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MOLECULAR AND GENETIC TESTING OF HLA II CLASS GENES IN CELIAC DISEASE PATIENTS IN YAKUTIA

ABSTRACT

The article presents the results of molecular genetic study based on typing of class II HLA genes (*DRB1, DQA1, DQB1*) in patients in age from 8 months to 18 years with a referral diagnosis of celiac disease or with suspected celiac disease. The study of the gene HLA class II with three-locus haplotypes *DRB1-DQA1-DQB1* revealed carriers of the haplotypes associated with celiac disease. The researchers found a high frequency of carriers of the haplotypes *DRB1*04 - DQA1*03:01 - DQB1**03:02 (*DQ8* type) in the Yakuts compared to the Russians.

Keywords: celiac disease, *DRB1, DQA1, DQB1*genes, haplotype.

INTRODUCTION

Celiac disease is one of the common medical-social problems of modern gastroenterology. High frequency of complications and development of associated diseases causing the disability testify to necessity of studying this pathology and search of the latest technologies for detecting groups of risk and rehabilitation of patients [1].

Until recently the disease has been observed rarely (1:5000 – 10000). However, nowadays the disease is known to be identified in the majority of countries (from 1:184 to 1:500). According to the researches conducted in Europe and the USA the prevalence of celiac disease among children was 1:80 – 1:300. In Russia no clinical-epidemiological researches on this pathology have been conducted, its prevalence approximately estimated 1:1000 [1]. Due to a significant role of celiac disease in the etiology of many systematic diseases there is uncertainty of its diagnostics, treatment and rehabilitation that would promote treatment from celiac disease and diseases connected with it, prevention of oncological intestinal diseases [2].

Celiac disease and its complications have multifactorial pathogenesis detected by genetically associated features of metabolism, immune system and gluten hypersensitivity. Of all the theories of celiac disease pathogenesis the genetic theory is considered the most significant

one according to the World Society of Gastroenterologists. The disease progression is connected with genes *HLA-DQ2 (A1*0501 and B1*0201)* diagnosed at 90-95% of patients and *HLA DQ-8 (A1*03 and B1*0302)* at 5-10% of patients [3, 4]. But existence of these genes not always leads to the progression of celiac disease, as non-HLA genes can be evidence of predictive celiac disease as well [3].

The concept of molecular genetics concerning association of polymorphic genetic markers with predisposition or resistance of the pathology is noted to be one of the approaches of studying genetic risk factors at multifactorial diseases including celiac disease. These markers typical to concrete pathology can be revealed long before its clinical manifestation that will allow to detect risk groups, to organize their monitoring, and if necessary to appoint preventive therapy. Studying of candidate genes with a product of their expression (enzyme, hormone, receptor) involved directly or indirectly in the development of pathological process is of special interest [2].

Due to contemporary achievements in the field of molecular genetics, the study of impact of candidate genes on the disease progression, its clinical manifestations, variability of quantitative signs of immunity and metabolism in the formation of complications appears to be perspective and conductive to the search of risk criterion of celiac disease [1].

In the Republic of Sakha (Yakutia) the prevalence of celiac disease among children in 2008 was 1:1660, and 1:884 among the children's population in Yakutsk city [2]. The absence of unified diagnostic criteria in Yakutia, especially concerning the subclinical forms causing the higher rate of complications and shortcoming of molecular genetics foundations of celiac disease predetermine the expediency of carrying out this research. The topicality of studying of the haplotyping variety of genes HLA II *(DRB1,DQA1,DQB1)* among patients of various ethnic groups living in the territory of RS(Ya) is connected first of all with the necessity of accumulation of database on specific genotypes of patients with celiac disease in this region. The numerous researches conducted in the field of 'HLA and diseases' testify to some distinctions in the clinical course of the disease and development of the immune response depending on the patient's genotype. Detection of such correlations will allow to find out certain treatment of celiac disease by an individual pathogenetic approach in the nearer future and significantly reduce a number of oncological and other complications as well as improve quality of life of patients.

Thus, the aim of this work was the molecular and genetic research and haplotypic variety of celiac disease on the basis of typing genes *HLA II (DRB1, DQA1, DQB1*) in Yakutia.

MATERIALS AND METHODS

This research included DNA samples of the sick children taken by a gastroenterologist of the municipal establishment "Children's City Hospital" of Yakutsk. An informed consent for the genetic research was received from each participant of the research. In total 37 patients with initial diagnosis of celiac disease or with suspicion on celiac disease aged from 8 months till 18 years living in RS (Ya) have been investigated. Of them 24 (64.9%) were the Yakuts, 11 (29.7%) Russians, 1 (2.7%) Evenk and 1 (2.7%) Kyrgyz. On a sexual sign patients were divided on 18 (48.6%) female and 19 (51.4%) male patients (Tab. 1).

DNA purification was conducted from 0.5–0.6 ml of venous blood by means of commercial sets for DNA purification Extra – Gene I (BAG Health Care GmbH, Germany). All examined patients were genotyped on genes of *DRB1, DQA1 and DQB1* by means of commercial sets for HLA tissue typing of HISTO TYPE SSP alleles (BAG Health Care GmbH, Germany).

RESULTS AND DISCUSSION

Totally 37 people were genotyped with the initial diagnosis of celiac disease or with suspicion on celiac disease. As a result of genotyping the haplotypes associated with celiac disease (tab. 2) were found in 17 of 37 investigated. At the rest 20 people no haplotypes associated with celiac disease were revealed, 4 patients of them having a clinic of celiac disease. At Yakuts haplotypes associated with celiac disease were revealed at 11 people, the Russians had 6 people, at the Evenk and the Kyrgyz no haplotype was revealed (Tab. 2). The first haplotype *(DRB1*04 – DQA1*03:01 – DQB1*03:02)* was diagnosed at 6 patients (30%), of them 5 Yakuts (38.4%) and 1 Russian (14.3%). The second haplotype in the amount of 3 *(DRB1*03 – DQA1*05:01 – DQB1*02:01)* was found in equal quantities at both Yakuts and Russians, 6 patients as the whole (30%). The amount of the third haplotype *(DRB1*07 – DQA1*02:01 – DQB1*02:02)* made 5 (25%), of them 3 (15%) were found at Yakuts and 2 (10%) at the Russians, and the fourth haplotype *(DRB1*11–DQA1*05:05 – DQB1*03:01)* rated at 3 patients (15%), of them 2 were the Yakuts (10%) and 1 Russian (5%). As we see in the table 2, the *DQ2* type is presented with 3 haplotypes, and DQ8 type with 1 haplotype. The DQ8 type is found in 5 cases (31.1%) at the Yakuts and in 1 case at the Russians (11.6%). The DQ2 type rated 8 at Yakuts (49.8%) and 6 at Russians (69.3%).

The DQ8 type is noted at Yakuts 3 times (31.1%) more frequently than at Russians (11.6%). Three patients (the Yakuts – 2 people, the Russians – 1 people) are carriers of two celiac disease associated haplotypes (tab. 2). The first patient (the Yakut) has *DRB1*04 – DQA1*03:01 – DQB1*03:02 and DRB1*07 – DQA1*02:01 – DQB1*02:02* relating to DQ8 and DQ2 types, respectively. The second patient (the Yakut) has *DRB1*03 – DQA1*05:01 – DQB1*02:01 and DRB1*07 – DQA1*02:01 – DQB1*02:02* haplotypes (both DQ2 types), and the third person (the Russian) has *DRB1*04 – DQA1*03:01 – DQB1*03:02 and DRB1*03 – DQA1*05:01 – DQB1*02:01* (DQ8 and DQ2 types, respectively). The last patient (*) having DQ8 and DQ2 types at the same time has very high risk of celiac disease.

In various regions of the world the incidence rate of these alleles at celiac disease has specific features and changes from 50 to 97%. On the basis of E.N. Kasatkina's research [6] carried out among a group of children in Moscow 97.2% of patients with celiac disease had gluten enteropathy associated alleles. Thus the main share (88.6%) is presented by the molecule of DQ2 and 8.6% by DQ8 haplotype. In our work specific alleles are noted in 80.9% of cases low the data given above. At the Russians the DQ2 type meets in 69.3% of cases, and DQ8 type in 11.6%. At the Yakuts the DQ2 type is found in 49.8%, and DQ8 type in 31.1% that is 3 times higher, than at Russians. Comparing to the results received at the research of various population groups it is to be noted that there are no similar frequency rates of these alleles at Caucasian and Mongoloid races. So if in Europe the frequency rate of DQ2 amounts for 90-95%, at people of Mongoloid race it is much lower. For example, in A.T. Kamilova's research carried out in Uzbekistan DQ2 type was identified at 69,2% (according to the established allelic loci associated with DQA1*0501 \DQB1*0201 celiac disease – DQ2 type), and at 62% in T.K. Isabekova's works (Tab. 3) [6].

Despite the significant association of celiac disease with *DQ2 (DQA1*05-DQB1*02)* and *DQ8 (DQA1*03-DQB1*0302*) genes, there are data testifying to existence of other genes of HLA system causing the progression of celiac disease. According to the European researchers, 61 patients with celiac disease of 1008 (6. 05%) carried neither DQ2 nor DQ8 heterodimer. In our research, 4 patients of 21 are both DQ2 and DQ8 negative amounting for 19.1%.

At the same time certain Russian researchers specify that the genotype of patients in various regions can have the features and lack of alleles, characteristic for the European population, doesn't exclude the development of the disease. [2]

In this regard, the results obtained require carrying out further researches for establishing genotype features of patients with celiac disease in our region.

CONCLUSION

Thus, according to the contemporary researchers' points of view the existence of *HLA-DQ2 and HLA DQ-8* genes is the basic, but insufficient factor of the development of celiac disease. Lack of the genes almost excludes the diagnosis of celiac disease. If pathological alleles are identified in combination with serologic markers it is likely to predict celiac disease.

When typing the patients with celiac disease and suspicion of celiac disease on HLA II genes by *DRB1-DQA1-DQB1* three loci haplotypes 17 carriers of haplotype associated celiac disease are found out. 4 persons have no these haplotypes, but have the clinic of celiac disease. Three patients (Yakuts – 2 people, Russians – 1 person) are 2 haplotype carriers at once. The high frequency of the haplotype *DRB1*04 – DQA1*03:01 – DQB1*03:02 (DQ8* type) is found out at the Yakuts (31.1%) in comparison with the Russians (11.6%) and with earlier conducted researches (5–10%) that requires more thorough population and genetic research of the Yakut population on *DRB1 – DQA1 – DQB1* HLA II genes.

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Table 1.

Patients: ethnicity and sex, (%)

#	Ethnicity	Patients (%)	Sex	
			Male	Female
1	Yakuts	24 (64.9)	13 (54.2)	11 (45.8)
2	Russians	11 (29.7)	5 (45.5)	6 (55.5)
3	Evenks	1 (2.7)	1 (100.0)	-
4	Kyrgyz	1 (2.7)	-	1 (100.0)
5	Total	37 (100.0)	19 (51.4)	18 (48.6)

Table 2

The distribution of haplotypes associated with celiac disease in patients in Yakutia (Sakha Republic)

	Celiac disease: haplotypes (HLA genes) *DRB1 – DQA1 – DQB1*	Type	Yakuts (%)		Russians (%)		All haplotypes found (%)	Risk	
1.	*DRB1**04 – *DQA1**03:01 – *DQB1**03:02	DQ8	5***	31.1	1*	11.6	6 (30.0)	high	very high
2.	*DRB1**03 – *DQA1**05:01 – *DQB1**02:01	DQ2	3**		3*		6 (30.0)	high	
3.	*DRB1**07 – *DQA1**02:01 – *DQB1**02:02	DQ2	3**, ***		2		5 (25.0)	low	
4.	*DRB1**07 – *DQA1**02:01 – *DQB1**02:02 / *DRB1**11–*DQA1**05:05 – *DQB1**03:01	} DQ2	2	49.8	1	69.3	3 (15.0)	high	

- DRB1*03-DQA1*05:01-DQB1*02:01 and DRB1*04-DQA1*03:01-DQB1*03:02; **- DRB1*03-DQA1*05:01-DQB1*02:01 and DRB1*07-DQA1*02:01-DQB1*02:02; *- DRB1*04-DQA1*03:01-DQB1*03:02 and DRB1*07-DQA1*02:01-DQB1*02:02.*

Table 3

The frequency of HLA haplotypes in different populations

Populations	Haplotypes	frequency of occurrence, %
Finland	DQ2 and/or DQ8	97.0
Northern Europe	DQA1*0501 DQB1*0201	98.9
Israel	DQA1*0501 DQB1*0201	80.0
Kazakhstan	DQA1*0501 DQB1*0201	62.0
Uzbekistan	DQA1*0501 DQB1*0201	69.2
Russia, Tomsk	DQ2 and/or DQ8	70.0
The results of this study	DQ2 and/or DQ8	80.9

Data is taken from the article [Zakkarova, Borovik, Roslavceva et al., 2011].

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The Outcomes of Different Organ-Preserving Treatment of Uterine Fibroids

ABSTRACT

The article reports a prospective study of women with uterine fibroids. The patients went to the clinic for conservative myomectomy and uterine artery embolization. Endovascular UAE has proved to be the most effective method of UF treatment, having fibroid nodes in the size up to 10 cm with a good vascularization, as well as submucous nodes localization. Thus, UAE among patients with UF provides little traumatic intervention with good clinical effect and reduction in the size of the uterus, as well as preserves the uterus, which is especially important for women with unrealized reproductive function, having contraindications to surgery and categorical rejection of it.

In this way, the optimal outcome of organ-saving UF treatment is achieved not only due to the skill of the surgeon, the adequacy of the selected surgical approach, providing minimization of operational risks, but also due to a whole complex of measures, including diagnosing disorders in various links of reproductive system and rational management of pre- and post-operative stages in accordance with complex rehabilitation.

Keywords: uterine myoma, uterine artery embolization, ccomplex postoperative rehabilitation.

INTRODUCTION

The realities of modern reproductive surgery show that even taking into account all variety of treatment technologies, debates about the question of expediency, selection criteria, indications, contraindications, long-term results of treatment of hyperplastic diseases of the uterus are still going on to clarify the preferred embodiment of a particular intervention. The revision of priorities in favour of organ reconstructive plastic surgery can be explained by rejuvenation contingent of women with uterine myoma who are interested in saving their reproductive function but often have large or atypical arrangement of fibroids [1,2].

Efficiency of uterine fibroids (UF) treatment technologies is the most debated subject of scientific research. Not only the pace of the reduction of the amount of fibroids and clinical symptoms, but also the rate of complications and recurrence of myoma growth are subject to comparative analysis. Despite the ambiguity of the results of different interventions – laparotomic myomectomy, endoscopy and endovascular – it is obvious that the focus of efforts

must be to improve not only the manual skills, but also the scope of rehabilitation of patients' life quality. Putting endovideosurgical operations into practice determined trendiness of laparoscopic approach in treatment of reproductive-age women with uterine myoma – due to its high levels of efficiency and minimum risk of complications. However, the idea of laparoscopic myomectomy priority has changed with the appearance of reports about uterine rupture in the place of a scar during the process of giving birth (1%) [3], which indicated the need for a differentiated choice of surgical access. Stratification of laparoscopic surgery in complexity, with the release of high-risk category in multiple uterine fibroids, large tumor size, especially interstitial, proves it justifiable to make "energy-consuming" operations in subserous nodes on the stem or shallow wide basis.

Interventional radiology advances contributed to the effective implementation of routine practice in the treatment of UF uterine artery embolization (UAE). Result of its use convince us in practicing this alternative method when having technical complexity of the conservative myomectomy or unjustifiably high risk of trauma using other way of access[9].

Optimization of the quality of life of patients with UF requires not only the analysis of productive using of saving surgery opportunities, but recovery from operational stress [6]. Results of the analysis of quality of life (QOL) of women after treatment of UF using various rating scales: Nottingham Health Profile (NHP), Medical Outcomes Study Short Form-36 (MOS SF-36), Uterine Fibroid Symptom and Quality of Life questionnaire (UFS-QOL) are variable, which can be explained by the difference of samples, lack of post-operative rehabilitation or inadequate capacity [6].

The proof for the effectiveness of uterine artery embolization (UAE) in treatment of symptomatic uterine fibroids can be the data by AJ Smeets et al. (2012) [4] about the reduction of clinical manifestations of the disease among 70.6% of women 46 months later after endovascular impact, based on the results of the standardized questionnaire UFS-QOL. There are reports about long-term sustainable improvement in quality of life with a slight relapse – 6 years after the UAE at 17% [8]. Despite the advantage of non-invasive treatments for UF in comparison with hysterectomy [5], after the processing of personal data on the scale of UFS-QOL there were best indicators of quality of life after hysterectomy, despite the considerable relief among patients 12 months after different treatment options [7].

Considering ambiguity of the data on the improvement of quality of life after various options of sparing technologies, analysis of the reduction rate of the amount of fibroids and the

reduction of symptoms of UF is required to predict benefits of choosing options for intervention. The chance of reducing postoperative complications and recurrence of the disease is possible after the optimization of different approaches, adequate selection of UF treatment technologies, rational preoperative preparation and recreational activities after the intervention. The lack of evidence proving efficiency of the above-mentioned tactics defines the goal aimed at comparative analysis of the quality of life of women after different UF treatment technologies and outcomes of the disease, depending on the availability of rehabilitation.

MATERIALS AND METHODS

To achieve the goal a prospective study of 675 women with uterine fibroids was carried out. These patients went to the clinic for conservative myomectomy and uterine artery embolization. Depending on the technology of treatment and the presence of postoperative rehabilitation, entire contingent of women with uterine fibroids was divided into groups: I – after laparotomic myomectomy (LTM) ((n = 216) and after complex rehabilitation (CR), II – after LTM and without CR (n = 51), III – after laparoscopic myomectomy (LSM) and CR (n = 248), IV – after LSM and without CR (n = 36), V group – after UAE and CR (n = 108) , VI group – after UAE without CR (n = 26).

Comprehensive pre-operative examination included Doppler ultrasound, hysteroscopy, histological examination of scrapings of the endometrium, treatment of persistent chronic inflammatory diseases of genitals. Antimicrobial therapy was provided if needed (in cases of exacerbation of chronic inflammation of the genitals with the release of infectum in diagnostically significant titer). Complex rehabilitation after the intervention included prevention of adhesions (3000 IU Longidaza suppositories or intramuscular №10), immunocorrection (depending on the nature of the violation of non-specific resistance there were used endogenous interferon inducers №10, UFO autologous №7-10), antioxidants (tocopherol acetate 200 mg every day for a month), disaggregates (Curantyl 75 mg 2 times a day for 3 weeks), the restoration of genitals eubiosis (Gynoflor E, Normoflorin, Primadofilus).

To prevent recurrence of fibroids growth the following medicaments were prescribed in accordance with hormone-related diseases and interest in the subsequent implementation of the reproductive function: a GnRH agonist (Zoladex), intrauterine Levonorgoestrelum-releasing depot system "Mirena", low-dose hormonal contraceptives (Regulon, Jeanine).

UAE was carried out by the standard technique, with preliminary angiography research, units' sonography, Doppler; polyvinylalcohol (PVA) particles measuring between 350 and 900 or

hydrogel (AAA Co., Russia) were used as emboli. UAE was made when having contraindications to other organ-preserving treatment options or their inefficiency (hormone), nodes greater than 10 cm in diameter.

The treatment results were evaluated by the subjective self-esteem of women, patients' questioning about the dynamics of symptoms, menstrual cycle, the quality of life at baseline and 3, 6, 12 months after the treatment, as well as by ultrasound evidence and magnetic resonance imaging. Quality of life assessment was performed using a questionnaire before surgery (LTM, LSM, UAE) and after 3 and 6 months, according to the modified American Association of Obstetricians and Gynecologists Quality of Life Questionnaire UFS - QOL among patients with UF.

The duration of patients' observation and follow-up after the surgery was 12 months.

Statistical analysis of the data was performed using the statistical application package «Statistica for Windows» v. 6.0, Stat Soft Inc (USA). Descriptive statistics, criterion χ^2, Student's t test (t) for unrelated groups were used for the description of the indicators presented in the form of quantitative variables. Statistically correct was the factor, the significance level of which is less than 0.05 ($p < 0.05$).

RESULTS AND DISCUSSION

The results of the survey of patients 6 months after various UF treatment technologies showed mostly accurate reduction of negative symptoms, including prolonged and heavy menstruation, chronic glandular deficiency anemia, feeling of heaviness in the abdomen, violation of adjacent organs, being reflected in the decrease in the quality of life and the limit of working ability. The severity of clinical manifestations after UAE in groups with complex rehabilitation and without it was still different.

In general, the study of quality of life among patients after various treatment technologies correlated with minimizing the symptoms of dysmenorrhea and dyspareunia, disappearance of pelvic organs compression signs, reduction of menstrual blood loss, which prevailed in groups after complex rehabilitation course. Normalization of hematological parameters occurred 3 months after monitoring all patients with anemia caused by meno- and menometrorrhagia.

UAE efficiency in removing menometrorrhagia during the year was 92.5%, which can be regarded as a fairly high rate. Among 22 patients with symptoms of compression of adjacent organs (the heaviness in the abdomen, dysuria, constipation) leveling of symptoms was observed in 95.5%. 86.6% of women had regular menstrual cycle, amenorrhea developed among 13.4% of women 6 months later.

Normalization of hemoglobin by 12 months' time occurred in 46.1% - 76.9% cases with complex rehabilitation compared to 80.5– 91.7% without CR.

The criterion for the effectiveness of treatment techniques was considered significant reduction in severity of the condition index 6 months after compared to baseline: 50.7% after UAE ($p < 0,05$), 44.2% on average – after LSM and LTM, in the absence of rehabilitation – 36.7% on average.

Increasing the integral index of quality of life after the intervention took place due to the relief of symptoms and almost leveling of negative emotional reactions to the settings on the readiness to regular uterine bleeding and risk of endometrial malignancy.

Clinical benefit in the form of regression of symptoms and downsizing nodes was marked in most cases (up to 81.3%) after embolization of uterine fibroids. Dynamics of volume reduction of dominant subserous and subserous-interstitial nodes 3 months after was 42% in the group with CR, uterus – 45%, 6 months after – 57.8% and 65.4% respectively. Full devascularization of dominant myoma node (90%) one month after the UAE was observed among 83.6% of women at 95.5% after 3 months, 93.3% - after 6 months; with multiple nodes – among 60.4% of women. Intraoperative-pain syndrome of varying severity accompanied all parts of UAE, the combination of it with the blood leucocytosis was observed among 13 women. This condition was not regarded as a side effect or complication, it was interpreted as a manifestation of metabolic adjustment accompanied by myoma node tissue degradation, the consequences of which were not considered within adequate tactics of postembolizational period. The result of UAE together with submucous nodes or centripetal growth reveals in reducing their size more than doubled and expulsion of the uterine cavity (1-6 months after UAE), which was accompanied by an increase in menstrual blood loss and caused menorrhagia and metrorrhagia.

Spontaneous nodes expulsion that required hysteroresectoscopy took place in 15 cases. Hysteroscopic removal of fibroid necrotic mass at 8% was complicated by the development of acute endometritis treated conservatively (anti-bacterial, anti-inflammatory, detoxification therapy) in two patients. In one case, against the background of acute painful endometritis due to submucous node migration into the uterus 2 weeks after embolization, supravaginal amputation of the uterus was made, without appendages. 2 patients had a hysterectomy without appendages because of large growing node symptoms. Bleeding as UAE complication in the submucous uterine myoma was observed in two cases 3 months after the intervention, one – in 11 months and demanded hysterectomy without appendages.

Detailization of postoperative complaints showed gradual disappearance of pain and discomfort that occurred among the vast majority (96%) of women before the treatment: during 3 months after UAE – 26.1%, 6 months – 11.9%, a year – 8.9%. Still preserving moderate pain 3-4 months after UAE combined with node units reduction on average of 30-40% (n = 24) was observed mainly in the absence of a rehabilitation course, which determined a minor downward trend of QOL scales. After UAE in terms from a month to a year 26 patients were operated on (in addition, 5 – with the expulsion of nodes), from them, 6 – because of the absence of clinical effect, 10 – because of the progressive myoma growth. In the absence of clinical effect (n = 9) (among 6 patients without a rehabilitation course) 3 months after UAE LTM was performed in cases of four women (with two of them having adenomyosis of the III degree), 4 months – in cases of five women (with adenomyosis II and III having two and one of them, respectively). Additional coagulation of endometriosis, followed by prescribing GnRH agonists (GL), was required in one of the episodes. Short-term and small (on average, 20% of the original) amount of the node units reduction preceded preserving of symptoms and further nodes growth. Revascularization episodes occurred in cases of 19 women, which was the basis for hysteroresectoscopy 2 months after in cases of three women, LSM – two women, LSM and coagulation of endometriosis 4 months after in cases of two patients, repeated endovascular intervention – four patients. In one case, LTM coagulation of endometriosis was preceded by separate diagnostic curettage of the endometrium. A year after the UAE (node units decrease by 25% 6 months after turned to growth and revascularization) two patients needed radiotherapy without appendages, in one case gonadotropin supplementation has been effective.

In assessing the parameters of quality of life 3 months after UAE the highest regression of symptoms was determined in combination with CR, that was realized in positive dynamics of such parameters as "uneasiness decrease", "alertness / fatigability," "self-image" and "sexual function". 6 months later after various interventions UAE effectiveness was confirmed by statistically significant improvement in a number of increased parameters: "alertness / fatigability" (by 53,7%) ($p < 0,05$) – by one and a half times in contrast to LSM and LTM (on average , 37.5%); "Self-image" (by 62.2%) – by 1.2 times in comparison with the indicator for LSM, by 1.7 times – for LTM ($p < 0.05$); "Sexual function" (by 56.2%) – by 1.5 and 1.8 times ($p < 0.05$), respectively. Regardless of the type of intervention, the growth of "activity" parameter appeared to be comparably high – by 46.1% on average (with the CR after UAE – by 32% compared to its absence ($p < 0.05$), after LSM and LTM – by 17 1% on average), "control" – by 44.6% on average.

The morphology of endometrial samples before the operation turned out to be mosaic: glandular endometrial hyperplasia – among 133 women with UF, glandular fibrous endometrial polyp – among 149, ferruginous – among 75.

The frequency of separate diagnostic curettage of the endometrium after UAE in connection with endometrial hyperplasia prevailed when combined UF with adenomyosis – 5.7% with CR and a quarter in its absence ($p < 0.05$).

Identification of atypical endometrial hyperplasia (AEH) as well as focal hyperplasia with adenomatosis determined without the need for hysterectomy of the uterus, in both cases among patients without CR. The greatest number of UAE complications (n = 4) was revealed within submucous UF and caused hysterectomies without appendages (n = 3) and one supravaginal uterus amputation without appendages. Relatively slight and temporary reduction in the scales of quality of life within symptomatic UF and its combination with adenomyosis without CR after the operation was the reason for LTM among 4 patients, LSM among 4 patients; supravaginal uterus amputation without appendages among 4 women, repeated UAE among 4 women; the absence of clinical effect caused LTM among 9 patients.

In order to prevent recurrence of the disease more than a third of women after conserving surgery received hormone therapy by agonists of gonadotropin-releasing hormone for 4-6 months (Zoladex, Diferelin), with the restoration of the menstrual cycle on average within 28 days after their cancellation. The above-mentioned tactics has identified the reduction of menstrual blood loss and the relief of dysmenorrhea severity and frequency. In total, relapse during the observational follow-up was noted among 74.5% patients after LTM, 69.4% – after LSM, 73.1% – after UAE, mainly because of CR absence after the operation.

CONCLUSION

Taking into consideration the ambiguity of long-term UAE results, we have to provide details of the possible causes of nodes relapse, paying respect to pathogenetic aspects. Thus, despite the episodes of relapse, the causes of which we have to clarify, UAE presents a highly effective organ-saving treatment of uterine fibroids among women of fertile age planning pregnancy. It is also an alternative to radical hysterectomy among premenopausal women with multiple nodes.

In this way, the optimal outcome of organ-saving UF treatment is achieved not only due to the skill of the surgeon, the adequacy of the selected surgical approach, providing minimization of operational risks, but also due to a whole complex of measures, including

diagnosing disorders in various links of reproductive system and rational management of pre- and post-operative stages in accordance with complex rehabilitation.

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The Characteristics of the Connective Tissue of the Pelvic Floor at the Collapse of the Genitals

ABSTRACT

The objective of our study is to clarify the distribution of immunohistochemical marker expression of MMP-1, MMP-2 and TIMP-1 in the sacrouterine and round ligaments of the uterus among women with genital prolapse.

The research was performed on the material of biopsies of sacrouterine and round ligaments of the uterus on both sides taken during vaginal hysterectomy from 15 women with genital prolapse aged 42 to 65 years old. It was found that the decrease in the accumulation of TIMP-1 on the background of high expression of metalloproteinases in the POP contrasts with a moderate level of expression of MMP-2, low MMP-1 and moderate TIMP-1 in the control group, which affects the density of the VCR. Connective tissue loosening, reducing of its elasticity and tensile strength was accompanied by degradation of fibers and increased degradation of collagen, defining pathobiochemical disorders in the pelvic dysfunction.

Keywords: genital prolapse, matrix metalloproteinases, tissue inhibitors of matrix proteinases.

INTRODUCTION

The problem of genital prolapse which is considered to be crucial due to increasing morbidity and severe dysfunction of pelvic organs seems not only medical, but also a serious social problem [2,4]. Dysfunction of pelvic organs, combined with incomplete emptying of the bladder and the bowel, which manifests itself in a variety of symptoms - feeling of heaviness and a foreign body in the lower abdomen, dysuria and dyspareunia - causes patients significant physical and mental suffering.

Hidden epidemic - that is the definition that has formed about the problem of pelvic floor failure not only because of the prevalence of older women segment among patients and, according to foreign researchers, because of their highly active way of life. There is also a forecast about doubling the number of requests for medical help in the next 30 years [2].

We have to mention a pessimistic conclusion about the growth rate of genital prolapse among women of reproductive age and poor quality of life that require surgical correction. Despite the vast amount of methods of surgical treatment of pelvic floor dysfunction, none of

the practiced techniques can be considered stable and effective due to frequent statements of recurrence of the disease, followed by a succession of plastic interventions and partial or total patients' disability.

According to literature, the need for repeated surgical treatment of genital prolapse occurs in one third of cases, reaching the anatomy of the pelvic floor 61.3% within a period of three years after the rapid restoration [2]. These facts point to the need for in-depth study of aspects of etiology and pathogenesis of the disease, for which there is still no consensus [14]. Alongside with contradictory and ambiguous judgments, debates about the damage of any single anatomical structure, which determines the lack of fixation of pelvic organs, are constantly going on. We discuss the existence and nature of damage to the muscle layer as a key factor in the development of genital prolapse and pelvic floor failure accompanied by isolated or combined dysfunction of pelvic organs. This theory, first advanced by J. Halban and J.Tandler in 1907, disagrees with the teachings of Schultze (1881) about the leading in the development of omission, and then prolapse failure supporting ligaments, namely - the round ligament, according to a further submission - retaining ligaments - cardinal and sacrouterine. However, at the present stage of medicine development the idea emerged that taking into account ensuring of the fixing process and the normal functioning of pelvic tissues of different "phenotypes" - connective tissue component and striated muscle, their involvement in genital prolapse development is sure to be mutual.

Recent-year studies have allowed to study the genesis of genital prolapse from the standpoint of the role of molecular-biological factors [11]. Development of the theory of connective tissue dysplasia (CTD) - states with different clinical manifestations of this disease, with certain congenital viscerotomy lesions arising embryonically and postnatally, with progressive course and a number of dysfunctional manifestations, has defined a new direction of scientific research in the perineology sphere [3]. Due to the conclusion of a multi-organ involvement in CTD and metabolism disorder - a defect of synthesis or degradation of extracellular matrix (ECM) and dysregulation of morphogenesis structures of the pelvic floor, tissues and their histological and immunohistochemical features were the subject of careful study at genital prolapse [1].

It is obvious that the manifestations of pelvic dysfunction such as stress incontinence and genital prolapse may have a common pathophysiological basis due to violation of the anatomical

relationships and unspecified changes in the functional activity of the pelvic floor structures at not only the macro- and micro-levels.

The basis of connective tissue ECM is presented by gel medium elastin and collagen fibers [3]. The content of collagen and elastin - the main proteins of connective tissue in genital prolapse - varies dramatically. Type I collagen can be found in bones, scars, tendons, cartilage, II is the main component of cartilage, III is found in reticular fibers, IV prevails in subepithelial layer and in basal membrane. Elastic fibers provide flexibility and elasticity of tissues; collagen contributes to their strength and integrity. [10] According to data, patients with genital prolapse have violations of the ratio of their content. Due to lower total collagen and elastin the number of fractions of crude, more "fragile" collagen increases [6,13].

Having taken into consideration the current knowledge about the molecular and biological mechanisms of genital prolapse it is important to study matrix metalloproteinases (MMPs) - enzymes performing the degradation and remodeling of connective tissue with high biological activity by regulating homeostasis VCR expression during wound healing in normal and pathological cases [4, 12].

MMP-1 is synthesized by fibroblasts and connective tissue monocytes and is involved into catabolism of fibrillar and non-fibrillar collagens, mainly in the supporting apparatus of pelvic organs [7]. MMP antagonists include proteins tissue inhibitors of matrix proteinases (TIMP), expressed in the tissues of pelvic organs to preserve the dynamic balance [15]. Despite the small number of messages, there is evidence of excess activity of specific MMPs involved in the collagen tissues decay process, not compensated by TIMP, among patients with genital prolapse [5]. It is believed that the contribution of the increase in MMP collagenolysis may be associated with features of genetic polymorphisms, mutant forms of their predominant among women with genital prolapse. [13] However, complicated biochemical interactions of enzymes, proteins and molecules still have to be recognized.

The increasing interest of experts to study the importance of ECM components imbalance - MMP and TIMP - in the genesis of pelvic floor failure can be explained not only by the possibility of clarifying the molecular mechanisms predisposing to the disease, but also by prediction the likelihood of relapse.

The objective of our study is to clarify the features of the distribution of immunohistochemical marker expression of MMP-1, MMP-2 and TIMP-1 in the sacrouterine and round ligaments of the uterus among women with genital prolapse.

MATERIALS AND METHODS

The research was performed on the material of biopsies of sacrouterine and round ligaments of the uterus on both sides taken during vaginal hysterectomy from 15 women with genital prolapse aged 42 to 65 years old. The control group was presented by biopsies of ligaments (sacrouterine and round) from 15 women without genital prolapse aged 35 to 52 years old who also underwent abdominal hysterectomy. 4 samples of tissue were obtained from each patient: right and left sacrouterine ligaments and right and left round ligaments of the uterus. Biopsies were fixed in 10% neutral formalin and embedded in paraffin, and then paraffin sections were made 4 microns thick. The samples were stained with hematoxylin and eosin, with picrofuchsin according to Van Gieson and fuchselin according to Weigert. Additional non-stained sections on polylysine glass were produced and immunohistochemical reactions by the standard method with thermal unmasking of antigens using primary antibodies to MMP-1 and MMP-2 (LabVision, readytouse), TIMP-1 (LabVision, 1:50) were carried out.

The results of immunohistochemical reactions were scored according to the percentage of stained cells or the percentage of stained VCR.

Mathematical processing of the obtained results was carried out by methods description and a parametrical statistics on a personal computer with the aid of the program «Statistics 7.0».

RESULTS AND DISCUSSION

According to the information received, COP and CCM expression of MMP-1 and MMP-2 was observed in the form of lumps of brown staining in the extracellular matrix, fibroblasts, ligament apparatus and in vascular endothelium within pelvic connective tissue structures. A similar tendency was observed in connection with marker TIMP-1 visualization (Fig.).

Ligamentous apparatus among patients with genital prolapse can be characterized by increased levels of metalloproteinase activity in comparison with indicators in the group of healthy women. Expression of MMP-1 in genital prolapse turned out to be twice as big (4± 1.2), compared to the rate in the control group (2 ± 0.8). The expression level of MMP-2 in genital prolapse was 6 ± 0.3 points, which is half as significantly higher than the rate of enzyme accumulation among healthy women (4 ± 0.5 points). The increase of metalloproteinase activity in genital prolapse went along with decreased expression of the natural inhibitor TIMP-1, the level of which amounted to 1.5 ± 0.5 points versus 4 ± 0.7 points in the control group.

Thus, the reduction of TIMP-1 accumulation alongside with high expression of metalloproteinases in genital prolapse contrasted with moderate level of MMP-2 expression, low

MMP-1 and moderate TIMP-1 within a control group. It affected the density of VCR as well. Connective tissue loosening, reducing of its elasticity and tensile strength was accompanied by degradation of fibers and increased degradation of collagen, defining pathobiochemical disorders in the pelvic dysfunction. Preservation of tissue homeostasis among healthy women was observed on the background of high content of metalloproteinase TIMP-1 inhibitors and a slight but optimal for maintaining tissue strength expression level of MMP.

The results obtained agree with the data concerning the important role of violation of dynamic equilibrium processes of synthesis, postranslation transformation and IMF and SST degradation in the tissues of the ligamentous apparatus - COP and CCM among patients with genital prolapse. The presence of misbalance between MMPs and their inhibitors, initiating remodeling of the ECM in the ligaments of the uterus in genital prolapse is proved by the works of other studies [7, 10]. Increase in the expression of MMP-1, MMP-2 and MMP-9 in the CCM and vaginal tissues is reported to be found among patients with genital prolapse as compared to the control [9, 12]. Conclusions about overall excess of MMP activity and significant TIMP decrease in vaginal tissue among white women with premenopausal genital prolapse present vivid evidence of the violation of tissue metabolism components of connective tissue and the VCR [8].

CONCLUSION

The research conducted proves a significant role of connective tissue in fixation and normal functioning of pelvic organs. It also points out that mechanical properties of the ligament apparatus are determined by the level of proteolytic enzymes expression. We put forward the idea about pathogenetic importance of degradation and synthesis activity of connective tissue components in genital prolapse. Identified molecular biological processes of tissue remodeling are accompanied by changes in the activity of enzyme complex ECM and allow to considerimmunohistochemical diagnostics as widening of predictive capability referring to risk of recurrence of the disease after surgery. Continued research in this area is promising for the development of innovative reconstructive surgery and preventive measures to reduce the risk of genital prolapse relapse.

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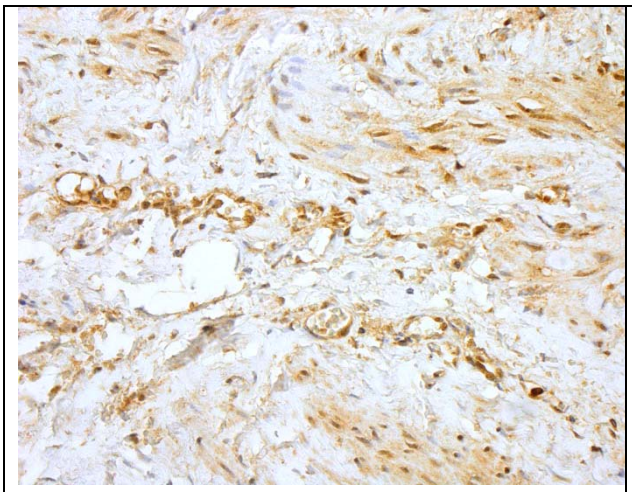

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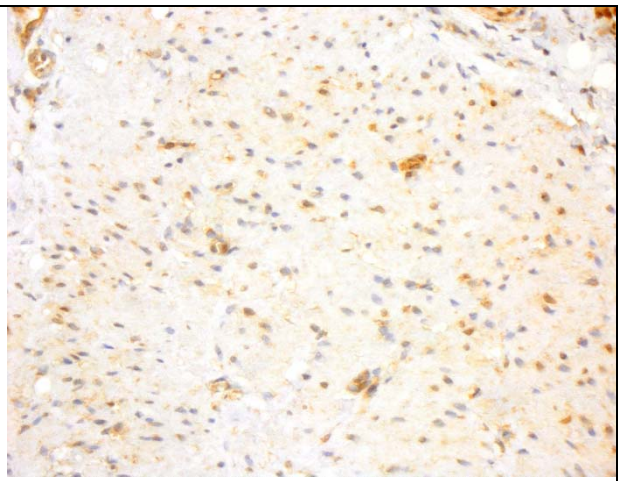

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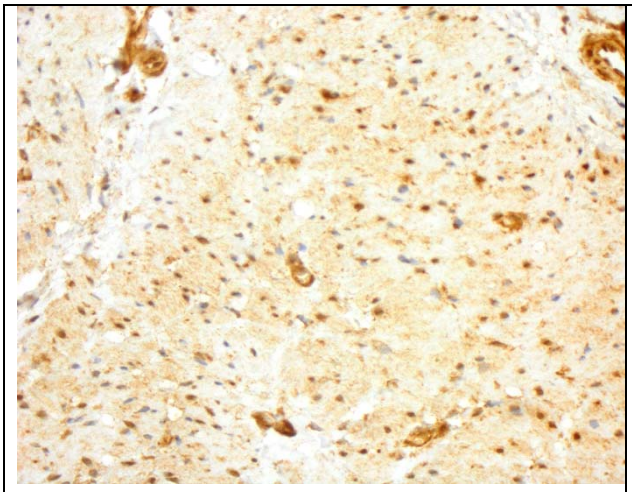

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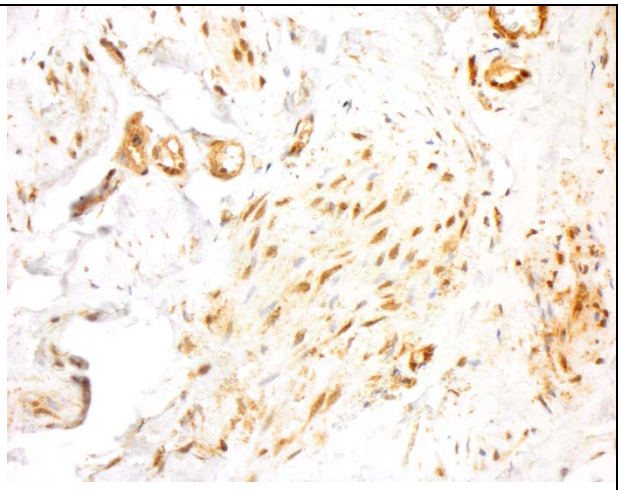

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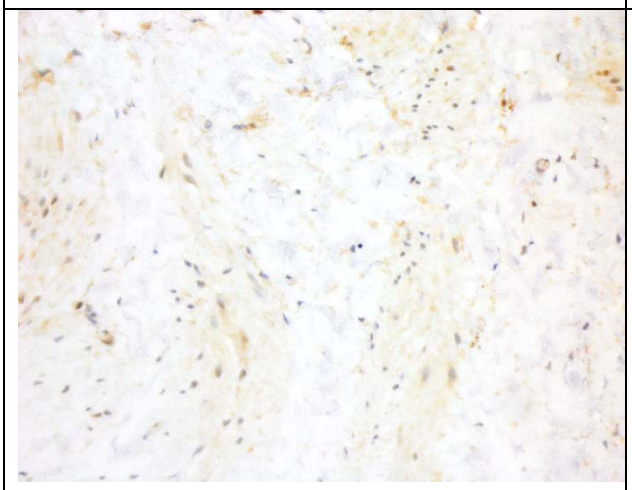

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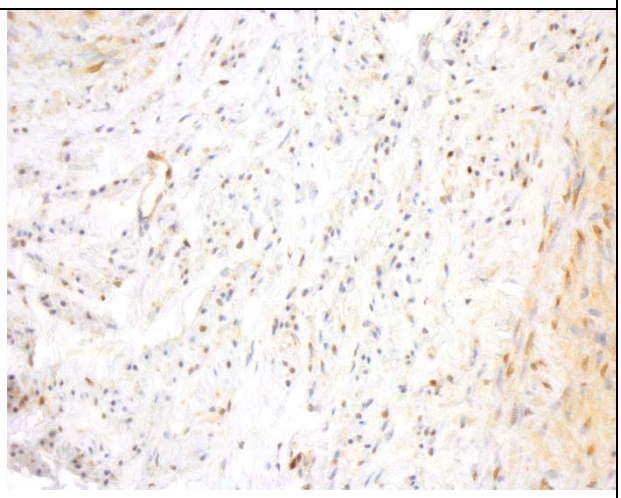

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Figure. MMP-1 MMP-2 TIMP-1in round ligaments of the uterus, *400:main group (aMMP-1, c MMP-2, e TIMP-1), control group (b MMP-1, dMMP-2, f TIMP-1).

B.M. Gasanova, N.I. Duglas

Features of Cytokine Status of Pregnant Women with Chronic Pyelonephritis, Depending on the Placenta Morphological Characteristics

ABSTRACT

It has been shown that for an objective appraisal of the impact of active influence of chronic pyelonephritis on the feto-placental complex is possible in determining the constituents of pro- and anti-inflammatory cytokines. The results of this research on cytokine status give an evidence of the unstabilized nature of the immune system in women with CP. In spite of the complete clinical and laboratory remission of the disease, contributions to the development of gestational complications were due to the lack of pregravidal training and early prevention of placental insufficiency. It has been established that, despite the absence of specific features in the placenta of women with chronic pyelonephritis that highlighted to the compensatory and sub-compensatory changes against the backdrop of dystrophic, microcirculatory and other disorders, reflecting not only the provision of the required conditions for the existence of the fetus, but as well as the degree of destructive lesions and severe shift in immunological equilibrium.

Keywords: chronic pyelonephritis, cytokines, placental insufficiency, pregravid preparation.

INTRODUCTION

Chronic pyelonephritis (CP) is one of the most common kidney diseases, especially among the female population of reproductive period.

The correlation between chronic infectious and inflammatory diseases of the urinary tract with local and systemic immunity damages proves the results of the previous studies. However, the detailed nature of the immune-pathological reactions remains unknown. It is obvious that the immune response of the mother is formed in accordance with the need to limit and eliminate an infectious process, along with pre-gestational immunological restructuring on one hand and implementation of genetically determined program of childbearing on the other hand.

A disorder of thin inter-systemic correlations at CP was implemented due to the inadequacy in the production of humoral and cellular immune factors. Moreover, the functional activity of immune-competent cells varies depending on the severity of the inflammatory process. The available data and difference in the versions of cytokine imbalance in pregnant women with CP are rare and this makes it almost impossible to create a complex representation

for further course of study during pregnancy and the outcome of the disease. Taking into account, the negative impact of CP on a fully formed feto-placental complex, the risk of preeclampsia and premature birth, anemia, placental failure, chronic fetal hypoxia and the delay in intrauterine development is very important for the clarification of cause-effect relationships that serve grounds in the birth of unhealthy children. Early detection of groups with high risk of developing gestational complications can lead to the possibility of their timely correction, which is extremely important taken into account the likelihood of developing placental insufficiency (PI), which is not depended on the course of CP.

Thus, detecting the regulation within the intercellular communication, mediated system cytokines in women with CP will help clarify the current status of their immune system, the severity of the disorder and further, this will help us get an idea of pathogenesis of the obstetrical complications. Cytokines based on their biological effect are divided into pro-inflammatory regulators of immune response (IL-1, IL-2, IL-6, IL-12, TNF-a), and those involved in the formation of the inflammatory response and as well as offer a protective effect (IL-4, IL-10, IL-13, INF-g, pg / ml). Management of cytokine balance seems to be a new direction of impact in pregravidal training, in connection with what has been delivered.

Aim of our research: to study the dynamics of cytokine status in pregnant women with HP and different morphological characteristics of the placenta.

MATERIALS AND METHODS

In accordance with the purpose of our scientific work, 120 pregnant women were examined. 30 of them - with normal pregnancy (control group). The group consisted of women between the ages of 20 to 32 years (average age -26. 1 ± 1.2 yrs).

Criteria for exclusion were: the absence of chronic infectious and inflammatory diseases in exacerbation stage, diseases associated with impaired immune surveillance (neoplastic processes, allergic, immunoproliferative and autoimmune diseases).

With the aim of studying and assessing the prognostic significance of the immune status in the pregnant women and its variability based on morphological characteristics of the placenta, 90 women with chronic pyelonephritis in the clinical and laboratory remission stage (duration of disease ranged from 3 to 7 years) were examined. The women were between the ages of 22 to 37 years (mean age – 26.7 ± 1.8 yrs).

The grouping was performed based on the morphological characteristics of the placenta and the types of PI:

1. Compensatory - with the appropriate degree of maturity of the villi in gestational age, normal vessel lumen, hyperplasia and hypertrophy of the terminal villi.

2. Subcompensatory - with a maturity mismatch villi of the gestational period, architectural destructions of the villous tree, anemia, arteriolar narrowing and dilatation of the veins, small foci of hemorrhage and thrombosis in the inter-villous space, infarction and pseudo-infarcts

3. Destructive lesions in the placenta - due to inflammatory infiltration, foci of productive inflammation are localized on the basement membrane of the placenta and circulatory disorders, severe dystrophic changes and impaired maturation of the villous tree.

Group I (n = 32) included pregnant women with pregravidal training and prophylaxis of PN in the early stages of pregnancy.

Group II (n = 58) consisted of patients, in whom the said strategy did not yield any results, among them 34 women were in sub compensatory type of PI. 24 - with destructive changes in the placenta. In the presence of pregravid training, changes in the placenta were described as compensatory. Cytokine concentration in serum was determined in an immunological complex Stat-Fax 2100 with the help of enzyme immunoassay system test (LLC "cytokine" St. Petersburg), in accordance with the manufacturer's instructions. Sampling of plasma and the Study of cytokines (IL-1β, IL-8, TNF-a, IL-10, IFN-γ, IL-10) was performed in 22-24 weeks of examinees' pregnancy.

Morphometric and the morphological study of the placenta was conducted in a standardized scheme (A.P. Milovanov, 1999), which included macroscopic analysis, incised material and histological study in three phases.

Mathematical processing of the obtained results was carried out by methods description and a parametrical statistics on a personal computer with the aid of the program «Statistics 7.0».

RESULTS AND DISCUSSION

In studying the cytokine status in pregnant women with CP, differences in the level of the studied parameters were detected, depending on the morphological characteristics of placenta and type of PI. IL-1β - multifunctional cytokine with a broad spectrum effect plays a key role in the development and regulation of non-specific and specific defense of the immune system, the immediate release of which is regarded as a response or defense reaction of the organism to the action of pathogenic factors. Significant differences in the content of inducers of protein synthesis during the acute phase IL-1β were determined in the control group (21.8 ± 1.12). In the absence of pregravid training: in sub-compensatory type of PI its level seemed to have increase

by 1.8 times (38.4 ± 2.4) (p <0.05), destructive changes in the placenta - 2.4 times (52.8 ± 3.6) (p <0.05).

The content of IL-8 - cofactor of the acute phase reaction during the inflammation significantly exceeded the rate of healthy pregnant women (42.4 ± 3.86) in the absence of pregravid training in women with CP: in the group with sub-compensatory PI – one and half (62.2 ± 3.5) (P <0.05), with destructive changes in the placenta (74.7 ± 3.3) (p <0.05) - 1.8 times.

According to the canons of the immune regulation of TNF-a, which has the ability to stimulate the production of other pro-inflammatory cytokines - IL-1, IL-6 and to activate humoral and cellular immune responses with the tendency of bringing about hypercoagulability and hemodynamic impairments, to provide non-specific cytotoxic effect as an integral marker of inflammation. Its level in the group with HP, where no pregravid training was practiced, has shown substantial increase as compared to the healthy pregnant women (12,2 ± 0,6): in sub-compensatory - 2.6 times (31.6 ± 2.5) (p <0.05), in severe PI conjugated with the presence of inflammatory changes in the placenta - 3.8 times (46.8 ± 2.3) (p <0.05).

Index of IL-10 in women with PI confirmed with the help of morphological study of the placenta was elevated as compared to that of healthy pregnant women (7.86 ± 0.8) (p <0.05). It turned out that sub-compensatory PI level of this cytokine amounted to 18.3 ± 1.4 (p <0.05), whilst destructive changes in the placenta was – 32.6 ± 2.8 (p <0.05). The distributions of IFN-γ, one of the potent inducers of cellular immune system and cytotoxicity in groups of women with CP turned out to be identical, with an increase of 2.7 times (43.8 ± 2.4) (p <0.05) and 4 times (68.4 ± 4.3) (p <0.05) in different PI – sub-compensatory and destructive changes in the placenta.

Study of the level of IL-4 enabled us to establish a significant increase in the development of sub-compensatory PI (9.4 ± 0.08) (p <0.05), and 3.2 ± 0.02 (p <0.05) – with changes of an inflammatory nature in the placenta, indicating low resistance of the body of pregnant women with foci of chronic infectious and inflammatory diseases.

A number of pro-inflammatory cytokine levels in the group of women with CP who received pregravid training and course on preventive measures of PN were almost identical with those of healthy pregnant women, except for a slight increase in the level of IL-1β.

Thus, the destruction of an adequate restructuring of cytokine balance may serve the cause of various complications of the gestational process – PI. Prematurely, increase in the activity of pro-inflammatory cytokines and shift of the immunological equilibrium towards Th-1

type in pregnant women with CP, significant indications of chronic stress adaption of the immune system prevailed in the absence of a comprehensive pregravidal training and prophylaxis of PI.

Prolonged existence of the foci of chronic infectious and inflammatory process that was initiated before pregnancy and sustainable to maladaptive state, characterizes the complexity of the pathogenic abnormalities in the "mother-placenta-fetus". Severe immunosuppression at the system level has a negative impact on the morpho-functional characteristics of the feto-placental complex and the outcomes of pregnancy and childbirth respectively. Consequently, the implementation of pregravidal training and prevention of PN(diet rich in protein and polyunsaturated fatty acids; stabilized the lipid-protein bi-layered cells (Essentiale, vitamin E / amount of tocopherols), correcting micro-biocenosis of the genital tract, improved cellular metabolism and utero-placental blood flow (aktovegin, Trental)) in the early stages of pregnancy helped retain the balance of producing pro- and anti-inflammatory cytokines and a significant degree of compensation in women with CP and high risk of recurrent disease course and gestational complications.

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Diseases of the Biliary System in Patients with Overweight

ABSTRACT

The results of the analysis of patients with increased body weight examination and state of their biliary system are presented. It is shown that a significant part of the observed patients are in risk group for the biliary tract diseases. Regardless of the degree of obesity these patients have disorders of fat metabolism: atherogenic dyslipidemia, impaired hormonal function. Significant amounts of the examined have pathology of the biliary system – non-alcoholic amyloid liver disease, the presence of bile heterogeneity (sludge) and the gallstones. It is revealed that the increased weight, together with serious cardiovascular system pathology and endocrine disorders affect the overall metabolism and, in particular, functional disorders of the biliary system.

Keywords: disease, biliary system, gastrointestinal pathology, overweight.

INTRODUCTION

The biliary tract diseases belong to the widespread gastro-intestinal pathology. Taking into consideration that diseases of the biliary system (cholecystitis, cholelithiasis) are often found in obese patients this problem is not only medical, but also an important socio-economic one [4]. The number of patients with the biliary system pathology has increased over the last decade in Russia for persons older than 50 years at 5%, and over 60 years – up to 20% [2]. In paper [3] it was noted a clear trend in the prevalence of cholelithiasis and the increasing number of operations on the occasion of cholecystolithiasis.

Doctors diagnose functional disorders of various organs and serious illness in obese patients: type 2diabetes, cardiovascular disease (CHD, GB), erosive-ulcerous defects of the digestive tract [5], polycystic ovary syndrome and syndrome of obstructive sleep apnea. For this group of patients it is more frequently diagnosed non-alcoholic fatty liver disease (NAFLD), atherogenic dyslipidemia [4], gastroesophageal reflux [6].

The aim of this work is the examination of patients with overweight and their biliary system status determination.

MATERIALS AND METHODS

We carried out the analysis of the biliary tract diseases for 51 patients who were examined and treated in the therapeutic Department of the hospital FCAN "MSU MIA of Russia in the Amur region" from 2008-2014. Among patients there were 41 employees and 10 retirees of the MIA, including 27 men and 24 women.

In the work to determine the degree of obesity examined we used the WHO classification on Kettle body mass index (1997, 2003), which, as you know, is determined by the formula:

$$BMI = m / h^2$$

where m – body weight in kilograms, h – the man's height in meters.

The calculation of Kettle BMI index allows determining the risk of accompanying disease according to table 1.

Table 1

Classification of obesity according to body mass index (BMI) according to the WHO classification, 1997, 2003

Classification	Body mass index (BMI) by Kettle, kg/м^2	The risk of associated diseases
The deficit of body weight	less then 18,5	Low
Normal body weight	18,5-24,9	Normal
Overweight (pre-obese)	25,0-29,9	Increased
Obesity of I degree	30,0-34,9	High
Obesity of II degree	35,0-39,9	Very high
Obesity of III degree	40,0 and more	Extremely high

The patients were divided by age into two groups: 1st group from 25 to 35 years old – 16 people, 2nd group from 36 to 60 years – 35 people. Kettle BMI index was calculated for each group and the number of patients in risk groups was determined (table 2). It turned out the body weight of all patients was increased, and 5 patients belong to the class of pre-obesity, 33 – to obesity of I degree, and 13 related to obesity of II degree.

Table 2

The proportion of patients' body mass index

Group	Age	The number of surveyed	Body mass index, kg/м^2		
			25,0-29,9	30,0-34,9	35,0-39,9
Group 1	25-35 years	16	3	10	3
Group 2	36-60 years	35	2	23	10

Analysis of anamnesis data, patient cards, and results of objective examination was fulfilled. For all the patients there was done an electrocardiogram (ECG), echocardiography, ultrasound of abdominal organs, renal ultrasound with Doppler of blood vessels, computed tomography (CT) of the abdomen, esophagogastroduodenoscopy (EGD), daily monitoring of arterial pressure (DMAP).

DISCUSSION

The prevalence of I degree obesity for surveyed people (see table 2) is as in the 1st group, for younger people (10 of 16, 62.5%) and for older people (23 of 35, and 65.7%). However, for the older people more often are II degree obesity (10 of 35. 28.6% against 3 of 16, 18.7%).

During the study, in 6 patients of the 2nd group there was diagnosed type 2 diabetes. Atherogenic dyslipidemia – high cholesterol levels, low density lipoprotein (LDL), triglycerides, lowered high density lipoprotein (HDL) is observed in the 1st group in 12 of 16 patients, and in the 2nd group – in all patients.

Using diagnostic ultrasound of the abdomen found for 43 people (84.3%) the nonalcoholic steatosis, for 4 people – the presence of biliary sludge (7.8%), for 9 people – the stones in the gallbladder (17.6%), confirmed by CT scan of the abdominal cavity. Esophagogastric reflux was observed in 10 (19.6%) patients of the 2nd group.

During the observation an increase in blood pressure was registered in 14 patients of the 2nd group. Daily monitoring of arterial pressure (DMAP) showed daily average increase in blood pressure (BP), Doppler ultrasound of renal vessels found a diffuse increase high-speed indicators and the increase of the resistance index. For 37 patients BP changed within normal limits. Doppler sonography of renal vessels for these patients did not identify any hemodynamic disturbances of blood flow in the renal arteries. The echocardiography revealed a mitral valve for one patient of the 1st group and extension chord valve apparatus for two patients of the same group.

CONCLUSION

Data of fulfilled observation showed that a significant portion of the observed patients are at risk for diseases of the biliary tract. First of all, it is persons who are overweight with fat metabolism disorders: atherogenic dyslipidemia, impaired hormonal function (5 women with polycystic ovary syndrome), functional disorders of the biliary tract: nonalcoholic fatty liver disease (NAFLD) for 43 of 51 (84.3%) patients, the presence of heterogeneity of bile (sludge) for 4 (7.8%) cases, the stones in the gallbladder for 9 (17.6%) patients.

For older patients (2nd group) in addition to pathological changes in the biliary tract there were selected 14 patients (40.0%) with arterial hypertension and 6 patients (17.1%) with type 2 diabetes. Obviously, overweight, a serious disease of the cardiovascular system, endocrine disorders affected the overall metabolism and, in particular, the functional disorders of the biliary system.

Thus, we found that patients with overweight are at risk group not only for the biliary system diseases, but also hypertension, diabetes and hormonal function diseases, and this is observed both for the young and the older patients. Of course, obesity and other risk factors are interconnected with each other and each of them makes some contribution to the development and progression of heart and blood-vessel diseases (HBVD) and diabetes mellitus. For all identified patients there was planned secondary prevention of cardiovascular complications and the formation of their commitment to the treatment with lipid-lowering drugs.

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The Functional State of the Cardiovascular System of the Ammosov NEFU 1st Year Girl-Students

ABSTRACT

The adaptive capacity of the circulatory system of the NEFU named after M.K. Ammosov 1 st year she-students in terms of adaptation to training in high school was studied.

In the girls somatometric data (height, weight) and hemodynamic parameters (heart rate, blood pressure) by conventional techniques, as well as indicators of circulatory system adaptive capacity (AP) and double product (DP), or Robinson index were determined.

DP analysis showed that the functional reserves of the cardiovascular system has been stretched and depleted in 55.5% of cases. AP in 98.5% of cases was unsatisfactory.

Indicators of reserves of the cardiovascular system of the 1st year students were worse than in the control group, indicating the emergency power of stress or of its long duration.

Thus, the adaptive reserves of an organism of students are characterized as unsatisfactory. The observed decrease in the adaptive capacity of the organism, even in the absence of the manifested disease testifies a lower level of health and increases the risk of disease.

Keywords: students, adaptive capacity, the cardiovascular system, the Robinson index.

INTRODUCTION

At the present time the researchers use methodological approaches to assess the state of adaptation to determine the health of both the individual and organized groups [4- 7].

The body composition and functionality of the body can be measured to evaluate the adaptive capacity of the organism. Parameters which are characterised the state of metabolism, the immune status of the organism, the state of the adaptive potential (AP) of the circulatory system were passed for assessment of adaptive reserves [2, 3].

The circulatory system plays a leading role in ensuring the adaptation of the organism as a general indicator of adaptive reactions. This role is defined by its function of transport of nutrients and oxygen – the main source of energy for cells and tissues. Energy mechanism has a leading position in the process of adaptation. Energy deficit is the trigger signal that triggers the

whole chain of regulatory devices that form the necessary adaptive capacity at the new homeostatic level.

Research and evaluation of the AP of the circulatory system allows determining the distribution (%) of individuals with varying degree of adaptation to the specific conditions of life.

In high school freshmen first of all are to adapt to a large teaching load, the volume of information, the length of the school day.

Research aim: to study adaptation potential of the circulatory system of the 1st year she-students to the terms of educating.

MATERIALS AND METHODS

476 she-students of different faculties of the Ammosov North-Eastern Federal University (NEFU) aged 15 to 22 years were involved in the study (mean age 18.2 ± 0.9 yrs). The number of Yakut girls amounted to 85.9%, other nationalities - 14.1%.

Control group consisted of young women (n = 156) aged 24 to 29, on average 26.3 ± 1.6 years.

Work performed in the Institute of Health NEFU, Department of propaedeutic and faculty therapy with endocrinology and physical therapy Medical Institute NEFU. The study was approved by the Ethics Committee FGBI "YSC ILC" SB RAMS. Participants provided written informed consent before entering the study. The work was performed as part of the base portion of the governmental assignment of Russian Ministry of Education on "Adaptive potential and health of the indigenous population of Yakutia in the modernization of the social and economic system."

The girls 1st year NEFU determined somatometric data (height, weight) and hemodynamic parameters (heart rate, blood pressure) by conventional techniques, calculated body mass index (BMI). BMI is determined by the formula Kettle BMI = W / L2, where W - weight in kg, L2 - height in meters squared. BMI is considered to be insufficient for values below 18.5, normal – 18.5-25, redundant – 25-30, obese – 30-40, obese – above 40.

The heart rate can be seen as an integral indicator of the level of functioning of the cardiovascular system, which depends on the energy needs of the body. The higher the energy potential, the more stable the system. As the reduction of the reserve capacity of the organism and, therefore, the level of adaptation (which may be due to the impact of unfavorable factors of production, or age-related changes) to provide the energy needs of the body are included compensatory-adaptive mechanisms and, in the first place, there is an increase in heart rate. AP

of the circulatory system in the score is calculated by the formula AP = 1.238 + 0.09 * HR where HR – heart rate, beats per minute; 1.238 and 0.09 – coefficients of the equation. If the value is less than 7.2 points AP the level of adaptation is estimated as satisfactory, with the AP from 7.21 to 8.24 points – the strain of adaptation mechanisms, at the AP from 8.25 to 9.85 points – poor adaptation, with more than 9, 86 AP points – the failure of adaptation mechanisms [1].

A very important indicator of the circulatory function is double product or index Robinson (DP or IR), which reflects the level of hemodynamic load on the cardiovascular systems and characterizes the work of the heart muscle. DP describes the reaction of the individual to the load and is calculated by the formula: DP = SBP * HR / 100 (c.u.). If the value is less than 69 DP c.u. the functional reserves of the cardiovascular system are assessed in great shape, a value of DP 70-84 c.u.– OK, a value of DP 85-94 c.u. – Lack of functionality of the cardiovascular system, a value DP 95-110 c.u. – Deregulation of the cardiovascular system, at a value of more than 111 DP c.u.– Regulation of the cardiovascular system is broken [9].

RESULTS AND DISCUSSION

General characteristics of the students are presented in Table 1. Growth rate NEFU 1 students ranged from 112.5 to 176 cm. Body weight also varied over a wide range from 38 to 87 kg. BMI was in the range of 14.5 to 39.1. BMI: insufficient – 17.5 ± 0.9 (14.5-18.4) in 52 (11.0%) patients, normal – 21.3 ± 1.6 (18.5-25) in 378 (79.4%) of the participants, excess – 26.6 ± 1.2 (25.1-29.3) in 38 (8.0%), obesity – 33.2 ± 2.9 (31.2-39.1) in 6 (1.4%), obese students - 0.

Table 1

General characteristics of girls (M ± σ)

Characteristics	1st year student NEFU n = 476	Control group, n = 156
Height, cm	159.2±6,1	163.7±5.9
Weight, kg	54.4±7.1	61.6±12.7
BMI	21.5±2.8	23.1±47
SBP, mm Hg	104.2±10.8	104.2 ±14.9
DBP, mm Hg	66.4±8.4	70.5±11.6
P, beats per minute	83.4±11.7	69.6±10.3
HR per minute	83.4±11.7	69.6±10.3
AP, scores	8.7±0.9	7.5±0.9
DP, arbitrary units	87.1±14.4	72.9±14.2

Note: SBP – Systolic blood pressure, DBP – Diastolic blood pressure, P – Pulse, HR – Heart rate.

It is known that the adaptation of the body provides a coordinated in time and space and by subordinate to each other specialized functional systems. In this case, the main adaptive system, limiting mental and physical performance, is the cardiovascular system. Clear information on the degree of perfection of development and level of physical health of the individual gives a level of energy production, indicating the ability to adapt to the conditions of existence and the possibility to implement a program of development. The most valuable criteria for the energetic state of the reserve is the cardiovascular system. One indicator of this reserve is DP (IR), which characterizes the somatic work of the heart. The larger the figure at the height of physical activity, the greater is the functional capacity of the heart muscle [9].

So, the girls' systolic blood pressure ranged from 80 to 140 mm Hg, diastolic blood pressure – 50-102 mm Hg, heart rate – from 60 to 188 beats / min. One of the main indicators of the functional state of the cardiovascular system, determining the development of the adaptation of the whole organism, is the heart rate. This figure is traditionally used as a vegetative and correlate emotional stress. According A.V. Shakhanova et al. heart rate changed upward depending on the shape and control of the degree of emotional stress [8]. This indicates a sharp decline in the functional capacity of the circulatory system and reflects the presence of stress adaptation mechanisms, as evidenced by indicators of DP and AP.

DP analysis showed that 10.2% of the examined cardiovascular system functional reserves were in great shape, at 34.3% – normal, at 24.9% – failure, at 25.4% – a violation of the regulation, at 5.2% – regulation is violated, i.e. functional reserves cardiovascular system were tense and exhausted in 55.5% of cases (tab. 2). Thus, only 1.5% of AP was satisfactory, while in 98.5% of cases – poor (tab. 3).

Table 2

Indicators of double product of the NEFU 1st year students (M ± σ)

Double product, n=461	Conventional units
Great n=47	63.9±3.1
Good n=158	77.4±4.2
Average n=115	89.2±2.8
Poor n=117	100.5±4.6
Very bad n=24	120.0±5.7

Table 3

Indicators of adaptive potential of the NEFU 1st year students (M ± σ)

Adaptive potential, n=476	Points
Satisfactory adaptation, n = 7	6.8±0.2
Stress adaptation mechanisms, n = 118	7.7±0.3
Poor adaptation, n = 269	8.8±0.4
Disruption of the mechanisms of adaptation, n = 82	10.3±0.6

Somatometric data of the control group were as follows: growth ranged from 149 to 178 cm, weight ranged from 43-116 kg (Tab. 1). BMI varied over a wide range of 15.6 to 44.4 (Tab. 1). Hemodynamic parameters were as follows: systolic blood pressure was from 70 to 170 mm Hg, diastolic blood pressure – 40-115 mm Hg, heart rate – from 42 to 100 beats per min. (Tab. 1). AP figures ranged from 5.018 to 10.238 points, characterized by satisfactory only in 40% of cases (Tab. 5). DP varied within 37.8-108.57 c.u. which was satisfactory in 94% (Tab. 4).

Comparative analysis showed that the control group had better somatometric and hemodynamic parameters (the growth $p < 0.0000$, the weight $p < 0.0000$, BMI $p < 0.001$, DBP $p < 0.0000$, HR $p < 0.00$). Indicators of cardiovascular system reserves of the NEFU 1st year girls

students were worse (AP p <0.00, DP p <0.0000), indicating the extreme force of impact or a long duration. Overstrain of regulation system can lead to the disruption of adaptation to changes in the level of inadequate functioning of the heart and blood vessels, to disruption of homeostasis with the advent of pathological syndromes and diseases.

Table 4

Indicators of adaptive potential of the control group (M ± σ)

Adaptive potential, n=156	Points
Satisfactory adaptation, n = 62	6.8±0.6
Stress of adaptation mechanisms, n = 56	7.7±0.2
Poor adaptation, n = 37	8.6±0.4
Disruption of the adaptation mechanisms, n = 1	10.2

Table 5

Indicators of double product of the control group (M ± σ)

Double product, n=156	Points
Great n=66	60.0±7.6
Good n=58	76.1±4.6
Average n=22	89.7±3.1
Poor n=10	101.2±4.7
Very bad n=0	-

Thus, adaptive body reserves of NEFU students are characterized as unsatisfactory. The observed decrease in adaptive capacity of the organism even in the absence of the manifested disease indicates a lower level of health and increases the risk of disease.

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Remaxol in the Correction of Lipid Peroxidation Processes of Biomembranes Induced by the Cold Exposure

ABSTRACT

In experimental conditions the possibility to correct free radical lipid oxidation of rats' organism membranes was studied with the introduction of the succinate containing drug called remaxol. The animals were divided into 4 groups and each of them had 30 rats: intact animals which were held in standard conditions of vivarium; the control group in which rats were exposed to cold during three hours daily; the experimental group in which before cooling animals had a daily intake of the remaxol in a dose of 50 mg/kg; the experimental group in which before cooling animals had a daily intake of the remaxol in a dose of 100 mg/kg. It was found out that in the blood of experimental animals a daily cold exposure during three hours contributes to the increase of lipid hydroperoxides level (by 25 – 41%), of diene conjugate (by 38 – 54%), and of malonic dialdehyde (by 27 – 74%) against the decrease of antioxidant system activity in the blood of intact animals.

The introduction of the succinate containing drug to rats in the conditions of cold exposure contributes to the reliable decrease in the blood of lipid hydroperoxides by 8-25%, of diene conjugates – by 10-29%, malonic dialdehyde – by14-38% in comparison with the rats of the control group. While analyzing the effect of the remaxol on the activity of the components of antioxidant system it was shown that the level of ceruloplasmin in the blood of animals was reliably higher by 10-50%, of vitamin E by 8-31%, of catalase by 7-28% in comparison with the same parameters of the rats of the control group.

During the comparative pharmacological analysis it was established that remaxol produced a direct antioxidant effect according to a dose during cold exposure on the organism of the experimental animals.

Keywords: remaxol, cold exposure, lipid peroxidation biological membranes, products of peroxidation (lipid hydroperoxides, diene conjugates, malonic dialdehyde), antioxidant system.

INTRODUCTION

Modern environmental conditions dramatically increased the level radicalopathy processes in the body [1, 8, 10]. Cold exposure stimulates the generation of reactive oxygen species that initiate the process of lipid peroxidation (LPO), due to the development of hypoxia, based on the increase in the rate of consumption of tissue oxygen necessary for energy supply,

in conditions of increased heat production [4, 7]. In these circumstances the use of the succinatecontaining antihypoxants is appropriate since the conversion of succinic acid in the body is associated with the production of energy necessary for life support, and under conditions of increasing load on any of the body systems, in particular during cold exposure, the maintenance of its work is provided mainly by the oxidation of succinic acid [3, 5, 7]. Given the above, the experimental evaluation of the effectiveness of polyionic infusion solution remaxol, comprising the salt of succinic acid, riboxinum, methionine, nicotinamide and excipients (magnesium chloride, potassium chloride, sodium chloride) in optimum concentrations developed by the scientific–technological pharmaceutical firm "Polysan" approbated on the clinical bases of the Department of anesthesiology and intensive care, St. Petersburg medical Academy of postgraduate education, for the correction of peroxidation processes induced by the effect of cold, is relevant and opens perspectives in the regulation of various stress factors.

The aim: to examine the effect of succinate containing preparationremaxol in doses of 50 mg/kg and 100 mg/kg on antioxidant state of warm-blooded organism in the conditions of cold exposure.

MATERIALS AND METHODS

To study the effect of remaxol in doses 50 mg/kg and 100 mg/kg on the organism of the experimental animals (white rats-males) cold model of the experiment was made [4]. In the experiment 4 groups of animals with the weight of 180g took part. There were 30 rats in each group: 1- intact group, the animals were in standard conditions of a vivarium; 2 – control group, the animals were exposed to the prolonged cooling in the climatic chamber "Fentron" (Germany) at the temperature -15°C during 3 hours daily within 21 days; 3- experimental group, before cooling the animals were made intraperitoneal introduction of remaxol in the dose of 50 mg/kg during 21 days; 4 – experimental group, before cooling intraperitoneal introduction of remaxol in the dose of 100 mg/kg was made to the animals during 21 days.

The investigation was conducted simultaneously in all groups during 21 days, slaughter of the animals was made by means of decapitation on the 7 th, 14 th, 21 th days of the experiment. The intensity of LPO processes was estimated during examination of the content of lipid hydroperoxides, dien conjugates (according to methods, worked out by I.D. Stal'naja), malonic dialdehyde (according to colored reaction with thiobarbital acid) and the main components of AOS(ceruloplasmin – according to methods of V.G. Kolb, V.S. Kamyshnikov, vitamin E according to methods of R.Zh. Kiselevich, S.I. Skvarko, catalase and glucose-6-phosphate dehydrogenase

according to methods in modification of Ye.A. Borodin) in the rats' serum. Statistical processing of biochemical data was conducted by means of parametrical method with the use of "t" Student criterion.

RESULTS AND DISCUSSION

In the conditions of the prolonged cold exposure during the experiment a reliable increase of the content of dien conjugates (DC) in blood by 38-54% regarding intact animals was observed. Introduction of remaxol in the dose of 100 mg/kg in the conditions of cold model promotes a stable reliable decrease of DC content in the blood of the experimental animals during all days of the experiment on the average by 25% in comparison with the control. During the introduction of remaxol in the dose of 50 mg/kg considerably less expressed decrease of this index was observed at the end of the second (by 16%) and the third weeks of the experiment (by 10%).

In the control group of animals a reliable accumulation of lipid hydroperoxides (LHP) in the blood by 28%, 41%, 25%, on the 7^{th}, 14^{th}, and 21^{st} days of the experiments was observed correspondingly regarding intact rats. In the experimental group of animals receiving remaxol in the dose 50 mg/kg before cold exposure some decrease of LHP in the serum by 8%, 21%, 19%, was observed on the on the 7^{th}, 14^{th}, and 21^{st} days of the experiment correspondingly. The increase of remaxol dose to 100 mg/kg led to more pronounced reliable decrease of LHP in the serum during all days of the experiments in comparison with the control group average by 16%-25%, the best result was received by the end of the second week of the experiment, on the 21^{st} day of experiment the level of LHP content in the blood of experimental animals is comparable with analogous index in the intact group.

Thus, by the end of the experiment LHP content in the serum in the group of animals receiving remaxol in the dose of 100 mg/kg unlike experimental animals, receiving remaxol in the dose 50 mg/kg, became equal with the initial LHP content in the serum of the animals of the intact group. It shows the absolute stabilization of LPO processes.

Table 1

Content of LPO products in the rats' blood in the conditions of the prolonged cold stress against the background of applying remaxol in the dose of 50 and 100 mg/kg

Indices	Periods of experiment	*Group1* intact n = 30	*Group 2* cold (control) n = 30	*Group 3* Remaxol in the dose of 50 mg/kg + cold n = 30	*Group 4* Remaxol in the dose of 100 mg/kg + cold n = 30
Hydroperoxides(nmole/ml)	the 7th day	26,0 ± 1,8	33,2 ± 1,1* $P_{1,2} < 0,01$	30,6 ± 1,0 $P_{2,3} > 0,05$	27,9 ± 2,0 $P_{2,4} > 0,05$
	the 14th day	25,0 ± 2,7	35,2 ± 1,2* $P_{1,2} < 0,01$	27,9 ± 1,7** $P_{2,3} < 0,01$	26,4 ± 1,3** $P_{2,4} < 0,01$
	the 21th day	28,6 ± 1,5	35,6 ± 1,1* $P_{1,2} < 0,01$	29,0 ± 1,9** $P_{2,3} < 0,05$	28,6 ± 1,2** $P_{2,4} < 0,05$
Dien conjugate(nmole/ml)	the 7th day	35,2 ± 4,3	48,7 ± 3,3* $P_{1,2} < 0,05$	38,1 ± 2,8** $P_{2,3} < 0,05$	37,8 ± 1,9** $P_{2,4} < 0,05$
	the 14th day	35,4 ± 3,0	49,2 ± 2,6* $P_{1,2} < 0,01$	41,2 ± 1,2** $P_{2,3} < 0,05$	35,1 ± 1,4** $P_{2,4} < 0,01$
	the 21th day	31,2 ± 2,6	48,1 ± 3,4* $P_{1,2} < 0,01$	43,2 ± 2,3 $P_{2,3} > 0,05$	36,8 ± 1,1** $P_{2,4} < 0,05$
Malonic dialdehyde (nmole/ml)	the 7th day	3,8 ± 0,1	6,1 ± 0,2* $P_{1,2} < 0,001$	4,6 ± 0,3** $P_{2,3} < 0,05$	4,0 ± 0,1** $P_{2,4} < 0,05$
	the 14th day	3,8 ± 0,2	6,6 ± 0,4* $P_{1,2} < 0,001$	4,6 ± 0,2** $P_{2,3} < 0,05$	4,1 ± 0,2** $P_{2,4} < 0,01$
	the 21th day	4,4 ± 0,3	5,6 ± 0,4* $P_{1,2} < 0,05$	4,8 ± 0,1 $P_{2,3} > 0,05$	4,4 ± 0,3** $P_{2,4} < 0,05$

Notes: * and **– differences, reliable regarding the intact group*and the control group of animals **

Table 2

The content of AOS components in the rats' blood in the conditions of the prolonged cold stress against the background of application of remaxol in the dose of 50 and 100 mg/kg

Indices	Periods of experiment	*Group1* intact n = 30	*Group 2* cold (control) n = 30	*Group 3* Remaxol in the dose of 50 mg/kg + cold n = 30	*Group 4* Remaxol in the dose of 100 mg/kg + cold n = 30
Ceruloplasmin (mkg/ml)	the 7th day	30,0 ± 1,9	20,5 ± 1,8* $P_{1,2}$ < 0,01	22,6 ± 4,6 $P_{2,3}$>0,05	26,6 ± 2,8 $P_{2,4}$ >0,05
	the 14th day	28,8 ± 1,4	19,1 ±1,2* $P_{1,2}$ < 0,01	28,7 ± 2,6** $P_{2,3}$< 0,05	27,7 ± 2,5** $P_{2,4}$< 0,05
	the 21th day	26,8 ± 1,4	20,3± 1,0* $P_{1,2}$ < 0,01	26,5 ± 1,1** $P_{2,3}$< 0,05	27,7 ± 2,1** $P_{2,4}$< 0,05
Vitamin E (mkg/ml)	the 7th day	48,7 ± 3,6	37,3 ± 1,5* $P_{1,2}$ < 0,05	40,2 ± 0,8 $P_{2,3}$>0,05	44,8 ± 1,7** $P_{2,4}$< 0,05
	the 14th day	47,5 ± 2,2	34,0 ± 1,6* $P_{1,2}$ < 0,01	40,9 ± 1,5** $P_{2,3}$< 0,05	44,7 ± 1,5** $P_{2,4}$< 0,05
	the 21th day	45,8 ± 2,0	38,0 ± 1,8* $P_{1,2}$ < 0,01	41,5 ± 1,3 $P_{2,3}$>0,05	44,8 ± 1,4** $P_{2,4}$< 0,05
GL-6-PhDH (mcmoleNADFH $л^{-1}c^{-1}$)	the 7th day	6,9 ± 0,2	5,6 ± 0,2* $P_{1,2}$ < 0,01	5,8 ± 0,2 $P_{2,3}$>0,05	5,8 ± 0,2 $P_{2,4}$> 0,05
	the 14th day	6,8 ± 0,2	5,9 ± 0,2* $P_{1,2}$ < 0,05	6,5 ± 0,1** $P_{2,3}$< 0,05	6,6 ± 0,2 $P_{2,4}$> 0,05
	the 21th day	6,7 ± 0,3	5,6 ± 0,2* $P_{1,2}$ < 0,05	6,5 ± 0,2** $P_{2,3}$< 0,05	6,4 ± 0,2** $P_{2,4}$< 0,05
Catalase (mcmole H_2O_2 $г^{-1}c^{-1}$)	the 7th day	93,0 ± 2,7	78,6 ± 5,1* $P_{1,2}$ < 0,05	83,8 ± 6,1 $P_{2,3}$>0,05	85,2 ± 6,4 $P_{2,4}$> 0,05
	the 14th day	95,2 ± 3,2	72,8 ± 5,9* $P_{1,2}$ < 0,05	84,4 ± 5,1 $P_{2,3}$>0,05	86,8 ± 4,8 $P_{2,4}$> 0,05
	the 21th day	97,0 ± 3,5	71,0 ± 4,2* $P_{1,2}$ < 0,05	81,0 ± 4,9 $P_{2,3}$>0,05	91,0 ± 5,0** $P_{2,4}$< 0,05

Notes: * and **– differences, reliable regarding the intact group*and the control group of animals **

A reliable increase of malonic dialdehyde (MDA) content by 27-74% in the blood was observed during the experiment in the conditions of cold exposure on the experimental animals. In case of remaxol introduction in different doses the the content of MDA in the blood was reliably lower, that in the control animals on the 7th and 14th days of the experiment. Antioxidant effect is more pronounced in remaxol in the dose of 100 mg/kg during all days of the experiment (the decrease of MDA content made up 21%-38% regarding the control group), the level of index, against the background of remaxol introduction in the of 100 mg/kg on the 21st day of the experiment is comparable with the level of index of the intact group.

The pronounced decrease of concentration of ceruloplasmin by 24-34% in plasma was marked as a result of cold exposure on the organism of the laboratory animals. Against the background of the intraperitoneal introduction of remaxol in the dose of 100 mg/kg before the cold exposure the content of ceruloplasmin in plasma inereases by 30%, 45% on the 7th and 14th days of the experiment correspondingly regarding the control and it corresponds to the level of ceruloplasmin in the animals of the intact group by the end of the animals of the intact group by the end of the third week. Remaxol introduction in the dose of 50 mg/kg leads to small increase of ceruloplasmin content in plasma by 10%, 50% and 31% on the 7th, 14th and 21st days of the experiment correspondingly regarding the control.

Against the background of remaxol in the dose of 100 mg/kg a reliable increase of vitamin E content by 20% and 31% is marked on the 7th and 14th days of the experiment correspondingly regarding the control group. Remaxol in the dose of 50 mg/kg affected considerably less the level of this index (by 8%, 20% and 9%) on the 7th, 14th and 21 days of the experiment correspondingly, these differences regarding the control group were not authentic. Thus, there is a direct dependence of vitamin E content on the dose of preparation, but in the groups receiving remaxol in the dose of 100 mg/kg the effect is achieved and it allows to suppose stimulating effect of this dose of preparation on the intensified production of endogenous vitamin E, it may be a significant factor in prophylaxis of the cold stress.

Cold exposure causes (by 13-19%) the decrease of GL-6-PhDH activity in the blood of laboratory animals in comparison with the intact group. The partial normalization of enzyme activity is observed during all days of the experiment (by 4-14%) against the background of remaxol introduction in the dose of 100 mg/kg. Remaxol in the dose of 50 mg/kg leads to less pronounced effect partially normalizing GL-6-PhDH activity by the 7th day of the experiment to

4%. By the end of the second week the level of GL-6-PhDH activity is lower that the level of the control group index by 10% and by the 21st day of the experiment GL-6-PhDH activity during remaxol introduction in the dose of 50 mg/kg corresponds to the level of the intact group.

Thus, remaxol in the dose of 100 mg/kg in comparison with remaxol in the dose of 50 mg/kg gives more pronounced effect on normalization of GL-6-PhDH activity during its decrease against the background of cold exposure in the control group of animals.

A considerable decrease of catalase activity from (16%, to 27%) regarding group of the intact animals' takes place during the experiment in the conditions of cold exposure. Remaxol in the dose of 100mg/kg prevents from the decrease of catalase activity in the blood-partially after the first week of low temperature action (by 8%). In this case level of the intact group is not achieved. After the second week and by the end of the third week of cold exposure the enzyme activity increased by 19-28% in comparison with the control group correspondingly. Effect of remaxol introduction in the dose of 50 mg/kg is less pronounced on the 7th, 14th, and 21st days of the experiment, catalase activity increased by 7-16% correspondingly.

As a whole, the examination of LPO products content in the blood, content and activity of AOS components in the conditions of cold exposure and influence on these indices of remaxol in the dose of 50 and 100 mg/kg allows to establish antioxidant effect which is more pronounced in the dose of 100 mg/kg.

CONCLUSIONS

1. The possibility of the cold stress correction by means of introduction of preparation remaxol which contains succinic acid is confirmed experimentally for the first time.
2. Intraperitoneal introduction of remaxol to the laboratory animals (rats) decreases the intensity of LPO processes biomembranes induced by the prolonged cold exposure normalizing stationary level of peroxidation products against the background of a reliable increase of activity of the main AOS components.
3. Statistically significant differences of changes of indices of LPO processes and components of AOS depending on the dose of remaxol and the duration of its application are determined (direct dose dependence – in case of application of remaxol greater dose, the antioxidant effect is more pronounced).

4. The results of the investigation give the grounds to recommend remaxol as an antioxidant as well as regulator of adaptation reactions of an organism at a low temperature.

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The Incidence of Ulcerogenesis Exogenous Factors in Patients with Newly Diagnosed Stomach Ulcers, Complicated with Bleeding and Perforations

ABSTRACT

The purpose of the study. To study the incidence of exogenous factors and ulcerogenic topical features of newly diagnosed gastric ulcers in the KhMAO-Yugra residents.

Materials and methods. A total of 32 residents of Yugra Khanty-Mansi Autonomous with newly diagnosed stomach ulcers were under study. All patients in the examination of stomach ulcers are diagnosed based on the EFGDS results.

Results. There was revealed a predominant localization of ulcer bleeding from newly diagnosed gastric ulcers - the body of the stomach. It was noted the high frequency of alcohol-related new cases of stomach ulcers, complicated with bleeding. Perforations of new cases of stomach ulcers are not exceeding the rate of exogenous factors of ulcerogenesis compared with bleeding and uncomplicated new cases of stomach ulcers.

Conclusion. It is noted the high frequency of alcohol associated newly diagnosed gastric ulcers complicated by bleeding. Mixed Hp-invasion and NSAIDs for bleeding ulcers of new cases are less common than in patients with uncomplicated disease.

Keywords: ulcer, stomach, bleeding, perforation, H. pylori.

INTRODUCTION

Ulcers in the stomach are found in four times less than in the duodenum [3,12]. At the same time ulcers in the stomach are characterized by often recurrent course, the severity of complications [6,9], a longer period is necessary to restore the integrity of the gastric mucosa [7.13].

The formation of ulcers in the stomach is associated with the action of the numerous exogenous factors: invasion of Helicobacter pylori (Hp), the action of non-steroidal anti-inflammatory drugs (NSAIDs), alcohol [4, 11, 15].

The complexity of the problem of diagnosis of ulcers in the stomach and predict their risk of morbidity due to the fact that the formation of ulcers in the stomach is often accompanied by morphological rearrangement of the gastric mucosa with the formation of metaplastic, dysplastic, and paraneoplastic changes [1,14], reducing its regenerative capabilities and resilience to exogenous ulcerogenic factors [2, 10].

Histological study of biopsy specimens of the gastric mucosa is a must study the detection of gastroduodenal ulcers [8]. At the same time great importance is the timely detection and elimination of exogenous ulcerogenic factors [5,15].

Objective: to study the incidence of exogenous factors and ulcerogenic topical features of newly diagnosed gastric ulcers in the KhMAO-Yugra residents.

MATERIALS AND METHODS

A total of 32 residents of Yugra Khanty-Mansi Autonomous with newly diagnosed stomach ulcers in KhMAO-Ugra "County Hospital" in 2011-2012: 17 men, 15 women, aged 54 ± 13.9 yrs, were under study. The first group consisted of 15 patients with newly diagnosed stomach ulcers, perforations and bleeding complications: I subgroup (11) and subgroup 2 (4 people), respectively. The comparison group consisted of 17 patients with newly diagnosed gastric ulcers not accompanied by a complicated course.

All patients in the examination of stomach ulcers are diagnosed based on the results EFGDS. At the same time in all patients a stomach ulcer or duodenum were not previously detected.

Among ulcerogenic factors were evaluated: the availability of HP-invasion, non-steroidal anti-inflammatory drugs (NSAIDs), alcohol intake before diagnosed gastric ulcer.

At the diagnosis of ulcers their localization was recorded and assessed: cardiac, antrum and gastric body.

EFGDS was carried out in the usual manner with gastroscope «OLYMPUS GIF-Q 160".

The presence of Hp-invasion was verified by morphological study of biopsy material of gastric mucosa in the Hp and using enzyme-linked immunosorbent serologic method.

Statistical analysis was performed using Statistica '99 Edition (Statsoft). The statistical significance of differences between groups was assessed using Pearson's chi-squared test - $\chi 2$. The critical level of significance when testing statistical hypothesis $p < 0.05$.

The study complies with the principles of the Helsinki Declaration on Human Rights, reviewed and approved by the local ethics committee members BU "Khanty-Mansiysk State Medical Academy".

RESULTS AND DISCUSSION

In the patients with newly diagnosed stomach ulcers we revealed bleeding and perforation at the complicated disease in 73 and 27%, respectively. At the same time, bleeding

ulcers of the gastric mucosa in the examined patients is found significantly more often than the perforation of ulcers (χ^2 = 6.53 p = 0.0106).

When analyzing ulcerogenesis factors patients of comparison group their frequency is 53% of cases (Table). The most important factors are: HP-invasion and NSAIDs (89% identified ulcerogenic factors), exceeding the rate of gastric ulcers associated with alcohol (χ^2 = 10.89 p = 0.0010).

Mixed HP-invasion and NSAID in the comparison group is 56% of the total number of identified ulcerogenic factors (Table).

At the comparing of the frequency of exogenous ulcerogenic factors in patients of group 1 and comparison group we revealed no statistically significant differences (p> 0.05; Table).

Table

Comparative analysis of ulcerogenic and topic factors in newly diagnosed gastric ulcers complicated by bleeding and perforation

	Patients with newly diagnosed gastric ulcer (group1-15)			Patients with first identified universe-gastric ulcer (comparison group - 17)		
	bleeding complica-tions 1st sub-group (11)	χ^2 * p	complica-tions of perforation 2nd subgroup (4)	comparison with subgroup 1 χ^2 * p	number of patients 17	compared to subgroup 2 χ^2 * p
Factors of ulcerogenesis	8 (73%)	2,78 0,0952	1 (25%)	1,10 0,2951	9 (53%)	1,01 0,3141
1.Helicobacter pilori	2 (18%)	0,84 0,3596	0 (0%)	0,00 0,9712	3	0,82 0,3642
2.NSAIDs	2 (18%)	0,84 0,3596	0 (0%)	0,45 0,5027	5	1,54 0,2140
3. Alcohol	4 (36%)**	1,98 0,1590	0 (0%)	4,23 0,0397	1	0,25 0,6192
4.Mixed: Helicobacter pilori + NSAID	0 (0%)	2,95 0,0861	1 (25%)	3,94 0,0472	5	0,03 0,8605
Localization of newly diagnosed ulcers						
gastric antrum	2 (18%)	1 (25%)		6 (35%)		

the body of the stomach	8 (73%)	3 (75%)	11 (65%)	
cardia	1 (9%)	0 (0%)	0 (0%)	
Factors of ulcerogenesis	**15**		**17**	
1.Helicobacter pilori	2 (13%)		3 (18%)	0,11 0,7373
2. NSAIDs	2 (13%)		5 (29%)	1,21 0,2722
3. Alcohol	4 (27%)		1 (6%)	2,61 0,1061
4. Comparison of the frequency of ulcer bleeding: Antrum / body of stomach	2/8**		-	
5. Comparison of the frequency of ulcer perforation: Antrum / body of stomach	1/3		-	

Note: * - χ^2- Pearson's chi-squared test; ** - Statistically significant excess incidence of criterion when comparing the 1st and comparison group ($p < 0.05$).

A more detailed analysis revealed that in the patients of the 1st subgroup alcohol-associated gastric ulcers were significantly higher than those ulcers in the comparison group. Wherein mixed Hp-invasion and NSAIDs in patients with newly diagnosed ulcers, complicated with bleeding, we revealed statistically rarely than those of the comparison group ($\chi^2 = 3.94$ $p = 0.0472$).

The analysis of topic features of newly diagnosed gastric ulcers complicated by bleeding, we found their predominant localization in the stomach compared with its cardiac and antral departments ($\chi^2 = 7.20$ $p = 0.0073$).

In the analysis of the frequency of occurrence of exogenous ulcerogenic factors in patients with newly diagnosed gastric ulcers complicated by perforation statistically significant differences from the control group are not revealed ($p > 0.05$). It should be noted a relatively low level of occurrence of ulcerogenic exogenous factors, mainly due to mixed HP-invasion and NSAIDs - 25% in the 2nd subgroup (Table).

We did not detect topic laws at perforations of newly diagnosed gastric ulcers in the studied patients (p> 0.05 cm. Table 1).

When comparing the frequency of detection of ulcerogenesis exogenous factors in the patients of the 1st and 2nd subgroups no statistically significant differences have been revealed (p> 0.05).

CONCLUSIONS

At the non - complicated course of the newly diagnosed gastric ulcers among ulcerogenic exogenous factors, account for 53%, the most significant are Hp-invasions and NSAIDs as mono and mixed ulceration factors.

In the patients with newly diagnosed stomach ulcers, with bleeding complications statistically significant excess of the alcohol - associated ulcers when compared to the comparison group. At the same time it is found that bleeding is associated with ulcers mainly in the stomach body, exceeding antral and cardiac localization of gastric ulcers complicated by bleeding.

Complication in the form of newly diagnosed ulcer perforation, is associated with exogenous factors only in 25% of cases associated with simultaneous action on the gastric mucosa of Hp invasion and NSAIDs, and has apparently deeper mechanisms concerning the state of the gastric mucosa and endogenous factors having antiulcergenic properties.

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Two-Level Immunocorrection Therapy of Acute Destructive Pancreatitis in a Multidisciplinary Surgical Hospital

ABSTRACT

This work is based on the analysis of complex treatment of patients with pancreatic necrosis treated at the surgical department of the Republican Hospital №2 - Emergency Center of the Sakha (Yakutia) Republic in the period from 2010 to 2015. The study allowed adapting and improving a duplex immunocorrection in pancreatic necrosis in a multidisciplinary surgical hospital that along with the other constituents of intensive therapy has allowed in a whole to reduce the amount of intra- and extra abdominal complications and lethal outcomes in a sterile pancreatic necrosis phase and in the phase of infectious complications.

Keywords: pancreatic necrosis, immunocorrection therapy.

INTRODUCTION

The last decade is marked with a qualitatively new stage of comprehensive research in the area of abdominal surgery such as urgent pancreatology, in the structure of which, acute destructive pancreatitis ranks first [1, 10, 11]. The range of the main directions of scientific and practical research includes not only the study of various aspects of pathogenesis and tanatogenesis disease and its complications, and improved methods of diagnosis, intensive care choices and tactics of surgical procedures [2-4, 13].

A significant part of the researchers involved in the problem of the treatment of acute destructive pancreatitis found that the risk of complications, including purulent destructive processes directly related to developing this category of patients with secondary immunodeficiency [1-6, 12 - 14]. It is for this reason that one of the main problems facing the surgeon is timely, reasonable and adequate immunotherapy. Consequently, the question of choice of tactics of treatment of patients with different clinical and pathologic forms of complications sterile and infected pancreatic necrosis and the inclusion of a comprehensive treatment program immunotherapy require further research and development, which was the basis for the implementation of this work.

RESEARCH MATERIALS

This work is based on a comprehensive analysis of the results of conservative and surgical treatment of 497 patients with pancreatic necrosis treated at the surgical department of the Republican Hospital №2 - Center for Emergency Medical Aid of the Republic of Sakha (Yakutia) in the period from 2010 to 2015.

All patients included in the study cohort were separated into two groups and three subgroups in each group, depending on the fact of infection and embodiments of pancreatic necrosis pathomorphogenesis. The first group of observations - the group «A», consisted of patients with sterile clinical and pathologic forms of pancreatic necrosis. The second group of observations - the group «B», consisted of patients infected with clinical and pathologic forms of pancreatic necrosis. Group «A» is divided into three subgroups: the subgroup «a» - those with enzymatic ascites-peritonitis; subgroup «b» - patients with the formation parapancreatic infiltration, morphological basis which was "aseptic" abscess of various departments of the retroperitoneal fat; subgroup «c» - patients with pseudocyst formation postnecrotic alternatively the evolution of necrosis occurring in abacterial conditions (time of formation of a false cyst usually accounted for more than 4 weeks from the onset of the disease, provided these posts with large formations of pancreatic duct). In turn, the group «B» is divided into three groups depending on the different options for transforming the sterile clinical and pathological forms in infected necrotizing pancreatitis: a subgroup «d» - patients with abscess formation pancreatogenic; subgroup «e» - patients with infected pancreatic necrosis formation; subgroup «f» - patients with infected pancreatic necrosis formation in conjunction with pancreatogenic abscess.

The diagnosis of pancreatic necrosis and the development of its complications was verified based on a comprehensive survey include: clinical findings, laboratory tests (including an assessment of the level of endogenous intoxication (EI) on the content of low and medium molecular weight (SL & AMW) by the method M.Y. Malakhova [7] and oligopeptide (ARS) by Lowry [9] in plasma, erythrocytes and urine with the release of five phases of EI, as well as control and accounting of important biochemical markers of pancreatic tissue necrosis and retroperitoneal tissue, systemic inflammatory response (SVR), and infection of pancreatic necrosis (LDH , C-reactive protein, procalcitonin). Instrumental methods of diagnosis include ultrasound and radiopaque computer scan of the abdominal cavity, retroperitoneal fat, videolaparoscopy, transdermal therapeutic and diagnostic puncture liquid formations of the pancreas, abdominal and retroperitoneal tissue under ultrasound followed by microbiological and cytological analysis of the resulting material. Assessment of the severity of the general condition and the severity of multiple organ failure in patients with pancreatic necrosis was performed using integrated systems scales, APACHE II [12] and TFS [10].

Immune status was evaluated by the number of lymphocytes and their subpopulations (T lymphocytes and B lymphocytes).

To study the T-system of immunity were determined by plaque subpopulation of T cells: T helper (Th), T-suppressor (TS), and calculates the immunoregulatory index (IRI), equal to the ratio Tx to Tc (Th / Ts) [8].

Analysis of B-immune system included its quantitative characteristics - determination of B-lymphocytes in the blood (the percentage and absolute content) [8] and functional characteristics - determination of serum immunoglobulin classes A, M, G by radial immunodiffusion on C. Manchini [8].

Statistical analysis of clinical material produced using the software package Stat Plus 2007 for Windows XP. In assessing the totality of the average value (μ) and standard deviation (σ); confidence factor differences (p) was determined by the Mann-Whitney test.

RESULTS AND DISCUSSION

According to several authors [1, 3, 4, 6, 10], in 24-68% of patients with necrotizing pancreatitis immune system disorders and functional impairment of the liver develop, which greatly exacerbates the severity of the disease due to the development of secondary immunodeficiency and eventually worsens its prognosis.

The causes of immunodeficiency in necrotizing pancreatitis are: significant loss of proteins with exudate, pus; insufficient intake of complete proteins from food (forced starvation, malnutrition); toxic inhibition of liver function, including protein-synthesizing; immunosuppression drug due to prolonged administration of antibiotics and etc [4,5, 14].

The object of our study was to evaluate the immune status of 188 (37.8%) patients with a sterile and in 57 (82.6%) patients with positive clinical and pathologic forms of pancreatic necrosis. Cellular (T-lymphocytes and their subpopulations immunoregulatory index (IRI)), and humoral immunity (B-lymphocytes, immunoglobulins A, M and G) were evaluated during the first day after admission and then every 3-5 days.

Studies on the first day, showed a violation of the immune status in all representations of groups and subgroups of patients (Table 1).

Table 1

Immune status of patients -sterile (group A) pancreatic necrosis in the first days of intensive care

Indicator	Control	Subgroup «a» (n=75)	Subgroup «b» (n=102)	Subgroup«c» (n=11)
Leukocytes(·10^9/л)	6,7±1,3	12,6±1,4**	15,1±1,8***	8,2±1,3*
Lymphocytes (%)	20,1±2,1	15,3±2,3**	12,1±3,5**	17,4±1,5*
(·10^9/л)	1,4±0,1	0,7±0,4*	0,6±0,3*	1,1±0,6*
T-lymphocytes (%)	44,9±2,3	22,3±1,5**	19,3±1,2**	36,6±2,4*
(·10^9/л)	1,1±0,9	0,7±0,4*	0,5±0,2*	0,9±0,7*
T-helpercells (%)	39,6±3,3	28,1±3,3**	26,1±3,4**	31,4±2,3*
(·10^9/л)	0,8±0,8	0,4±0,3*	0,3±0,4*	0,6±0,8*
T-suppressors (%)	25,5±2,8	19,5±2,7**	18,1±3,1**	22,3±4,1*
(·10^9/л)	0,7±0,4	0,4±0,2*	0,3±0,4*	0,5±0,5*
IRI (y.e.)	1,6±0,1	1,4±0,3*	1,4±1,6*	1,4±0,4*
B-lymphocytes (%)	27,3±2,6	17,4±7,1**	15,3±4,1***	24,6±1,6*
(·10^9/л)	0,7±0,3	0,4±0,9*	0,3±0,5*	0,6±0,1*
IgA (г/л)	2,4±0,1	3,7±1,1**	4,1±0,3***	3,2±1,5**
IgM (г/л)	1,48±0,7	1,0±0,1*	0,9±0,2**	1,1±0,4*
IgG (г/л)	14,2±2,6	17,6±4,1**	19,8±1,5***	16,5±2,4**

* - index significantly different from control (p<0,05),

** - index significantly different from control (p<0,01),

*** - index significantly different from control (p<0,001)

Presented in Table 1 data show that major shifts in sterile pancreatic necrosis characteristic of cellular immunity and appear absolute and relative decline in the number of lymphocytes, predominantly T-lymphocytes and their subpopulations. Absolute content of T lymphocyte Th and Tc, in patients, especially in the subgroups «a» and «b» is reduced as compared with the control value of 1.5; 1.6 and 1.4; 1.3 times, respectively. It may be noted that among the subpopulations of T-lymphocytes, Tx quantity change, compared with T is somewhat more pronounced. Presented changes have led to a decrease in IRI, which has made in these subgroups values 1.4±0.4 and 1.4±0.3 c.u. respectively, which could indicate a moderate immunodeficiency. In the subgroup «c» change of cellular immunity were much less pronounced in comparison with the subgroups «a» and «b» and generally approached the check digit.

Changes in the immune system in the presented study groups were less pronounced and expressed decrease in absolute and relative content of B-lymphocytes. The indicator of its functional characteristics - blood levels of immunoglobulins, usually remained within normal limits, except for IgA and IgG, the absolute values exceeded in 1.6-2.5 times or more check digits. This fact, in spite of dissimmunoglobulinemia, according to the literature, is characterized as increased activity of humoral immunity [5]. It should be noted, since the voltage of the immune system of the human body is realized in the North, mainly due to the activation of B-cell level [8], therefore, we can expect its early failure.

More significant changes were observed in the immune status of subgroups «e» and «f» patients in the phase of infected pancreatic necrosis. Against the backdrop of severe general condition of patients and the manifestation of clinical signs of systemic inflammatory response of the body, these changes correspond to a pronounced degree of secondary immunodeficiency (SID). Thus, in patients subgroups «e», and «f» content absolute and relative amount of T-lymphocyte populations and Tx and Tg significantly below as reference numbers and indexes of patients subgroup «d». The most pronounced decrease in Tj and Tc, the absolute content in the blood was 0.3±0.5 (10^9/l), 0.4±2.4 (•10^9/l) and 0.2±1.2 (•10^9/l), 0.3±0.9 (10^9/L), respectively, which is lower almost in 1.5 times than the values of the subgroup of patients with «d» and check digits in 2 times. Analyzing changes in IRI, it may be noted that its value amounted to 1.4±0.5 and 1.5±1.1 c.u. respectively, which is also lower than in the subgroup of patients with «d» and the reference values in the presented study groups.

The total number of B-lymphocytes in infected pancreatic necrosis forms (Table. 2), especially in the subgroups «e», and «f» were significantly lower than those in the subgroup «d», and compared with values in a group of patients with clinical sterile pathomorphological forms an average of 2.5-3 times. Quantitative values of immunoglobulins, especially IgA and IgG, quite clearly correlated with the severity of sepsis and pancreatogenic above the reference value and the subgroup «d» in 3-4 times. However, Table 2 shows that in patients with sepsis pancreatogenic greater variation of the standard deviation of the mean is noted, which can be explained by the different severity of sepsis.

Table 2

Immune status of patients infected (group B) pancreatic necrosis in the first days of intensive care

Indicator	Control	Subgroup «d» (n=9)	Subgroup «e» (n=28)	Subgroup «f» (n=20)
Leukocytes(·10^9/л)	6,7±1,3	7,6±1,1*	19,3±2,8***	16,1±1,1**
Lymphocytes (%)	20,1±2,1	15,5±1,8*	11,1±3,3**	11,9±3,3**
(·10^9/л)	1,4±0,1	1,0±1,6*	0,4±2,4*	0,5±1,6*
T-lymphocytes (%)	44,9±2,3	34,1±2,2*	19,2±3,5**	18,1±2,2**
(·10^9/л)	1,1±0,9	0,8±0,3*	0,5±0,3*	0,6±1,7*
T-helpercells (%)	39,6±3,3	29,4±1,3*	24,2±1,3**	25,4±1,4**
(·10^9/л)	0,8±0,8	0,5±3,1*	0,3±0,5*	0,4±2,4*
T-suppressors (%)	25,5±2,8	20,1±2,1*	16,8±2,1**	17,5±3,3**
(·10^9/л)	0,7±0,4	0,4±1,5*	0,2±1,2*	0,3±0,9*
IRI (y.e.)	1,6±0,1	1,4±0,6*	1,4±0,5*	1,5±1,1*
B-lymphocytes (%)	27,3±2,6	22,5±1,3*	15,7±3,5**	16,1±2,1**
(·10^9/л)	0,7±0,3	0,5±3,1*	0,3±0,1*	0,4±0,2*
IgA (г/л)	2,4±0,1	4,6±3,5**	6,3±4,1***	5,5±1,6**
IgM (г/л)	1,48±0,7	1,0±0,2*	0,8±0,9*	0,9±1,2*
IgG (г/л)	14,2±2,6	18,1±1,4**	21,8±1,1***	20,3±2,5**

* - index significantly different from control (p<0,05),

** - index significantly different from control (p<0,01),

*** - index significantly different from control (p<0,001)

For patients with severe sepsis pancreatogenic except pronounced decrease of T-cell immunity, there is significant, compared with the control and with the patients with uncomplicated, reduction in the absolute and relative number of B-lymphocytes. Thus, the content of B lymphocytes in the blood of an average amounts at 0.2±0.1 (·10^9 / L), significantly lower than control values and the «d» subgroup. Reduction of IgM and in some cases, especially in severe pancreatogenic sepsis, IgA and IgG require uniform application of immunomodulation tactics.

Thus, the analysis of the immune status of patients with necrotizing pancreatitis shows the development of VID, due mainly to deficient T cell immunity. At the same time we observed that immune deficiency is more pronounced in the transformation of sterile clinical and

pathological forms in infected pancreatic necrosis, the development of pancreatogenic sepsis, and in general, it depends on the nature of the clinical course of the disease. The ongoing evaluation of the immune status in the course of the treatment process and revealed SID character allowed drawing up a program for immunotherapy of patients with necrotizing pancreatitis.

Immunotherapy of patients with sterile pancreatic necrosis, often had a preventive focus and included therapeutic doses of thymus peptides (Taktivin) during the period of the patients in the ICU and was recommended after their transfer to relevant department (for 7-10 days). On the contrary, an immunomodulating treatment in patients with infected pancreatic necrosis and generalization of infection is a more complicated task, requiring individual approach and includes two levels (Table. 3).

Table 3

Immunotherapy of patients with pancreatic necrosis

Methods of immunotherapy	**The number of patients**	
	absolute	%
Immunotherapy first level		
Passive replacement therapy		
Freshfrozenplasma	57	100
Immunoglobulins	44	77,2
Immunostimulatory therapy		
Taktivin	15	26,3
Immunotherapy second level		
Immunocorrectors complex action		
Polyoxidonium	54	94,7

At the initial stage (1-3 days), expressed in terms of the inflammatory syndrome, SID correction was conducted with a focus on passive, replacement therapy. Correction of deep disorders of immunity in patients was carried out by introducing to subgroups «e» and «f» of fresh frozen plasma, intravenous immunoglobulin.

It should be noted that only after the improvement of the general condition, normalization of central and peripheral hemodynamics, reduce signs of inflammatory syndrome and a stabilization of the immunity indices we prescribed immunotherapy second level. As a rule, it happened not earlier than 7-10 days after the operation and the beginning of immune therapy. So, against first- level immunotherapy, further, to activate cellular immune defense mechanisms 54 (94.7%) patients received Polioksidony. Thus, the usefulness of the presented immunotherapy scheme was confirmed by the stabilization of the immune status at all stages of treatment (Table. 1, 2).

Summarizing the results of the study it can be **concluded** that the main changes of the immune status in necrotizing pancreatitis are characteristic T-cell immunity and mainly are most pronounced in patients with common clinical and pathologic forms of pancreatic necrosis as sterile, and the phase of infection in which there is a decrease in more than twice of the absolute and relative number of T lymphocytes and T helper cells in 1.5 - immunoregulatory index. These violations demonstrate the need for immunotherapy, the choice of which is determined individually and depends on the nature and extent of the identified changes.

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The New Device and Method for the Treatment of Congenital Clubfoot in Infants

ABSTRACT

A new method for correction of congenital clubfoot without surgery in the infants, developed and used in the practice of Department of orthopedics and Traumatology, Pediatric Center RH №1 - NCM Yakutsk in 2012i is presented in the article.

The technique is based on the anatomical features of nerve pathways in children of the first months of life and constant multiplanar foot traction by new device with a functional effect on certain muscle groups. This method eliminates the main drawback of conservative treatment of congenital clubfoot such as possible necrosis of the skin and soft tissues due to the lack of control over soft tissue located under the circular plaster cast.

The proposed method and device can be widely used in outpatient service.

Keywords: clubfoot, a device for the treatment of clubfoot, multiplanar traction, foot correction, sleeve, leather orthosis, rubber tourniquet.

INTRODUCTION

Clubfoot is a complicated congenital complex foot deformity. It manifests itself in the following variations: plantar flexion of the foot in the ankle joint (equinus), the outer edge of the foot lowering (supination), adduction, torsion of leg bones of the foot and contracture of foot joints.

Congenital clubfoot is one of the most common birth defects in children. From one to three out of 1.000 live births have this deformity. Pathology can be seen on ultrasound at 3 months of pregnancy.

Treatment of congenital clubfoot is complex and the not completely solved problem of modern orthopedics. Conservative treatment of congenital clubfoot is known more than 2000 years, from the time of Hippocrates, his tactics and methods have passed through a long evolution. Modern principles of conservative treatment are based on studies of J.H. Kite (1932), Ignacio Ponseti (1950), V.A.Shturm (1956), V.Ya. Vilenskij (1973), M.V. Volkov (1983) and et al. It means a gradual, phased correction of clubfoot components, beginning from the deformation of the forefoot, and ending it on equinus with the fixation of the limb with gypsum casts. To fix the

limb in the treatment of congenital clubfoot it is recommended to use the traditional longuet - circular plaster bandage from the fingertips to the upper one-third of the thigh at the angled 90^0 in the knee joint of the shin (Fig. 1).

Fig. 1. Phased plastering

It should be noted that the use for the treatment of true congenital clubfoot of truncated plaster casts and bandages with recesses and voids in the foot is unacceptable (Fig. 2).

Fig. 2. Improper application of a plaster cast

At the present time in modern orthopedics, there are only two main methods of conservative treatment of infants with congenital clubfoot: the Ponseti method and phased plastering by Volkov.

The main disadvantage of these methods is possible necrosis of the skin and soft tissues, due to the lack of control over soft tissues located under the circular plaster cast. Using plaster

casts eliminates at the long term possibility of therapeutic exercises, massages, baths and physiotherapy as well as significantly worsens the tone and trophism of leg and foot muscles. These techniques were associated with a significant prolongation of treatment and pretty frequent complications from skin and soft tissues (Fig. 3). Caring for a child in a cast requires parents’ patience and a lot of attention.

a

b

Fig. 3. Complications of the skin and soft tissues

New method of treatment of congenital clubfoot in infants with the use of device for multiplanar, dynamic, permanent extension of the foot in position of correction.

The new device consists of a removable sleeve made of 3 mm thick Polivik (Fig. 4). The sleeve (2) fixes the thigh and shin by two Velcro (1) in flexion of the knee angle of 90^0; since at the bent knee joint calf muscle attachment points become closer and foot, freed from the pull of muscles, is easier to correct.

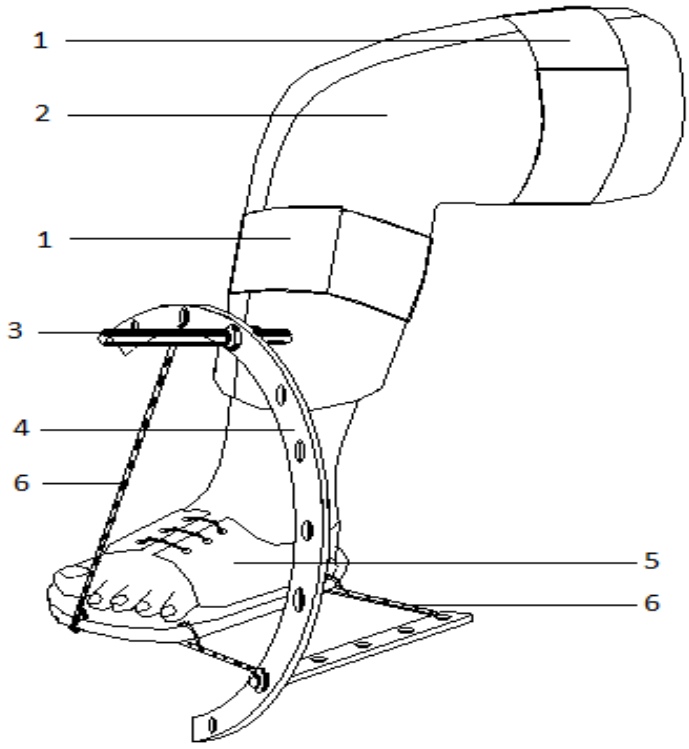

Fig. 4. The device for the treatment of congenital clubfoot

In the shin segment at the sleeve bottom part (3) rod is installed up to 8 - 10 cm length threaded on the entire length with screw - nut to "10" key. Into the rod semicircle with several holes with a diameter of 100 to 120 mm is mounted (4). The installed semicircle is adjustable in length, width and height depending on the degree of deformity.

We put on leather orthosis with a hard sole on feet (5). The brace must strictly match the size of the foot, as there should be free space inside.

Next, multiplanar traction with a rubber band (6) behind of the brace taking into account components of the foot deformities (equinus, adduction, supination, torsion) is done. The

diameter and strength of the tension of the rubber band are selected depending on the severity of the deformity and the child's age.

We have developed this method of correction of congenital clubfoot without surgery for the first time and it is used in practice in the Department of Orthopedics and Traumatology Pediatric Center RH №1 - NCM Yakutsk in 2012.

We obtained two patents of the Russian Federation to the device and method for the treatment of congenital clubfoot. The positive results of the formal examination are received.

Podiatrists are already not at risk to carry out phased corrections with plaster bandages from the first days of life due to severe complications such as necrosis of the skin and soft tissues, impaction by circular plaster bandage of the entire limb.

The new technique is based on the anatomical features of nerve pathways in children of the first months of life and the use of permanent multiplanar extension by new device, which is functionally acting on certain muscle groups.

Starting treatment of clubfoot by our method is recommended as soon as possible after birth. The earlier treatment is started, the better and faster the correction of a deformed foot.

After installing the device orthopedist with parents gradually make redressing towards deformity correction under the control of the muscular sense, stretching the soft tissues and ligaments of the foot. Passive corrective exercises are performed without pain and violence. This device is not only capable of holding the foot in position of obtained correction, but also constantly works to eliminate deformation. Periodically, parents can withdraw device by their own to control and care for the skin condition of the limb and receiving child warm baths and physiotherapy.

The above-described device is applied to the period from 1 to 2 months. As the baby grows up - the sleeve is changing, the strength and direction of traction are regulated.

Results of the study. We have treated 7 patients. Treatment was started at the age of 5 days to 2 weeks. There were no girls among patients. All the children were diagnosed with bilateral clubfoot, severe degree. The results of treatment in all cases were assessed as "excellent". Complete elimination of the deformation took 3 to 4 months (Fig. 5). After the

deformation eliminating the foot retention was conducted using another device in order to fix the foot.

a

Fig. 5. Patient K.: a - before treatment

b

b- after installation of multiplanar, dynamic, permanent extension of the foot during treatment;

c - side view;

d

e

d, e - after treatment

CONCLUSIONS:

1. The proposed in the article treatment of congenital clubfoot does not have the above mentioned disadvantages of the treatment of congenital clubfoot by phased gypsum plasters (by Volkov, Ponseti).

2. The use of this device and the method of treatment ensure the restoration of normal support ability of the limb to walking start of the child.

3. Treatment of congenital clubfoot by means of by our suggested method should be started from the first day of birth.

4. This device and method of treatment allows in a short time to correct foot deformities and get an excellent functional result without complications.

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Characteristics of the “Yagel” Preparation Antimicrobial Activity at the Edge Gingival Inflammation

ABSTRACT

The prevalence and intensity of parodontium diseases among children of school age and also teenagers of educational institutions of Yakutsk have been studied. Their high level of frequency in these examined groups where mostly chronic catarrhal gingivitis and rarer localised chronic periodontitis of mild case were defined. On the other hand, the unsatisfactory oral cavity hygiene was revealed in these groups of children that accordingly characterized insufficient level of sanitary culture of children and their parents. We’ve chosen preparation "Yagel" for the research. It is made of native vegetative raw materials of frond lichens extract of Cladina family. It has a high maintenance of usnicand other lichen derivative acids in clathrate shape with lichen β - oligosaccharides and possesses the antimicrobial action which hasn’t been studied earlier in clinical dentistry. Taking it into account we’vestudied antibiotic action of "Yagel" to conditional-pathogenic microflora incase of gingivitis. The microbiologicassessment of this medication has revealed certain features of minimum inhibiting concentration and minimum bactericidal concentration. So, the use of "Yagel" affected on quantitative and quality indicators of gram-positive, gram-negative microorganisms and also Candidainfection. The revealed inhibiting and bactericidal concentration of "Yagel" allowed to assert that it could promote reverse development of inflammatory process of gum tissues in the clinical plan and accordingly, reduce period of treatment and help treatment-and-prophylactic efficacy. In this connection this preparation could be applied in complex gingivitis therapy as alternative medication. Thus "Yagel" is produced in Yakutsk that defines its low cost price and availability for a wide range of the population. There is a necessity of further researches of clinical efficacy of "Yagel" in pathological processes of parodontium tissues of inflammatory-destructive character.

Keywords: gingivitis, periodontitis, hygiene index, sanitary culture, dental help, lichen extract, microorganisms, nutrient medium, antimicrobial action.

INTRODUCTION

Nowadays parodontium diseases are still topical problem of dentistry and medicine that is wide spread and unsolved problem of treatment and prevention [4, 7]. Thus one of principal causes of teeth loss are parodontium illnesses of inflammatory-destructive and exchange-

dystrophic character that is frequently in the form of chronic oral cavity infection promote development of the focus-caused diseases of parenchymatous organs [2, 8].

It is necessary to note that a bad oral cavity hygiene where initial signs of irritation and inflammation are hyperemia, hypostasis and bleeding [1] has the special role in the development of inflammatory process of marginal gum. Further there is a clump of microbes in the form of tooth plaques with admixed gram-positive and gram-negative bacteria, fungus, etc. [5]. The substantial growth of gram-negative rods happens in subgingival microflora at the long gingivitis treatment. Feature of anaerobes and saprophytic microorganisms in the development of inflammatory gum process are allocation of ectotoxins and endotoxins which damage cells, connective tissue formations and basic substance which, as a rule, are connected with the decrease of specific and nonspecific mechanisms of native and general organism reactivity [3, 6].

Unsolved problems of gingivitis prevention and treatment dictate the necessity of constant search of new effective remedies and methods. Thus studying and assessment of the antimicrobial action of "Yagel" to microflora in inflammatory diseases of parodontiumtissues has important theoretical and practical value in dentistry, especially when similar researches have not been made earlier.

Research objective: to define the minimum inhibiting and minimum bactericidal concentration to microorganisms in inflammatory process of marginal gum on the basis of themicrobiologic analysis of results of the antimicrobial action of "Yagel".

MATERIAL AND METHODS

The complex clinical-epidemiological research of 1853 schoolboys at the age from 7 till 17 years in schools №9, 30 and 31 of municipal district "city Yakutsk" have been done at the first stage. The special card, recommended byWHO (1997) was used for the assessment of dental status. The hygienic state of oral cavity was defined by index IGR-U (1964). Prevalence and severity of parodontium tissues diseases were defined by index PMA (Parma, 1960).

The second stage included the assessment of the antimicrobial action of "Yagel" in case of gingivitis. The research was made on the basis of studying-scientific microbiologicclinicallaboratory of medical institute of the North-eastern federal university named after M.K.Ammosov. Material from the inflammatory locus of sulcus gum in gingivitis has been received by means of a tampon which was placed intransport medium with coal.

Primary materialinoculation was carried out on anaerobic blood agar, "chocolate" agar and Saburo medium. Incubation of inoculation was carried out at 37^0C during 24-48 hours. Plates

with anaerobic gemagar were incubated in air-locked containers for gas generators atmosphere and anaerobic atmosphere «GENbagAnaer» (Bio-Merieux). Inoculation on "chocolate" agar were also placed in air-locked containers, but with gas generators for micro obligate aerobes «GENbagMicroaer» (Bio-Merieux).

Inoculation for calculation of microorganisms’quantity was made byMelnikova-Tsareva method: a tampon put inoculatedmaterial on the 1st sector of Petri dish with a nutrient medium. After that a bacteriological loop in diameter of 3 mm made 4 shaped inoculations from the 1st sector into the 2nd, then from the 2nd sector into the3rd, burning a loop after reinoculation of each sector. Quantity of bacteria in the material was defined by means of the special table. Identification of discharged cultures was carried out by morphological, tinctorial and biochemical properties. Smears were taken from evolved colonies and coloured by Gram ’s Method. Pure growth was accumulated on the conforming medium in suitable atmosphere, then identified on the microbiologic evaluator «Vitek-II Compact» with application of identification cards «Vitek 2 GN», «Vitek 2 GP», «Vitek NH», «Vitek 2 YST» and «Vitek 2 ANC» (Bio-Merieux).

The biological preparation "Yagel" has been developed in the Institute of biological problems of cryolite of the Siberian Branch of the Russian Academy of Science (Yakutsk) and has the certificate of the state registration in Federal Agency of control in sphere of consumers’rights protection of the Russian Federation №77.99.23.3. У.3522.5.08 on 5/4/2008; technical specifications 9219-002-36971185-08; sanitary-and-epidemiologic conclusion of Federal Agency of control in sphere of consumers’rights protection of the Russian Federation №77.99.03.003. Т.000928.05.08 on5/4/2008; the certificate of the state registration, customs union of Byelorussia, Republic Kazakhstan and the Russian Federation №RU.77.99.11.003. Е.051236.11.11 on 11/17/2011; the Russian Federation patent №2006100978 on 8/1/2007. It is made of frond lichens extract of Cladina family and contains: basic active materials – amino - β-oligosaccharides, formed from amino - β-polysaccharides processing by water in Carbon dioxide medium in the state of supercritical liquid. It contains also a complex of substances of antioxidant actions: orselic, lecronic, griphoric, xiatic acids and quinones; vitamin B_{12}, folic acid; natural antibiotics – usnic acids and their derivatives. Preparation of suspension on the basis of "Yagel" was made by method of refrigerator centrifuging on device "К-70Д" (Germany) at rotating speed of 3500 turns a minute and temperature 70+2ºС within 40-45 minutes.

RESULTS AND DISCUSSIONS

The analysis of the received data testifiedgingivitis prevalence in the examined groups of children where the tendency of increase of inflammatory processes frequencyin marginal gum was defined. So, 7-year-old children had index 41.23±0.63 % and in teenagers' group of 17 years old – 85.57±0.15 %. Thus the mean index of gingivitis prevalence among children living in the Central Yakutia was 63.08±0.18%. It is necessary to emphasize that intensity of inflammatory process byPMA index among children from 7 till 12 years old was characterized as mild case and from 13 till 17 years old – moderate severity level. Meanwhile the arithmetic-mean index is interpreted as a mean level of marginal gum inflammation in the examined groups of schoolchildren. But at the same time, 6.43±0.45 % had localized chronic periodontitis of mild severity level.

Gingivitis prevalence among children of school age and also unsolved problems of its treatment and prevention dictate necessity of constant search of effective methods and medications. We've researched for the first time antimicrobial action of "Yagel" in clinical stomatology. The received results of microbiologic research characterized some peculiarities of antimicrobial action of "Yagel" to parodentium pathogenic microflora in case of gingivitis (tab.1). At the beginning of the research the definition of the minimum inhibiting concentration of this preparation has been made. The minimum concentration of inhibiting effect on microorganisms, taking part in the development of inflammatory process of marginal gum has been revealed. So, concentration of "Yagel" which renders an inhibiting effect onCandidaalbicans10^3 and Candidadubliniensis$10^3$was 0.07 mg/ml whereas in group of Candidadubliniensis104 it was 2 times more and was 0.15 mg/ml. Meanwhile minimum inhibiting concentration of "Yagel" for Candida infection was at level of 0.31 mg/ml.

It is necessary to note, concentration of "Yagel" action for Neisseriasicca10^7 was equal to 0.6 mg/ml and Neisseriasicca10^6 – 0.31 mg/ml. Thus mean concentration, Neisseria growth-retarding was 0.5 mg/ml. But at the same time the minimum inhibiting concentration and mean index of this preparation was at the level of 0.07 mg/ml. at various levels of colony-forming units of streptococci (Streptococcusoralis10^5, Streptococcusmutans10^6)

Thecharacteristic of antibacterial action of "Yagel" to parodentium pathogenic microflora in case of gingivitis

Species of microorganisms	Minimum inhibiting concentration (mg/ml)	Minimum bactericidal concentration (mg/ml)
Candida albicans10^3	0.07	0.15
Candida dubliniensis10^3	0.07	0.15
Candida dubliniensis10^4	0.15	0.3
Mean concentration for Candida fungus	0.31	0.66
Neisseria sicca 10^7	0.6	1.2
Neisseria sicca 10^6	0.31	0.6
Mean concentration for Neisseria	0.5	1
Streptococcusoralis 10^5	0.07	0.15
Streptococcusmutans 10^6	0.07	0.15
Mean concentration for Streptococcus	0.07	0.15

It is necessary to notice that the revealed minimum inhibiting concentration of "Yagel" on conditional-pathogenic microflora in gingivitis promoted us to further researches on its minimum bactericidal concentration. Some features which characterize its variability have been defined. So, minimum bactericidal concentration was 0.15 mg/ml at various quantity indicators of Candidaalbicans10^3 and Candidadubliniensis10^3 whereas Candidadubliniensis10^4 concentration raised in 2 times and was 0.3 mg/ml.

The analysis and assessment also promoted definition of mean bactericidal concentration of "Yagel" for Candidainfection2 times more, than minimum inhibiting concentration and was 0.66 mg/ml.

It is necessary to notice that Neisseriasicca10^6 minimum bactericidal concentration to gram-negative microorganisms was rare faction of 0.6 mg/ml. But at the same time in quantitative values Neisseriasicca10^7index raised in 2 times and reached level of 1.2 mg/ml. Mean bactericidal concentration of "Yagel" for Neisseria was 1 mg/ml. To such gram-positive microorganisms Streptococcusoralis$10^5$and Streptococcusmutans10^6 Minimum bactericidal concentration was 0,15mg/ml. The similar index also was defined at mean concentration for Streptococcus.

CONCLUSION

Our first research of antimicrobial action of "Yagel" to gram-positive and gram-negative microflora and also to Candida infection in case of gingivitis has characterized its efficacy. In this connection it could be applied in clinical dentistry for the treatment-and-prophylactic help of pathological processes of parodontium tissues of inflammatory-destructive character as alternative medication. The high level of gingivitis among various age-groups of school children and the received results of the minimum inhibiting concentration and minimum bactericidal concentration of "Yagel" in their practical application will have positive effect in prevention and treatment of inflammatory processes of marginal gum.

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S.S. Pavlov, G.A. Palshin

Experience of Rivaroxaban Application for the Prevention of Thromboembolic Complications after Prosthetics of Large Joints

ABSTRACT

The article presents an analysis of the rivaraksoban application after replacement of large joints held in the Republican Hospital №2, Yakutsk from January 2012 to December 2013. Studies have shown that rivoraksoban intake reduces the number of complications and increases the level of commitment in these patients.

Keywords: prevention of thromboembolic complications, rivaraksoban.

INTRODUCTION

Venous thrombosis and pulmonary embolism are the most important medicine problem, which importance in the practice of doctors of various specialties cannot be overestimated [1, 3]. The problem of thromboembolic complications in traumatology is determined by considerable frequency of their occurrence, latent clinical course, the difficulty of treatment and high mortality. The relevance is due to the fact that one of the main areas of specialization - prosthetics is currently on the rise not only abroad, but also in our country. The percentage of total hip and knee joints to other operations conducted in the trauma hospitals is growing every year. With increasing numbers, the number of complications is growing, among of which a leading position are taking a thromboembolic complications. The frequency of symptomatic thromboembolic complications in total hip replacement on the background of thromboprophylaxis is, according to various estimates, from 1.3% to 3.4%, in total knee arthroplasty - from 1.7% to 2.8% [2]. Fatal thromboembolism frequency is ranging from 1% to 2.3%, nonfatal thrombosis develop in 7,9-15,2% cases [6]. When hip arthroplasty, median time to development of deep vein thrombosis is approximately 21 days prior to the development of pulmonary embolism - 34 days [7]. Numerous foreign clinical studies convincingly demonstrated that primary prevention of venous thromboembolism is highly effective and significantly reduces the incidence of deep vein thrombosis (DVT) and pulmonary embolism (PE) [5]. At the moment the use of rivaroxaban (Ksarelto) is sufficiently studied for the prevention of DVT and PE among patients with trauma and orthopedic profile

[4]. Interest to rivaroxaban (Ksarelto) dictated by a number of its advantages over the known forms of injectable anticoagulants:

- Release tablet form, which eliminates the need for additional injection, especially at home after discharge from the hospital;
- Ease of reception - one tablet (10 mg) once a day;
- The lack of need for ongoing monitoring of blood coagulation parameters;
- High safety and tolerability, which is extremely important in the prevention of thrombosis after discharge from hospital;
- Absence of clinical trials, evidence of impaired liver function medicinal origin, associated with the use of the drug.

MATERIAL AND METHOD OF RESEARCHES

From January 2012 to December 2013 in the orthopedic department of the Republican Hospital №2 of Yakutsk, 665 operations on knee and hip joints concerning degenerative-dystrophic diseases were performed.

Age of patients ranged from 17 to 86 years. Average age was 57.62 years. There were dominated patients with knee arthroplasty (n-349). In both groups operation was performed under subarachnoid anesthesia.

After surgery, all patients received combined therapy with analgesics, anti-bacterial drugs. Given bed rest during the day after the operation, as well as limiting the axial load (walking with crutches to three months), we paid special attention to the prevention of postoperative thromboembolic complications. For this purpose, all patients underwent anticoagulation therapy and it was recommended elastic bandaging of both legs or wearing compression underwear for 6 weeks after surgery.

Patients were divided into 2 groups: the first group consisted of 136 patients, for the prevention of thromboembolic complications it was used nodraparina calcium (fraxiparine) 3800ME / 0.4 ml or 5700 IU / 0.6 ml, if body weight was 70 kg it was used nodraparina calcium with subsequent transition to antagonist potassium (warfarin) 5 mg once a day to control coagulation (bridges prevention).

The second group included 289 patients treated with rivaroxaban (Ksarelto) orally at a dose of 10 mg once a day (from the date of surgery up to remove the sutures, i.e. within 11-12 days) without monitoring indicators of blood clotting.

On average, the patients were in the hospital 11 days after surgery, after which they are discharged to ambulatory treatment, with detailed recommendations mandatory prevention of thromboembolic complications 10 days after knee replacement and 20 days after hip replacement in each group with appropriate medication. Also it was recommended INR control when receiving indirect anticoagulants (warfarin).

Initial visual inspection of patients was carried out one month after the operation: check the state of patients, found out real terms of anticoagulant prophylaxis on an outpatient basis, whether to hold control of coagulation (INR) when taking an indirect anticoagulant.

Repeated examinations conducted after three months and six, twelve months from the execution of the control radiographs.

THE RESULT OF RESEARCHES

All patients had been warned about the risks and possible complications both during hospital stay and after discharge. Inspection was carried out in the trauma and orthopedic department in an outpatient surgery center of the Republican Hospital №2 or by telephone.

As a result, the control survey was conducted among 272 patients. According to the survey it was revealed that in the first group, prophylaxis of venous thromboembolism with recommended medicine continued 53 patients (60.22%), mostly women. From them, the control of coagulation was performed only 11 patients (12.5%). This is mainly due to the lack of laboratories in remote villages of the country, or the inability to go to the clinic for tests. The situation was different in the second group: from 184 patients prophylaxis of venous thromboembolism continued 167 patients, that amount 90.76%. The survey revealed that in the first group 3 patients replaced medicine to dabigatran etaksilat (pradaksa) 110 mg per day. 2 patients treated with indirect anticoagulants had epistaxis and 1 patient had clinical manifestations of venous thrombosis of the lower extremity. This patient Doppler has not been made. In the second group 2 patients were transferred to nadroparin calcium and 1 patient had manifestations of venous thrombosis (Doppler was not done). 3 patients had nosebleeds.

CONCLUSION

According to the results of our survey it was revealed that the standard prevention of thromboembolism after total hip replacement of large joints when using rivaroxaban revealed bleeding events. In general, the rate of complications associated with the use of rivaroxaban was 1.8%, significantly lower than the figures of the first group (5.6%). Is also an

important indicator of commitment to anticoagulation, which in the first group was 60.22%, in the second group 90.76%. This is because rivaroxaban is convenient to use and does not require the control of blood clotting.

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The Level of Availability of High-tech Medical care for Acquired Heart Defects in the RF and the FEFD. Trends over the Last 10 Years

ABSTRACT

The analysis of statistical data on morbidity and surgical treatment of acquired heart defects in Russia and the Far Eastern Federal District for the 2004-2013 to assess the dynamics and the potential development of this type of care was done. From 2004 to 2009 there was a trend decrease in the etiology of rheumatic valvular heart disease in the Far East and Russia, and from 2012 patients from this group for the first time accounted for less than half of the all operated with valvular heart disease. The growth rate of the number of prosthetics and renovations increased significantly in 10 years, as well as the number of simultaneous use of prosthetic valves and reconstruction, combined with coronary bypass surgery. The growth of operational activity in the Far East has not led to significant changes in its position among the regions of the Russian Federation. The revealed ambiguity of postoperative mortality indicators points to the contradictions in the principles of evaluation in various institutions of the country.

Keywords: acquired heart diseases, high-tech medical assistance, cardiovascular surgery, endovascular interventions.

INTRODUCTION

The prevalence of cardiovascular diseases requiring the use of surgical and endovascular treatments determines the need for this kind of assistance, well beyond the level of security of the population in our country. Meanwhile, the possibilities of cardiovascular surgery in morbidity and mortality reducing are proven an experience of the developed countries of Europe and the United States [2].

Valve surgery is a kind of high-tech medical care that dependson high cost, appropriate technical equipment and implantable materials. However, the profitability of cardiac surgery is very high and is 15: 1 for each ruble invested in the industry [5]. As one of the most significant trends in cardiac surgery, surgical treatment of acquired heart disease (AHD) requires a special approach to the organization and functioning of this service.

The world statistics are now prevalent degenerative valvular etiology. Decrease in rheumatic etiology among the others (infection, syphilitic, degenerative, ischemic, post-infarction and traumatic genesis) is particularly clearly seen on the background of a life expectancy increasing and the overall aging of the population in the developed countries of

Europe. However, in developing countries, according to the World Heart Federation (WHF), especially those with low and extremely low standard of living, rheumatic etiology of AHD is still leading: from 20 to 30 cases per 1,000 patients undergoing an annual medical examination with the use of diagnostic ultrasound and is the most common cause of valvular insufficiency in developing countries [7,8,9,10,11,13].

Thus, the main factors influencing the high prevalence of AHD varying etiology are socio-economic situation and changes in life expectancy [10].

The analysis of statistical information on AHD surgery could allow to evaluate their opportunities objectively and to plan activities for the improvement and development of medical service [2].

MATERIALS AND METHODS

The data of dynamics of morbidity and surgical treatment of AHD in the Russian Federation (RF) and the Far East Region (FER) for the period 2004-2013 years calculated on 100,000 adult population were analyzed. The calculated parameters were compared to the corresponding period. The growth rate of surgical activity for the population of the FER and in Russia as a whole and was detected and their year dynamics was estimated. A comparative analysis of the dynamics of postoperative mortality in surgical treatment of AHD among Russian hospitals over the past 10 years was performed. Statistical processing was performed using the statistical software package Microsoft Excel Statistic. Statistical significance was based on the results of reliability indices due to error of representativeness of intensive indicator and confidence intervals of the relative data of the universal set. Indicators were evaluated as valid at the level of statistical significance of $p < 0.001$ (CI: 99.7%).

RESULTS AND DISCUSSION

The Russian Ministry of Health annual reports (reporting form № 12) contained information about rheumatic valvular disease and the clinical examination of these patients up to 2009 (Table 1).

Table 1

Acquired valvular disease of rheumatic origin in Russia and the Far East Region in 2004-2009 (cases per 100 thousand population of corresponding age) [1, 3, 4]

Year	Adults				Children 15-17 years				Children up to 14 years			
	Total		Revealed for the first time		Total		Revealed for the first time		Total		Revealed for the first time	
	RF	FER	RF	FER	RF	FER	RF	FER	RF	FER	RF	FER
2004	185,2	140,1	7,7	8,4	29,3	29,1	5,8	8,7	11,4	11,3	2,0	3,3
2005	181,2	137,4	7,8	8,7	26,8	31,8	4,6	6,8	11,6	9,9	2,5	2,7
2006	174,8	135,3	8,7	6,6	25,9	20,6	4,3	2,2	12,6	9,6	2,6	3,3
2007	165,9	126,5	8,7	8,3	25,7	21,1	4,9	4,8	12,5	10,6	2,6	2,0
2008	160,8	121,0	8,3	8,1	27,8	23,5	4,8	5,4	11,1	9,2	2,0	1,6
2009	150,9	122,8	7,4	8,4	29,8	27,1	4,7	6,6	10,9	8,9	1,9	1,9

The tendency to reduce rheumatic etiology of AHD similar to the global one was observed in Russia from 2004 to 2009 (except total cases in adolescents 14-15 years). The trend of decreasing in the total number of cases and new cases was observed in all age groups in the FER.

In 2007-2009 the proportion of patients with valvular defects due to chronic rheumatic heart disease in adults was 80.8% among all patients, in children 15-17 years - 47.7%, in children up to 14 years - 46.5%. In 2009 this figure rose in all age groups respectively to 82.7%, 55.2%, 50.0%, and number of cases of rheumatic heart disease was 178623. Unfortunately, since 2010 any information on the incidence of AHD (including post-infarction ones) in Russia has been absent. And it is doubtful these data are totally missing in statistical reports of the Ministry of Health will be available in the near future. Only details are available to find in the health authorities of subjects of the RF (e.g. the waiting lists for the provision of high-tech medical care). But the algorithm for creating these registers must be fundamentally different from the existing clinical practice of the advisory opinions of specialists [2, 6]. At the moment an approximate idea of the prevalence of AHD is available to get based on the information of surgical activity and the number of hospitalized patientsonly. The need of the population in the surgical treatment of AHD in this case is difficult to assess.

Note that in 2012 patients with surgical correction of rheumatic valvular diseases first made less than half of all operated (47.2% compared with 52.9% in 2011 and 50.4% in 2010). In

view of the genesis of valvular disease in 2013 surgery of AHD in the ratio of "the total number of cases: degenerative defects: infective endocarditis" was 8.9: 3.5: 1.0 (16351: 6455: 1843). There were recorded 48.1% prosthetics and 46.7% reconstructions in 2013 (Table 2).

Table 2

Surgery of acquired heart disease in Russia (the number of patients)

Type of correction	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Prosthetic valve*	5642	6154	6881	7892	8818	9421	9357	10164	10157	10534
Incl. 2-3 prosthetic valves	873	1020	1179	1346	1322	1267	1453	1348	1310	1236
Reconstructions	1526	1616	1937	2382	2672	3009	3379	3920	3920	3038
Incl. combined valve surgery	1254	1317	1593	1856	2039	2205	2331	2676	2503	2360
Commissurotomy	310	238	246	175	132	103	155	66	43	70
Incl. operations on "open heart"	119	141	127	109	65	59	104	54	35	65
Total operations on 2-3 valves	2036	2199	2522	2968	3165	3356	3576	3847	3709	3692
Total cases combined with coronary bypass	441	652	721	1023	1238	1510	1550	1847	2001	2226
Total cases of infective endocarditis**	721	815	979	1090	1410	1470	1464	1585	1520	1407
Endovascular interventions	24	28	10	25	30	42	71	123	210	267
Total cases with AHD	6542	6990	7855	9077	9828	10637	10822	11812	11921	12624

*operation on valves by complications of myocardial infarction, aneurysms of the ascending aorta are not included; **the cases of infective endocarditis of prosthetics are included [1].

According to the received data for 10 years the number of patients operated for AHD increased almost two times (92.97%), both due to valve replacement - by 86.71%, and valve reconstruction - 2 times (by 99.08%). The frequency of the combined applications of valve replacement and reconstruction increased 3.2 times.The growth rate of the total number of annually patients operated for AHD in the country for 10 years was 92.97%,valve replacement - 86.71%, valve reconstruction - 99.08%.

The introduction of multi-component reconstruction allowed to carry out correction of the defects of two or three valves to minimize the use of replacement (when it is indicated) [2]. Such dynamics is due to certain advantages of the method and a lower cost. However, from 2010 the number of reconstruction decreased slightly by 10.09% and from 2011 the number of reconstruction combined with the correction of the other valves decreased by 11.81%. The increase in the simultaneous multiple valve replacements was observed from 2004 to 2010 (873 to 1453) with a gradual reduction of their number to 1,236 by the year 2013. The overall increase

in surgery for 10 years was 41.58%, and the proportion of patients with combined valve intervention (replacement + reconstruction) increased by 81.34%. At the same time in 2013 the operations for AHD 5 times more often combined with coronary bypass grafting (CABG) than in 2004: the proportion of such cases increased from 6.74% to 17.63% of the total number of operations forAHD. According to the register maps' data the proportion of patients with AHD who need CABG in Russia ranged from 4.69% in 2006 to 6.39% in 2013, an average for 10 years it was 5.66%. If we take into account that the minimum number of needing CABG is 500 per 1 million population, the minimum requirement for combined surgery (CABG + AHD correction) will be more than 28 per 1 million population. However, in 2013 compared to 2004 the application of the technique of commissurotomy (mainly in mitral position) decreased significantly 4.4 times, while the proportion of such patients decreased 8.5 times.

Total in 2013 in Russia there were conducted 11416 cases of AHD surgery (88 operations, including 74 replacements per 1 million population) and 12,288 manipulations on the different valves, the ratio "replacement / reconstruction" on average for the mitral valve (MV), aortic valve (AV) and tricuspid valve (TV) was 72.7: 27.3; for MV - 76.5: 23.5; AV - 98.5: 1.5; TV - 13.3: 86.7 [1].

The number of the substituted valves for 10 years increased by 83.39% (from 6478 to 11880) and 79.58% based on 100,000 adult population, includingincrease of biological prostheses 3.5 times, mainly due to the increase in implantations in mitral and aortic position: 1.44 times and 2.25 times (per 100,000 adults) respectively. The replacement of TV increased 2 timescompared with 2004. In 2004 the ratio of kinds of prostheses TV: AV: MV was 1: 13: 16.8 and changed by 2013 upward the AV implantations - 1: 14.7: 12.1. These surgeries (replacement + reconstruction) reflect the predominant involvement of the AV degenerative processes almost 1.5 times more in 2013 (3313 AV cases vs 2228 MV cases). In 2013 infective endocarditis of AV with impaired function occurred 1.15 times more often than MV (776 vs 677).

The growth of valve reconstruction (per 100,000 adult population) from 2007 by 72.97% has been recorded because of increasing of the MV reconstructions 2.27 times and the TVreconstructions- 1.5 times, when the number of the AV reconstructions was constant (0.8 per 100,000 adult population). As a result, the ratio of AV: MV: TV in the country in 2013 changed due to a significant increase in the number of patients with the reconstruction of TV and MV (1: 16.7: 29.2) compared to 2007 (1: 6, 4: 18.8). In 2013 the ratio "reconstruction / valve replacement" was: total - 1: 2.6; MV - 1: 3.3; AV - 1: 66.0; TV - 1: 15.9. At the same time the most

frequent combination of simultaneous reconstruction was MV and TV (16.7% - 637 cases) with the mortality of 1.88%.

The clinical effect of surgical treatment depends on the individual patient's comorbidities and surgery-related factors. Surgical risk and early postoperative mortality is mainly determined by the patient's age, reconstructive operations, the use of combined surgery with prolonged cardiopulmonary bypass time (CABG; reconstruction /replacement of TV, treatment or prevention of atrial fibrillation etc.) [12].

The postoperative mortality from AHD surgery in the country in 2013 was averaged 4.63%, in 2012 - 4.59%, in 2011 - 4.6%, in 2010 - 4.7%, in 2009 - 4.7%, in 2008 - 5.6%. Only in comparison with 2008 (5 years) decrease in the overall postoperative mortality from AHD surgery can be mentioned by 17.32%.

In 2013 the average level of the postoperative mortality in patients with prosthetic valve amounted to 4.61% and was higher than in 2012 - 4.45% (in 2011 - 5.0%, in 2010 - 4.7%, in 2009 - 4.9%). Over 4 years the mortality decreased by 5.92%. The mortality from surgery on two or three valves over 4 years increased by 31.77% (in 2013 - 8.17%, in 2012 - 8.24%, in 2011 - 8.01%, in 2010 -7, 7%, in 2009 - 6.2%), which cannot be explained by an increase in the number of operations (Table 2). The mortality in the most frequent combination of MV and AV replacement in 2013 was 8.1%, in 2012 - 7.3%. In addition, if the correction of defects with two and three valves in different ways shows the positive dynamics in mortality reductionfor five years (in 2013 - 5.28%, in 2012 - 5.69%, in 2011 - 5.9%, in 2010 – 6.1%, in 2009 - 6.3%), the average mortality in isolated reconstructive operations is rather contradictory: the lowest rate was observed in 2011 - 1.53% (in 2013 - 1.73%, in 2012 - 1.83%, in 2010 - 2.1%, in 2009 - 1.6%, in 2008 - 2.7%).

Last time the methods of endovascular correction of valve diseases are actively developing, indications for their useare expanding, that leads to the increasein the number of such interventions. Transluminal balloon valvuloplasty of the mitral and aortic valves and transcatheter implantation of AV are used very little in Russia, but interventions such as transcatheter implantation of MV and endovalvuloplasty of valve failure are not still used. In 2013 the register maps noted 267 cases of endovascular interventions. The availability of this treatment strategy (especially in high-risk surgery) is no doubt. The main obstacle to develop it is the high cost of the endoprostheses (it is 5-6 quotas of high-tech medical care).

The rate "valvuloplasty / transcatheter implantation" in 2013 was 108:159 (in 2012 - 81:129, in 2011 - 63:60 cases). The index of postoperative mortality in transcatheter implantation

from 2013 to 2012 decreased more than 4 times (in 2013 - 1.89%, in 2012 - 7.75%), whereas the same index in balloon valvuloplasty decreased by 25.10% (in 2013 - 1.85%, in 2012 - 2.47%). From 2011 the number of transcatheter implantations actually increased (2.65 times). We suppose that a reduction in mortality is a result of development inimplantdesign, as well as the participation of technical advisers (proctors) in most operations, which obviously reduces the risk of complications in the hospitals mastering this method of treatment.

Infectious genesis of corrected valves occurredfrom 11.0% (in 2004) to 14.3% cases(up to 2013) on the background of the growth of the number of operations almost 2 times (1.95) that in 2013 was 9.82 cases per 1 million population [2]. In 2013 the mortality rate from valve replacement on the background infectiousendocarditis was an average 6.0%, decreased over the 6 years 2.26 times (in 2012 - 6.4%, in 2011 - 8.4%, in 2010 - 12.7%, in 2009 - 11.3%, in 2008-13,6%). In 2013 the mortality from reconstruction was 1.0%, but the one from intervention of several valves was 9.0% (for comparison, in 2010 - 0% and 10.5% respectively).

On average, the surgical mortality rate on the background of degenerative valve over the past year decreased to 3.7% (in 2012 - 4.3%). In 2013 the mortality for replacement (4.47%) was at the level of 2009 (4.5%), in 2011 - 3.1%, 2010 - 4.3%; for reconstruction it decreased slightly to 3.4% (in 2011 -3.8%, in 2009 – 3.9%). Most significantly and gradually the mortality decreased in interventions on several valves (2.27 times for five years compared to 2009): in 2013 - 5.1%, in 2012 - 5.6%, in 2011 - 5.9%, in 2010 - 6.9%, in 2009 – 1.6 %.

In 2013 the average level of mortality from combined CABG and AHD correction increased to 6.46% (in 2012 - 6.1%, in 2011 - 5.0%), which can probably be explained by an increase in the mortality from CABG and simultaneous surgery of multiple valves by almost 50% (46.89%): in 2013 - 13.22%, in 2012 - 9.0%, in 2011 - 8.0%, in 2009 - 9.0%.

Thus, the analysis of the dynamics of postoperative mortality for AHD noticed ambiguity of the indicators that definitely points to the contradictions in the principles of calculating the data in different hospitals in the country.

Table 3 presents the surgical treatment and postoperative mortality in AHD in the Russian regions.

Table 3

Surgical treatment of acquired heart disease and postoperative mortality in Russia

Region	Total operations for AHD						Valve replacement (number of operations)						Mortality in 2013	
	2011		2012		2013		2011		2012		2013		FromtheRelevantcommittee**	From the Ministry of Health of Russia
	Abs.	Per 100,000 adults	Abs.	Per 100,000 adults	Abs.	Per 100,000 adults	Abs.	Per 100,000 adults	Abs.	Per 100,000 adults	Abs.	Per 100,000 adults		
Central	3437	10,61	3745	11,56	3521	10,86	5,7	6,23	3282	10,13	2943	9,08	5,7	6,23
North-Western	1304	11,42	1156	10,12	1812	15,87	4,4	4,82	885	7,75	1491	13,04	4,4	4,82
South	1325	11,70	1247	11,00	1323	11,67	2,2	2,89	1104	9,74	1131	9,98	2,2	2,89
North-Caucasian	26	0,38	47	0,68	31	0,45	0,0	0,0	24	0,35	24	0,34	0,0	0,0
Privolzsky	2296	9,43	2275	9,37	2400	9,88	3,5	4,24	1929	7,94	2012	8,32	3,5	4,24
Uralsky	1213	12,44	1109	11,37	1100	11,28	3,5	3,29	943	9,67	890	9,13	3,5	3,29
Siberian	1989	12,92	2039	13,27	2090	13,60	3,5	4,44	1758	11,40	1746	11,40	3,5	4,44
Far East	222	4,41	303	6,03	347	6,91	4,6	3,90	232	4,62	297	5,94	4,6	3,90
Total in Russia	**11812**	**10,13**	**11921**	**10,23**	**12624**	**10,83**	**3,43**	**3,73**	**10157**	**8,72**	**10534**	**9,05**	**3,43**	**3,73**

* The calculations are performed on the data directed to the Relevant committee for Cardiovascular Surgery by p <0.001 (CI: 99.7%). ** Data received by the Relevant committee from the regions of the Russian Federation.

The most number of clinics performing the implantation of heart valves was noted in the Central region (24), but 0.07 per 100,000adult population, that 2 timeslower than in the North-WesternRegion (0.15 per 100,000adult population).The average index for the country is 0.08.

The increase in the total number of operations for AHD for the past 3 years is noted in four regions (Table 3). The North-Western Region showed the highest rates (15.87 per 100,000 adult population with an increase by 38.97%) and the FER (with the highest increaseby 56.69%, but at the much smaller number of operations - 6.91 per 100,000 adult population). An average index in 2013 in the country was 10.83 per 100,000 adult population.

The most number of valve implantation for 3 years was conducted in the Siberian Region (11.53-11.4-11.4 per 100,000 adult population), but in 2013 the North-Western Region was the leader: 13.04 per 100,000 adult population. The lowest number of operations carried out in the North Caucasus Region (0.25-0.35).

Different data of mortality from a variety of sources (Table 3) point to the lack of a unified approach to its assessment in different hospitals of the country once again.

In the FER from 2004 to 2013 a total of 5 hospitals have surgical care for patients with AHD. The number of replacements in the region is more than two times higher than the number of reconstructions (Table 4). At the same time, the share of reconstructions increased from 22.03% in 2008 to 35.43% in 2013 (by 60.82%).

Table 4

Correction of AHD in the Far East Region in 2004-2013 (the number of patients)

Type of surgery/year		RKH 1, Khabarovsk	RKH 1, Vladivostok	CSC ASMA, Blagoveshchensk	RH №1 NMC, Yakutsk	FCCVS, Khabarovsk	Total
Replacements	2004	10	8	25	30		73
	2005	23	8	19	55		105
	2006	50	8	19	59		136
	2007	32	10	15	81		138
	2008	38	19	1	80		138
	2009	42	14	1	88	-	145
	2010	36	13	16	85	6	156
	2011	22	1	15	54	100	193
	2012	10	0	8	72	142	232
	2013	4	0	13	72	208	297
Reconstructions							
	2008	7	0	0	32		39
	2009	6	0	0	33	-	39
	2010	13	0	1	35	0	48
	2011	5	0	0	27	27	59
	2012	6	0	1	23	101	141
	2013	0	0	1	23	77	101

NOTE: RCH - Regional Clinical Hospital №1, RH №1 NMC - Republican Hospital №1 of the National Medical Center, FCCVS - Federal Center for Cardiovascular Surgery, CSC ASMA - Cardiac Surgery Center of the Amur State Medical Academy.

Over the past 3 years the share of FCCVS, Khabarovsk, is the most essential, and by 2013 it has shown a progressive increase in replacement (in 2011 - 51.81%, in 2012 - 61.21%, in 2013 - 70, 03%). The chain growth rate for the period of 2011-2012 was 20.21%; for the period of 2012-

2013 it was 28.02%. The base growth rate forthe period of 2011-2013 was 53.89%. From 2004 to 2010 the growth rate of valve replacements in the FERamounted to + 113.70%, and for 10 years the base growth rate was almost three times higher (+ 306.85%). The share of FCCVS in valve reconstruction in the FER pointed to the more indicative dynamic: in 2011 - 45.76%, in 2012 - 71.63%, in 2013 - 76.24%. The chain growth rate increased significantly for the period of 2011-2012 (+138.98%), which was likely to determine a certain decrease for the period of 2012-2013 (-28.37%); the base rate of growth over the past 3 years (2011-2013) has been+71.19%, over the past 6 years (since 2008) it has been +158.97%. However, if in surgery of AHD the Far East showed a definitely positive trend in the whole according to the number of operations per 100,000 adult population it is still ranks one of the lowest positions among the regions of the RF.

CONCLUSIONS and RECOMMENDATIONS

Rheumatic etiology of AHD is losing the leading position in Russia that reflects the trend of redistribution of etiological factors for developed countries.

By 2013 in the Russia not only the total number of operations for AHD has increased, but the share of reconstructive surgery compared with replacement and the proportion of patients with simultaneous myocardial revascularization and correction of AHD have increased too, as well as combined operations on several heart valves. That reflects not only the overall growth of surgical activities, but also increase the level and quality of surgical treatment for AHD. However, these figures are still lower than the estimated needs in such kind of surgery that dictates the necessities for its further development in Russia.

One of the significant problems in surgery for AHD is that the level of need for surgical correction in the regions and in the country as a whole is not defined. The information about epidemiology (incidence and etiology) of AHD and patients who are under medical observation are unfairly ignored in the annual reports of the Ministry of Health (it's completely absent since 2009). Indirect understanding of the need for certain types of prostheses (the aortic, mitral and tricuspid prostheses) can be obtained only in the evaluation of the number of replacements in this or that position.The same situation is observed with age-contingent and etiology of the pathological process in operated patients (biological or mechanical device). To use this information in assessing the actual need for AHD surgery is rather difficult.

Contradictory data of postoperative mortality from AHD correction notes to the absence of a common approach in the evaluation of mortality, which complicates its dynamic comparative analysis.

According to the high social significance of AHD the data on prevalence of AHD and dispensary observation of patients should be included in the annual statistical reports of the Ministry of Health of Russia.

The real need for surgical interventions cannot be extrapolated even from one region of the country to the other, and determining the need for specific types of surgery should be based on the local situation [6]: the individuality of population, climatic and geographical peculiarities, the level of development of preventive medicine in the regions, etc.

It is necessary to define a common approach to the assessment of postoperative mortality in cardiac surgery in different hospitals in Russia.

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Effective Contract as Method of Optimization and Growth of the Income of Workers of Health care

ABSTRACT

The purpose of creation of any system of compensation is the motivation of workers on improvement of quality of the made production or service, in a case with health care this service is medical care, besides is solved, and a problem of attraction of new qualified personnel. In this article we tried to consider one of methods of optimization and growth of workers of health care, namely the conclusion of the labor effective contract. For this purpose we offer not only new functions, but also criteria of overall performance of the medical personnel, thus are surely considered also social guarantees of the worker. As a result of this work the data which allowed speaking about recommendations about effective use of a manpower and formation of an average salary above than in region economy were obtained.

Keywords: salary, efficiency, effective contract, health care economy, health care, labor relations, function of a medical position, social package, guarantees, indicators.

INTRODUCTION

For this purpose under the Decree of the Russian President of May 7, 2012 No. 597 "About actions for realization of the state social policy" "road map" according to which a certain wage level has to be provided to the health worker who is competitive with other sectors of economy was developed. For the solution of this task "the effective contract" – the employment contract with the worker in whom his functions, work terms of payment, indicators and criteria of an assessment of efficiency of activity for purpose of the stimulating payments depending on results of work and quality of the rendered state (municipal) services, and also a measure of social support are concretized is entered.

Updating of qualification requirements for positions of employees of healthcare institutions is provided; formation of system of professional standards on the basis of skill levels, specialization and the generalized requirements to workers determined by the corresponding indicators.

Concrete indicators of criteria of an assessment of efficiency of activity of the doctor are defined by the head of healthcare institution with number, density, age and sexual structure of

the population, an incidence, geographical and other features and have to be accurately measurable.

Now rationing of work of doctors in health care de facto doesn't exist, only norms of duration of reception and settlement indicators (which aren't establishing the actual size of a salary) of norm of business hours (loading) on medical sites for a salary rate are centrally established. As in health care all restrictions of limit volumes of medical loading are set by subordinate regulations, the established norms of function of a medical position for a rate of a salary serve only for work rationing, and is conditional for payroll calculation.

The program of improvement of compensation focuses on increase of efficiency of activity of each worker, establishment, and branch. In health sector the concept of efficiency needs to be corrected. Efficiency as economic category, as a rule, is the relation of useful results to the spent resources that assumes achievement more a good result concerning expenses, i.e. also and achievement of former result with the smallest expenses. The last is inapplicable to evaluation of the work of health workers whom there is a problem of improvement of quality, productivity (efficiency) of work, including with possible increase in expenses, for example, of labor costs, material investments, etc. On the basis of it there is actual a question of studying of introduction of effective contracts and development of recommendations about its results.

Purpose: to offer the introduction mechanism of "the effective contract" on the basis of State budgetary institution of the Republic of Sakha (Yakutia) "Medical center of Yakutsk". (MCY)

Research methods: analytical, statistical, and economic.

RESULTS OF RESEARCH AND DISCUSSION

At the first stage carrying out the detailed analysis by definition of functions, tasks and amounts of works of each worker which are formalized in the relevant departmental regulations is necessary. On the basis of what in the subsequent there is an entering into employment contracts of workers of more detailed conditions of payment of the compensatory and stimulating extra charges and surcharges. "The effective contract" counterbalances a reward with results of activity of a certain worker. Its payment isn't guaranteed, it can vary and essentially to differ for various workers. Its size directly depends on results of an assessment of individual work.

Table 1

Planning of fund of the district doctor

№ sector	Population Quantity	Number of points	Plan of the sum of expenses, 1.000 rubles
1	1236	449	258
2	1152	388	284
3	1296	416	270
……	……	….	
27	1238	446	299
Total	**68 236**	**11 135**	**3 297**

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In MCY the labor relations between the employer and workers based are accepted: on the volume of the state task and target indicators of overall performance (it is approved as the founder); on system of rationing of work of employees of institution (it is approved as standard industry acts); on system of the compensation considering distinctions in complexity of the performed work (it is approved as the employer); on quantity and quality of the spent work (it is approved as the employer).

As the second stage it is necessary to plan financial means for a forecast period. Each of points of the movement of financial means has to be counted on many indicators: For example, a hospital – on a profile of beds, number of hospitalization, treatment cost, expenses on a profile of beds, duration and a turn of beds, etc.; policlinic – on a visit profile (quantity, cost, etc.); paraclinic (laboratory, functional and radiodiagnosis, physiotreatment) – by types of medical services (quantity, cost).

For a bright example we will give calculation on the doctor of a therapeutic sector.

Total amount of expenses on a sector without division into components is planned (a hospital, paraclinic, "narrow" experts). At per capita financing when the district doctor is an asset holder, approximate calculation can be presented on the example of table 1 where one point is equal to number of visits. Discrepancy in points as on therapeutic sites the number of the population in various age groups is various is visible.

The number of medical services in certain age groups exceeds average figures in comparison with other age groups, for example: in group till 60 years – by 4,9 times; in group till 45 years – by 2,1 times.

The number of medical services in certain age groups exceeds average figures in comparison with other age groups, for example: in group till 60 years – by 4,9 times; in group till 45 years – by 2,1 times. Patients of the senior age groups are more often than others need preventive visits and to a thicket are ill. At a planning stage for the purpose of alignment of financing terms in these age groups conditional and estimated sizes were applied (UOV = 4,9 and 2,1). The local therapists having more patients on a district are more senior than 65 years; receive under financing calculation bigger number of points.

The 3rd Stage is the accounting of expenses. Primary documents of the operational accounting of expenses on sites are: out-patient card; statistical coupon; leaf of the accounting of medical services. All data on financial expenses are collected and processed in information and analytical department.

The 4th Stage is the analysis of expenses. The analysis of expenses is carried out on 3 main units: own activity; "narrow" experts; paraclinic, emergency medical service. The approximate structure of expenses on a therapeutic site is presented in table 2.

Table 2

Structure of expenses of a therapeutic sector No. 18

Kind of activity	Number of services	Expenses, 1.000 rubles	% от общих затрат
Local therapist	6210	168	54
"Narrow" experts	1661	32	10
Paraclinic	4580	40	13
Emergency medical service	43	71	23
Total	**12494**	**311**	**100**

Note. Number of adults on a site - 2357; the general incidence – 1957.0 on 1000; settlement expenses - 373 100 rub, additional points 4,9. On each site the actual expenses are compared to the planned means on the example of table 3.

Table 3

Accounting and actual expenses on sites in a quarter

№	Expenses, thousand rubles		
	Accounting	Actual	Deviation
1……	84,4	86,7	-2,3
27	98,8	81,2	+17,6
Total 1	**1113,0**	**1000,0**	**+111,3**

For local therapists the information and analytical department prepares output tables in which the movement of flows of patients together with financial means on all stages of delivery of health care is detailed. The district doctor has to have opportunity to analyze the actions and in due time to take measures for elimination of defects.

The 5th Stage is examination of quality of medical care, calculation of penalties. Penalties are applied only to an additional salary ("a bonus bonus"). The approximate list of penalties is given below:

1) mortality on a site is higher than the general, on establishment – deprivation bonus from 50 to 100%;

2) untimely or unreasonable direction: on hospitalization – from 10 to 30%; on consultation to the "narrow" expert – to 20%;

3) insufficient inspection in out-patient and polyclinic conditions – to 20%;

4) untimely or incomplete inspection on dispensary supervision – to 20%;

5) excessparaclinical actions – to 20%;

6) violation of labor discipline – to 30%;

7) reasonable complaints of the population – from 20 to 70%;

8) violation of volumes of preventive actions – to 30%;

9) violation of the sanitary and epidemiologic mode – to 30%.

During the pilot project, especially in its initial stage, penalties in relation to certain local therapists made from 10 to 40% of bonus fund.

The 6th Stage is change of methodological approaches in MCY to formation of fund of compensation:

a) calculation of volume of medical services in each profile, taking into account number of the medical services entering the standard is carried out:

Bedding set (i) × Sm (ij) = to Ohm (ij), where:

Bedding set (i) – planned number of patients according to the state task on an i-profile, Sm (ij) – number of the j-medical services entering the standard of delivery of health care on an i-profile, Ohm (ij) – the volume of j-medical services in an i-profile.

b) The total amount of the medical services chosen on each profile of the state task is calculated:

To ohm (ij) + …. + to Ohm (ij) = to Ohm (j), where:

To ohm (j) – the volume of j-medical services of the state task.

c) The fund of the working hours which is required on performance of volume on each medical service is counted:

To ohm (j) × Nvou (j) = Frv (j), where:

To ohm (j) – the volume of j-medical services of the state task, Nvou (j) – norm of time for rendering j-medical service (is defined by a settlement way, individually for each medical organization with the applied technologies), Frv (j) – fund of working hours on performance of volume of j-medical service.

d) The general fund of the working hours necessary for performance of the state task is counted:

Фрв (j) + … + Frv (j) = Frv, where:

Фрв (j) – fund of working hours on performance of volume of j-medical service,

Фрв – fund of working hours on performance of the state task.

e) Man-hour cost on region economy is calculated:

Szpr × 12/Frvg = Schch, where:

Szpr – an average salary in the region, Frvg – fund of working hours annual, is determined according to a production calendar for the corresponding year, Schch – man-hour cost by region economy.

e) The fund of compensation for the concrete medical organization is counted:

Фрв × Schch = FWH*, where:

Фрв – fund of working hours on performance of the state task, Schch – the average cost of a man-hour on economy in the region, the FWH – fund of compensation of establishment.

* Note: at calculation of FWHOS by 2018 it is necessary to increase the received result on 2.

Methodological approaches to formation of a salary of the personnel:

a) Payroll calculation of the personnel:

Odes × Frvi + Vskh + Vsp = ZPP, where:

Odes – a salary official, Frvi – fund of working hours individual, necessary for implementation of obligations of the worker according to the contract in a month, Vskh – payments of the stimulating character, Vsp – payments for a social package. At the conclusion of the contract the fund of working hours depends on the list of services which will be carried out by the specific employee. At this approach carrying out individual rationing of work on concrete specialties taking into account the medical and not medical technologies applied in the organization is necessary.

b) Calculation of an official salary:

Обчч (1-3) × Kdo = Odes, where:

Who – coefficient for additional education ("Khan"), with a minimum of value of coefficient 1, further for each additional education – 0,2. Kdo = (1,0 + 0, 2+ …. + 0,2),

Обчч – the salary basic for a man-hour, is determined by categories of the personnel as follows: Obchch1 – 1 category (not demanding secondary or higher vocational education), Obchch2 – the 2nd category (demanding secondary vocational education), Obchch3 – the 3rd category (demanding the higher vocational education).

Obchch1 = not less minimum wage rate × 12/Frvg, Obchch2 = not less than 0,25Szpr × 12/Frvg Obchch3 = not less than 0,5 Szpr × 12/Frvg where the minimum wage rate – the minimum wage, Szpr – the average salary in the region determined by Rosstat annually by the previous period, Frvg – the fund of working hours annual, is defined according to a production calendar for the corresponding year.

Methodological approaches to payments of the stimulating character (Vskh).

Definition of the list and the amount of the stimulating payments to the personnel will be individually carried out on each office, division. Detailed studying of functional duties has to become a basis for payments.

Methodological approaches to payments to the personnel for "a flexible social package". At the offered approach "the flexible social package" has to become the additional tool for fixing of the personnel in the medical organization. Includes obligatory compensation payments and various social measures of motivation of workers (tab. 4).

Table 4

Formation of payments for "a flexible social package"

Name of payments	Basis of payments
Compensation for nightwork	Percent from Job Salary (Art. 154 LC RF)
Payments to the workers occupied at works with harmful (dangerous) working conditions	payment in the sum is possible (Art. 147 LC RF)
Compensation in off days and holidays	Percent from Job Salary (Art. 153 LC RF)
Payments for work in the conditions deviating from normal	Percent from Job Salary (Art. 152 LC RF)
Payments for work in districts with special climatic conditions	payment in the sum is possible
Payment of time of disability	Proceeding from an average salary
Payment of a break on rest and a lunch	Proceeding from an average salary
Insurance upon accidents	Payment in the sum
Payments for the "scarce" specialties	Payment in the sum
Granting the free parking	payment in the sum is possible
The help in education increase, professional preparation, retraining	payment in the sum is possible
Journey payment (compensation of gasoline of an individual transport)	payment in the sum is possible
Granting in use to workers of objects of rest and entertainments	payment in the sum is possible

Methodological approaches to distribution of FWHOS in the medical organization.

The FWH is distributed on categories of the personnel as follows: not less than 60% – on the PHOT of the main personnel (doctors and SMP), no more than 25% – on the FWH of support

personnel (MMP and the other personnel), no more than 15% – on AUP FWH (the chief physician, deputies, accounts department, economists).

Payments for quality of the performed works for employees of institution are defined in proportion to a ratio of the sizes of monthly (quarter) fund of compensation of each structural division of establishment to the general wages fund which developed for the reporting period, in general the individual coefficients (a share from FWHOS) structural divisions which determine further the maximum volume of the stimulating payments for each structural division are determined by establishment.

For determination of the sum of payments of the stimulating character for quality of the performed works in general on establishment (except for the head of establishment) it is necessary to subtract from a monthly (quarter) wages fund of the reporting period the sums of basic salaries, the sums of payments of compensation character, payments with application of the raising coefficients and payments with application of coefficients of qualification, an experience, academic degree and honorary title, and also to subtract payments of the stimulating character of the head of establishment (to 2 percent of allocations from a wages fund).

The coefficients (share) of structural divisions estimated in the settlement way and by that the maximum volumes of the stimulating payments for each structural division are defined are applied to the received sum of payments of the stimulating character for quality of the performed works. Further the sums of the stimulating payments of structural divisions share on the greatest possible performance of number of points (the planned – 100%) and by that the planned cost of 1 point, individual for each structural division is defined. For determination of the real (actual) sum of payments of the stimulating character it is necessary to increase the planned cost of 1 point by the actual number of the points executed for the reporting period.

At non-performance of criteria for quality of the performed works money is subject to redistribution in reserve fund. Following the results of realization of stages of administrative mechanisms "the effective contract" for each worker is developed for MTsYa standard.

The main registration medical documents at an assessment of overall performance of the therapist of the district police officer are: medical record of the outpatient (registration form No. 025/u-04); the passport of a medical site (a registration form No. 030/u - I rubbed); the sheet of the accounting of medical visits in out-patient and polyclinic establishments, at home (a registration form No. 039/u-02); control card of dispensary supervision (registration form No. 030/u-04); coupon of the ambulatory patient (registration form No. 025-12/u); the card of the

citizen having the right to a set of social services according to the accounting of holiday of medicines (a registration form No. 030-L/u).

The following criteria of activity of the therapist of the district police officer are used: stabilization or decrease in level of hospitalization of the attached population, decrease in frequency of calls of an emergency medical service to the attached population;

increase in number of visits of the attached population with the preventive purpose; completeness of coverage by preventive inoculations of the attached population: against diphtheria – not less than 90% in each age group; against hepatitis B – not less than 90% of persons aged till 35 years; against a rubella – not less than 90% of women aged till 25 years; implementation of the plan of preventive inoculations against flu; stabilization or decrease in an indicator of mortality of the population at home: at cardiovascular diseases, at tuberculosis, at diabetes; decrease in number of the persons who died at home of blood circulatory system diseases aged till 60 years and not observed within the last year lives; stabilization of an incidence of diseases of social character (tuberculosis, arterial hypertension, diabetes, oncological diseases), completeness of coverage of actions for dynamic medical supervision over a state of health of separate categories of the citizens having the right to a set of social services, including provision of medicines, sanatorium and recovery treatment; validity of prescription of medicines and observance of an extract of recipes to the patients including having the right to a set of social services; number of medical examinations of the subject age groups.

Thus, the offered advanced system of work incentives promotes increase of efficiency of activity due to coherence of the general financial and economic results of their activity and individual quantitative and qualitative results of work of each worker. The size of the funds allocated for "the effective contract" is in full competence of the medical organization, is fixed in constituent documents, in the Provision on awarding.

Salary increase, including with application of additional incentive measures of workers due to existence at the employer of the flexible social package (SP) I involved new qualified specialists, and also allowed to hold skilled shots from change of a place of work. The structure of the joint venture is rather volume and isn't limited to the list which is given above. The employer establishes a concrete set of the privileges and compensations provided to workers itself depending on specifics of the activity and financial opportunities. Establish the joint venture the employer can as in labor (the Art. of Art. 9, 40, 41, 56 of the Labor Code of the Russian Federation), and in "the effective contract" (Art. 5 of the Labor Code of the Russian Federation).

Perhaps, this standard contract can provide the right of the worker to refuse some privileges that to it increased compensation by this sum.

Following the results of the carried-out work, having analysed the received information, we created a scale of indicators of an assessment of activity of "the effective contract" (tab. 5)

Table 5

Indicators of an assessment of activity of the effective contract

Indices	Indicators	Target value, %
Financial security	% from GNP	7, but not less than 5
Expansion of non-budgetary sources of financing	Share in the general consolidated budget	30
Salary increase	In comparison from an average economic salary on the region	200
Staffing	Completeness shots Ratio doctor / nurse	85 1/4
Satisfaction of the population with medical services	% of affirmative answers	on 6
Knowledge of the population of a place, look, terms of providing the medical services	Existence of Information on the site, in mass media, registry, a reception	100

Thus, the effective contract is aimed at providing interest of health workers in the end results of work. Introduction of this system of compensation will allow not only to keep, but also to increase the former level of a salary of health workers.

The positive moment of the effective contract is orientation of compensation depending on quality of the provided services, and also from a personal contribution of each employee regardless of length of service. For the first time for many years compensation in health care is attached to results of activity of the worker. Introduction of the effective contract is directed, first of all, on the new qualitative level of payment for work (by results). Besides, at the effective contract each head is interested in salary increase of the personnel as in this case also its salary

will grow. Official salaries of heads are established in the multiple relation to an average salary of employees of institution.

Thus, direct link between an average salary of the personnel and a salary of the head stimulates the last to increase of level of compensation of workers by minimization of number of the personnel. Establishments were granted the right to determine the sizes and conditions of payments of the stimulating character by collective agreements, agreements, local regulations. Payments of the stimulating character to the medical personnel for quality of the performed works are established according to criteria of quality of medical services. Criteria of quality are approved by the head of establishment taking into account opinion of a representative body of workers for concrete structural division. The amount of monthly earnings is determined in many respects by the stimulating extra charges which are based on a skill level and extent of performance or excess of standards taking into account the personified functions. Criteria and the principles of distribution of the stimulating fund are developed by establishment therefore this process has to be objective and open. The indicators developed by each establishment depending on objectives and order of stimulation have to be clear to each worker at an assessment of results of his work. The worker has to know, for as when the stimulating extra charges are paid to him, and also, how many he will receive for efficiency of the work. That is the clear algorithm of calculation of the stimulating payments has to work: on an entrance – work indicators which the employee can really influence, at the exit – the amount of its stimulating payment.

The adoption of the stimulating payments in establishment has to happen with participation and coordination with trade-union committee and labor collective. This process shouldn't be formalized. Consultations, negotiations, other processes of discussion of new system of compensation can be effective only at collective approach to it of the head, worker and public body. The main objectives which the new form of compensation has to solve: to raise the real income of employees of institutions, financially to interest the worker more effectively to work. According to the monitoring which is carried out in health care in 2013, the increase in an average salary is observed on all categories of workers: at doctors and pharmacists for 14,7%; at the medical and pharmaceutical personnel of the first level for 10,8%; at the average medical and pharmaceutical personnel for 13,8%; at working all-branch positions for 15,2%; experts and employees on all-branch positions for 10,7%. At decrease in total number of employees of institution the fund of compensation in comparison with 2012 grew by 17,1% and made more

than 36,5 million rubles, thus the fund of compensation of heads of establishment decreased by 1,1%.

Authors offered uniform recommendations about establishment and development of indicators and criteria of overall performance taking into account the following principles:

a) objectivity – amount of remuneration of the worker has to be defined on the basis of an objective assessment of results of his work;

b) predictability – the worker has to know, what reward he will earn depending on results of the work;

c) adequacy – remuneration has to be adequate to a contribution of each worker to result of activity of establishment, its experience and a skill level;

d) timeliness – remuneration has to follow achievement of result;

e) justice – rules of definition of remuneration have to be clear to each worker;

e) transparency – making decisions on payments and their sizes taking into account opinion of a representative body of workers.

Thus, for improvement of the operating system of compensation we suggest to develop methodical recommendations about establishment of criteria of an assessment of activity of employees of healthcare institutions for groups of positions: the health workers giving stationary help surgical, therapeutic, pediatric and other profiles, the health workers giving out-patient and polyclinic help, health workers of paraclinical services, workers of all-branch positions, pharmaceutical workers, etc.

CONCLUSIONS

We consider that introduction of this system of compensation will allow not only to keep, but also to increase the former level of a salary of health workers. It should be noted that at all appeal of "the effective contract" as way of motivated work, also a number of essential shortcomings and defects is defined:

1. The quantity of types of works and services in medicine is so great that for full their coverage it is necessary to form, establish, update and supplement with rationing tens and even hundreds of thousands norms and standards. Costs of establishment and maintenance of similar regulatory base are so great that they become commensurable with costs of carrying out types of rated works and services.

2. Not all types of medical works and services give in to a partition on uniform, same units for which norms and standards can be established.

3. Within service units same by the form on which standard standards of labor costs for branch of health care or even on separate medical institution are established, the considerable dispersion of labor costs which is objectively caused by specifics of diseases and the contingent of the served patients, level of ensuring processes of treatment can be observed.

4. There are methodical difficulties in achievement of compliance between desire of the employer and readiness of the worker for new forms of calculation of a salary.

5. Lack of stability on monthly obtaining identical level of a salary, and, as a result, difficulties of planning of the family budget of the worker.

6. Introduction of "the effective contract" involves the certain expenses caused by need of regular estimation of achievement of indicators of quality, productivity and overall performance of each worker. These expenses can be minimized by introduction of an automatic assessment by means of use of electronic technologies with the appropriate computer program.

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M. V. Lyadova

Analysis of medical-legal questions assessing the quality of emergency aid to for the injured with the musculoskeletal system lesion

ABSTRACT

Providing quality of medical care is the main objective of the health system. While in Russia the priority interests of the patient are fixed at the legislative level. In 2004 the World Health Assembly defined the main task of modern medicine to radically increase the safety and quality of treatment. Criteria of safe medical care were defined. The article attempts to determine the medical and expert criteria for qualifying an emergency trauma care on the basis of the analysis of a large number of medical records, the sociological poll, both of doctors and patients, assessment of regulatory initiative on the legal legislative documents. We defined algorithm for estimating the quality of medical care for the injured with the musculoskeletal system lesion.

Keywords: quality of health care, emergency trauma care, quality assessment, treatment defects.

INTRODUCTION

Ensuring quality of care is the main goal of the health system. The Federal Law №323 "On the basis of the health of citizens in the Russian Federation" revealed the inner meaning of the terms: health, health protection, medical care, the procedure for medical care, the standard of care and quality of care. Also, the above Act legalized the priority interests of the patient. In 2004 the World Health Assembly claimed to identify the main problem of modern medicine - to radically increase the safety and quality of care. The criteria of the safety of medical care were defined, the main of which is the adequate assessment of the balance of risks and potential benefits of intervention. This task was set not by accident, because according to experts on patient safety at Harvard medical errors each year in 13.6% of cases lead to the death of patients, and 2.6% to disability [6]. In Russia, due to inadequate provision of emergency medical care in the hospital each year the number of cases of harm to life and health of citizens is about 70 thousand [1]. Injury is also clearly distinguished and regulated at the legislative level concept. And it can be applied to light, medium and severe damage to the patient's health, which established rules for determining the severity of harm to human health in Minzdavsotsrazvitiya Order [5]. Depending on the degree of violation of the quality of the health care for the health

worker can occur both administrative and legal responsibility that given the gravity of unlawful actions of medical personnel, if it is proven, is qualified under the relevant articles of the Criminal and Civil Code. To determine the degree of medical officer guilt at the legislative level, the notion of MC quality examination "revealing violations in the provision of MC, including the assessment of the correctness of the choice of medical technology, the degree of achievement of the planned results and the establishment of cause-effect relationships identified defects in the delivery of health care" is implemented. Activity of doctor traumatologist on emergency trauma care involves significant legal risks, as emergency medicine - is an independent specialized type of care. Emergency trauma patients are characterized by transience of pathological conditions, especially in the acute period of traumatic disease that allocates emergency trauma care in a special section and requires special approaches to the organization, the nature and manner of use of health care resources [3]. Transformations in health care, including issues of standardization of the compulsory medical insurance, an increase of citizens on forensics bodily harm in cases of damage caused by illegal actions, steady growth in litigation on the quality of care makes it relevant to development evidence-based recommendations aimed at improving the evidence of expert evaluation criteria of quality emergency care to victims with injuries of the musculoskeletal system.

We performed a retrospective analysis of medical records to provide emergency care to patients with trauma injuries: sheets accompanying the ambulance, the form №114 / 350 from the victims brought to the N.I.Pirogov Clinical Hospital №1 in the period from September 2012 to August 2013; 180 inpatient medical records, a form №033 / y; 50 minutes of meetings of subcommittees of deaths suffered trauma Profile for 2013-2014; Reports of heads of departments of trauma the state hospital No 1 named by Pirogov N.I. the last 5 years; 50 commission MEA on materials of criminal and civil cases involving compensation for damage to health by providing medical assistance to the victims with injuries of the musculoskeletal system. Studied 237 "prisoners" forensic examinations at the Bureau of Forensic Medicine of the Department of Health in Moscow for victims, which were caused by non-dangerous life-threatening injuries, but entailed a lasting health disorder more than 21 days, and were regarded as damage entailing injury of moderate severity and where he participated as an expert trauma surgeon for the period from September 2011 to December 2013. To study the legal awareness of the doctors polled 80 experts trauma doctors to provide emergency medical care in Moscow. The age of respondents - from 27 to 62 years work experience - from 2 to 40 years, various

medical categories. The statistical study was carried out using the developed for this purpose questionnaire containing 38 multiple-choice questions. Among the questions of the questionnaire were the following: the existence of conflicts in the practice of doctors to provide emergency care, their causes and ways of solving them; knowledge of physicians regulations governing their professional activities; there is a requirement in their study on the protection of doctors from lawsuits from patients; the correctness of medical records. To study the degree of satisfaction of patients is currently provided emergency assistance and determine the approximate line of conduct in the event of conflict authors randomly surveyed 100 hospital patients who have received emergency trauma care. The patients - aged 18 to 82 years, of different social status. The survey was conducted by questionnaire from 25 questions.

Assessment of the quality of medical care to victims of trauma with injuries, carried out by the developed algorithm, which included several stages: information and analytical stage - evaluation and correctness of medical documentation; assessment of quality performance of diagnostic and treatment activities in accordance with the procedures and standards of emergency care at the stages of diagnosis and treatment; detection of defects rendering health care on stages of its delivery; assessment of the impact of objective factors on the process and outcome of care. Defects of medical documentation in victims of trauma Profile are important in assessing the severity of the damage to health by unlawful injury. Thus, in 40.9% of cases are not given information about the presence or absence of external manifestations of trauma in the form of abrasions, bruises, wounds. If they have been recorded, they are not given enough full morphological characteristics (color, size, contours, the state of the surrounding and adjacent soft tissues, crust color, etc.). In particular, 17.0% of bruises from a medical point of view are described unsatisfactory and replaces the concept of not carrying sufficient information; in 8.0% of cases, discrepancies in the interpretation of the presence of lesions in the form of bruises and hematoma: the primary medical examination indicated hematoma, and at repeated - a bruise, despite the fact that there is a common notion of these entities and their contents. Every third victim is no indication on the nature of the damage, and exhibited clinical diagnosis does not correspond to the complaints of the patient and according to clinical symptoms.

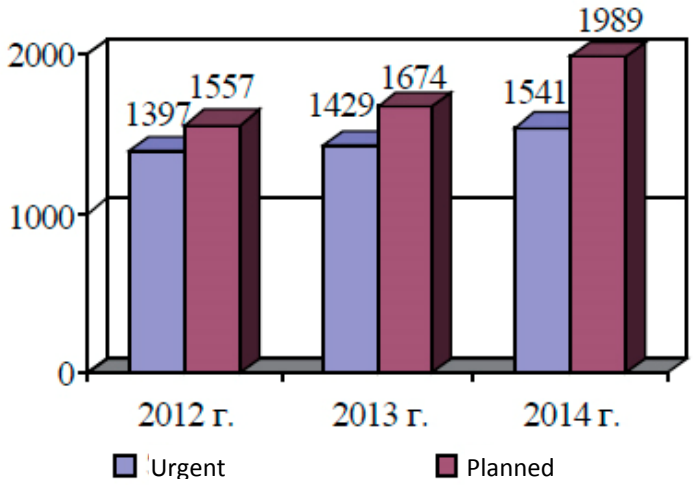

Fig. 1. The dynamics of the operational activity reports from Department Heads

Emergency trauma care becomes more specialized, technologically equipped and expensive, there is increase in surgical activity, and there is a rigorous growth in the number of emergency surgical procedures by an average of 25.0% per year (Fig. 1). According to the study commission examinations in criminal and civil cases the number of claims to doctors traumatologists is about 6.6% of the total number of examinations. The proportion of defects of medical care during hospital stay was 90.0%, pre-hospital, respectively 10.0%. Most often by patients to make a complaint to the provision of emergency trauma was 64.0% of health care. More than 90.0% of hospital mortality in victims of trauma related to the profile of the urgency of the hospitalization. According to the results of expert assessment of the causes of mortality of patients with trauma profile, delivered to the hospital for emergency indications are (data of protocols keels and drinking, as well as commissions of expertise): Late uptake in the hospital (not the principles of the "golden hour"), the patient has severe concomitant pathology, incurable patients, errors of doctors hospitals (unreasonable choice of treatment, improper assignment of medical treatment). The main criterion for the quality of emergency trauma patients is to achieve the best result of treatment. Fixed sets the standard in the diagnosis of subsequent treatment. In the study, we found that with respect to standards of care for patients the trauma profile, standardization of treatment is not perfect. There are certain limitations to standardize the diagnostic and treatment process. Medical science does not stand still, so a few years it seemed yesterday adopted the standards are out of date (for example, in the treatment of proximal femur fractures). Standards are constantly exposed to criticism from various schools

who have other medical approaches (for example, many questions remain in the standardization of the treatment of patients with associated trauma). In practice, compliance with the requirements of standards (rather - treatment protocols containing the algorithm of therapeutic and diagnostic measures) is only possible for a small number of emergency conditions. So prehospital the criteria on the basis of which can be given to medical expert assessment diagnostic and treatment process, namely the presence of immobilizing fractures, aseptic bandage on the wound, anesthesia, its value, the measurement of blood pressure, catheterization of peripheral veins, the presence of fluid therapy, its volume, an electrocardiogram in the elderly.

Analysis of defects health care phases of its provision reveals shortcomings in the organization of treatment and diagnosis, that in the future will provide an opportunity to develop appropriate recommendations for improving the organization of the treatment process for patients of trauma profile. For example, if the study of pre-hospital phase of providing health care revealed that of the 350 brought to the emergency department at 196 (56.1%) of the patients brought to the hospital ambulance teams, diagnosed the injury, which does not require hospitalization. In this group of victims, while more accurate pre-hospital diagnosis, medical care could be provided at the level of trauma points, which greatly reduce the workload of the hospital and save the financial costs. Currently, there is such a situation that the work of SMEs depends largely on the quality of health clinics and emergency station that was repeatedly emphasized by other researchers. Thus, one of the main causes of unjustified referral hospital is the lack of qualified medical staff of health facilities that use the work of the NSR as a transport, as ambulance teams who come to these challenges is a paramedic and has no right to challenge the exhibited doctor LPU diagnosis. There is a defect in the organization of the treatment process.

It was revealed that the dissatisfaction of those surveyed patients is not due to the quality of the medical care and treatment on the part of medical staff (Fig. 2). According to the survey, 86.0% of respondents aged 30 years, ie, those who have already applied for emergency assistance previously noted that the overall culture of service in hospitals, including the work of all parts of the medical personnel has decreased significantly from the point of view of ethics. An increased number of conflict situations with patients. Thus, virtually all surveyed physicians (98.0%) indicated their presence. It is obvious that the violations are not always associated only with the actions of doctors. Thus, the reception waiting time, which is considered the patients to provoke conflicts, regardless how it was found only on the quickness of the physician rather from

its work organization system. Next - the lack of expected outcomes, which is primarily due to the limited resource capacity of existing health systems as part of the policy medical institution. At the same time we should not forget that the majority of our population is no motivation for health saving behavior against the backdrop of increasing expectations and demands [2]. Our investigations have shown 18.7% applied for emergency assistance burdened with alcohol or drugs.

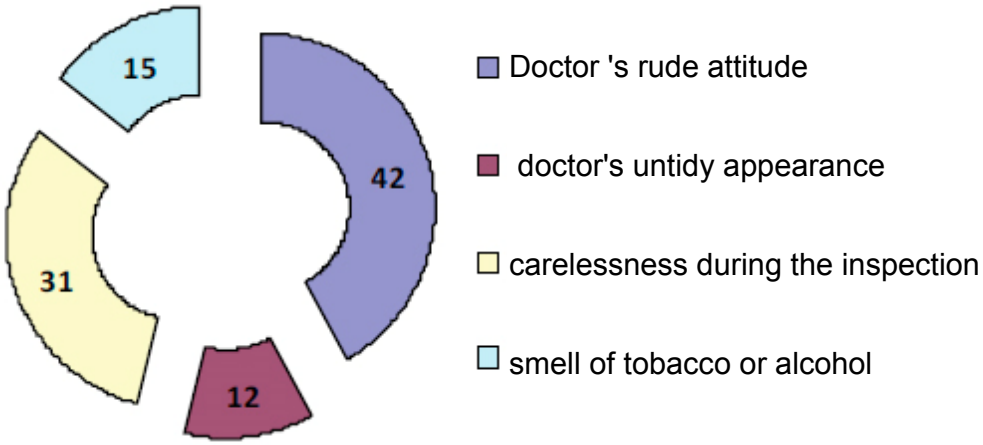

Fig.2. Assessment of quality of care among the potential patients of young age

The last few years in the national health care reform changes take place, aimed at its optimization. One outcome of reforms has become, for example, reducing the number of doctors on duty to provide urgent assistance. Currently undergoing public discussion of the draft order approving the typical industry standard time patient visits the doctor: over time the physician should establish contact with the patient at the level of understanding, then hold his examination (for example, in the case of injury it includes mandatory x-ray, ultrasound, general analyzes), prescribe treatment, direct hospitalization, fill the necessary documents [4]. The result is that the physician is not only "cargo" moral (for the life of the patient), but also legal liability. According to our research, in legal terms, medical staff is not sufficiently protected.

We believe that our analysis will improve the quality of trauma victims health care profile, as well as reduce the incidence of conflict between doctors and patients, to optimize the healing process, because «summum bonum medicinae sanitas» (Lat.) - The highest good of medicine is health.

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L.A. Aprosimov, D.A. Chichahov

Dynamics of Pediatric Service Staffing in the Republic Sakha (Yakutia)

ABSTRACT

The analysis of the dynamics of the supply of the Sakha (Yakutia) Republic population by physicians of all specialties, doctors-pediatricians, taking into account the pediatric surgeons, pediatric endocrinologists, pediatric oncologists for the 1995-2013 was done. In general in the Sakha Republic (Yakutia) during the analyzed period the increase of the children's population by doctors staffing of the pediatric profile was marked. This increase happened, both in Russia and in the Republic Sakha (Yakutia), mainly due to the reduction of the child population and, to a lesser extent, increasing the number of doctors themselves. The study has revealed the growth of doctors - pediatricians just in densely populated areas and the preservation of the unavailability of pediatric care in areas with low population density of the Sakha (Yakutia) Republic.

Keywords: medical staff, doctors staffing, nurses staffing, pediatric service, the ratio of doctors and nurses.

INTRODUCTION

Health is now the Republic Sakha (Yakutia) (RS(Y)) a powerful state structure having an extensive network of health care institutions. Significant is its contribution to the stabilization of the demographic indicators for the region. Today, the health care system of RS(Y), the efforts of the organizers of health during the difficult years at the turn of the century managed to retain its practical significance, restructured its resources, which ensured its continued development. But, at the same time, indicators of health of the population, slow population growth, lack of effectiveness of health systems require resource investment and, to a greater degree of human resources.

Uvarova T.E. and Burtceva T.E. [5], in a study of medical support areas densely populated by indigenous peoples in the Republic Sakha (Yakutia), noted the continued decline in core resources (number of health facilities, number of beds, frames, etc.). This reduction happened in sparsely populated areas of the RS(Y) with "excess" in comparison with common

federal, performance security of the population throughout the country. This situation demonstrates the inadequacy of rationing of medical support of the population, focused on the number of resident population, which is a violation of the constitutional rights of citizens of the Russian Federation (RF) to affordable health care. This fact is mentioned not only in the Far North, but also in other sparsely populated areas, in Siberia [3,4], in the central regions of Russia [2], and others.

Due to the fact that the rate of doctors is the most generalized criterion level of care, the analysis it is of particular interest to any of the regional health system. It should be noted that the most complex processes are currently taking place at the district health level. The staffing situation is tense in medical organizations at district level develops because that is where most of the focus problems of a systemic nature.

Objective: To analyze the dynamics of availability of RS(Y), physicians of all specialties, pediatric physicians, considering pediatric surgeons, pediatric endocrinologists, pediatric oncologists, per 10 000 of the total population, child population (0 to 17 years) for 1995-2013 years.

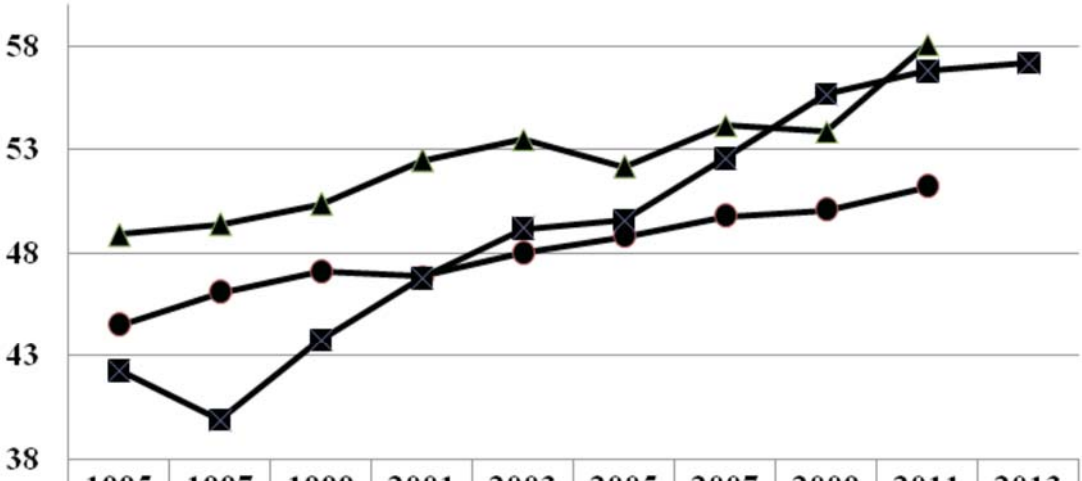
MATERIALS AND METHODS

A statistical analysis of the security of the population of RS(Y), physicians of all specialties, pediatric physicians, given the pediatric surgeons, pediatric endocrinologists, pediatric oncologists, per 10 000 of the total population, child population (0 to 17 years inclusive) for the 1995-2013 according to Rosstat, GBU RS(Y) "Yakut republican medical information-analytical center». A comparative analysis of the data of the Far Eastern Federal District (DFO) and the Russian Federation was done. To conduct the study, considering the medical and economic zoning of the RS(Y) [1], the areas of the country were divided into 6 groups: central, industrial, Vilyuisk, Northern and Arctic. Calculations were performed using software packages Statistica 6 and Excel. For the analysis of factors contributed most significantly associated with the studied parameters - providing the population of RS(Y), physicians of all specialties, pediatric doctors.

RESULTS AND DISCUSSION

Staffing of physicians of all specialties in the DFO and the RS(Y) is significantly higher than the Russian average, of doctors of all specialties in Yakutia before 2001 was significantly

(p=0.045) lower than in the Russian Federation, after steady growth - by data for 2011, the number of doctors in the Sakha Republic (Yakutia) was significantly (p = 0.012) more than in Russia, but less than in the DFO. Over the past 20 years in the Russian Federation number of physicians increased in all specialties was 15.1%, in DFO - 18.8%, in the Sakha Republic (Yakutia) - 34.3% (Fig. 1).



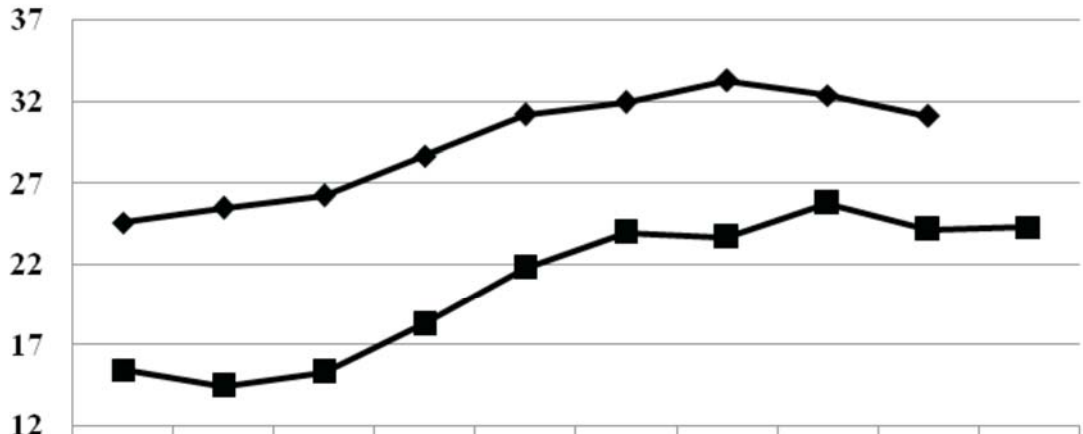
	1995	1997	1999	2001	2003	2005	2007	2009	2011	2013
RF	44,5	46,1	47,1	46,9	48	48,8	49,8	50,1	51,2	
EFD	48,9	49,4	50,4	52,5	53,5	52,2	54,2	53,9	58,1	
RS (Y)	42,3	39,9	43,8	46,8	49,2	49,6	52,6	55,7	56,8	57,2

Fig. 1. The number of doctors of all specialties per 10 000 population (according to Rosstat, 2013 - according to GBU RS(Y) YARMIATS).

The structure of the posts of health workers to ensure the availability of skilled medical care differs from the average. The ratio of doctors and nurses is 1: 2.7, which is slightly lower than the optimal value - 1: 3. The current ratio in the country due to the need to provide primary medical care to the population in remote localities, decreasing cost of air ambulance, as well as the introduction of new technologies in medicine.

Number of active physicians in view of pediatric surgeons, pediatric endocrinologists, pediatric oncologists in the SakhaRepublic (Yakutia) was always lower than in the whole of Russia, although there was an increase in the indicator for pediatricians 1999-2008. Performance security pediatricians child population of the Russian Federation has undergone rapid growth over the last 20 years: in Russia the number of pediatric physicians increased by

1.3 times, and in the RS(Y) for the same period - by 1.6 times (Fig. 2). Rising security pediatrician, as the Russian Federation and in the RS(Y) was mainly due to the reduction of child population and, to a lesser extent, increasing the number of doctors themselves. By the end of 2013 the number of physicians in pediatric RS(Y) per 10 000 children population was significantly lower (p = 0.023) than the average for the Russian Federation - 24.3 doctors per 10 000 children (RF in 2012 - 31, 1).

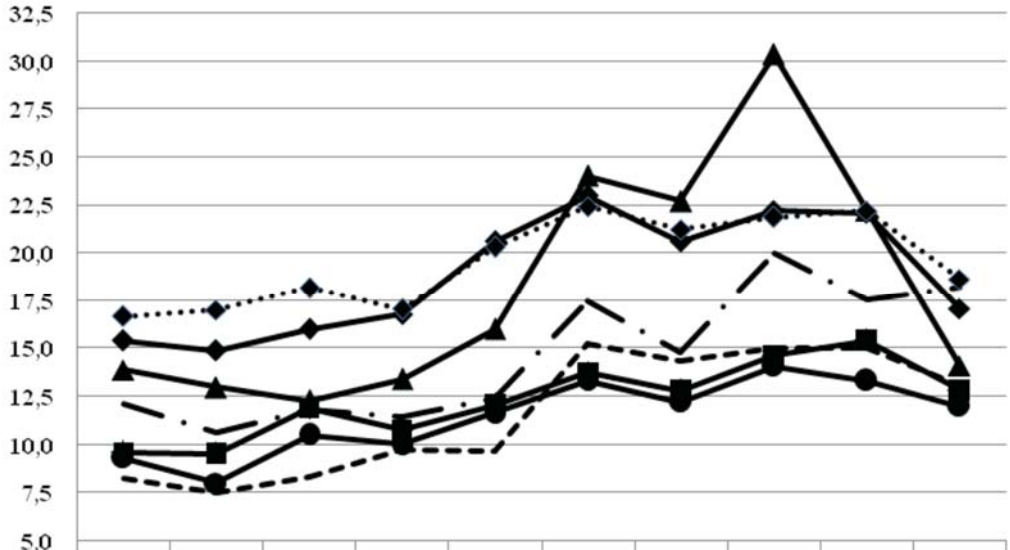


	1995	1997	1999	2001	2003	2005	2007	2009	2011	2013
RF	24,6	25,5	26,3	28,7	31,2	32	33,3	32,4	31,1	
RS (Y)	15,5	14,5	15,4	18,3	21,8	24,0	23,7	25,8	24,2	24,3

Fig. 2. Staff of pediatric physicians considering pediatric surgeons, pediatric endocrinologists, pediatric oncologists per 10 000 population (according to Rosstat, in 2013 - according to the GBU RS(Y) YARMIATS).

In general, the RS(Y) for the period 1995-2013 there is an increase of security of the child population pediatric physicians from 15.5 to 24.3 per 10,000 child population, which amounted to 56.7%.

In 2013, in health institutions of the RS(Y) 427 pediatricians and neonatologists operate. However, there are significant differences in the groups in the areas of security of pediatrics and neonatology (Fig. 3).



	1995	1997	1999	2001	2003	2005	2007	2009	2011	2013
RS (Y)	15,4	14,9	16,0	16,8	20,6	23,0	20,6	22,2	22,1	17,1
Arctic	13,9	13,0	12,3	13,4	16,0	24,0	22,7	30,3	22,2	14,1
northern	12,1	10,6	11,8	11,4	12,4	17,5	14,8	20,0	17,5	18,2
beyond the river	8,3	7,5	8,3	9,8	9,7	15,3	14,3	15,1	15,0	13,1
Vilui	9,3	8,0	10,5	10,0	11,7	13,4	12,2	14,1	13,4	12,0
central	9,6	9,6	11,9	10,8	12,1	13,7	12,8	14,7	15,4	12,8
RS (Y)	16,7	17,0	18,2	17,1	20,3	22,4	21,3	21,9	22,2	18,7

Fig. 3. Staff of pediatricians and neonatologists in the areas by groups per 10 000 population (according to the GBU RS(Y) YARMIATS).

Almost all groups of physicians to population areas pediatrics and neonatology not exceeded the average value of the index and only two it was higher for several years - in the industrial and Arctic groups. The highest rates are found in the unstable northern and arctic regions. In Arctic regions the group in 2009 had the highest security and pediatricians in 1997 - the lowest (30.3 and 13.0 per 10 000 children population, respectively). In the northern group, as there is a jump in the index: maximum security was observed in 2009, the minimum - in 1997 (20.0 and 10.6 per 10 000 population, respectively). In assessing the sufficiency pediatricians and neonatologists in these areas should take into account that the rate of security, calculated per 10 000 population, is uninformative because these groups cover 14 districts with the lowest population density.

Thus, in the arctic group, which includes five areas: Anabarsky, Bulunsky, Ust-Jansky, AllaikhovskiyNizhnekolymsky and, in 2009, there worked 21 doctors, and in 1997 - 15 doctors.

In the northern group of the 9 districts in 2009, 30 physicians were employed in 1997 - 17, while in some areas,we noted the lack of pediatricians.

During the review of 20 years the number of doctors pediatrics and neonatologists in the country increased by 11.0% (from 15.4 in 1995 to 17.1 in 2013). Most of all staffing was observed in 2005 (23.0 per 10 000 population, mostly due to staffing in the arctic regions of the group with an index of 24.0).

The highest growth rates of doctors pediatrics and neonatologists for the 1995-2013 was observed in the group of regions beyond the river: an increase of 57.8% (from 8.3 to 13.1 per 10 000 population, respectively).

The lowest rates observed in the Arctic regions of the group - an increase of 1.4% (from 13.9 to 14.1 per 10 000 population, respectively).

During the 1995-2013 the highest staffing of pediatrics and neonatologists were reported in 2005 in Ust-Maya area (security was 36.4 per 10 000 population worked in the area of 9 pediatricians) and in 2009 in the Allaikhovskiy area (provision totaled 54.6 per 10 000 population in the area worked 4 pediatrician).

Over the 20 years studied the lowest number of doctors pediatrics and neonatologists was reported in 1997 in the Amginsky area - 5.1 per 10 000 population (there worked 2 pediatrician).

CONCLUSION

Personnel shortage of physicians in pediatric rural and remote northern settlements imposes a very unique imprint on the organization of care for children's population. In general, it is organized primarily on a "reception residence", but differs from the urban schemes that patients have immediate access to medical services only paramedic FAP, pediatric specialty physicians do not, that may have the primary first aid, primary medical and emergency care. Help pediatrician, as well as specialized medical care can be obtained, in most cases, only in regional centers. The study revealed a growing number of doctors pediatric only in densely populated areas and the preservation of the unavailability of pediatric care in areas with low population density of Republic Sakha (Yakutia).

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Medical and Social Characteristics of Water Transport Workers of the Republic of Sakha (Yakutia)

ABSTRACT

The article presents the results of medical examination with questioning of workers of a water transport of Yakutia. This document provides information about age, nationality, sex. Moreover, the social characteristics (work experience, position, marital status), the attitude to health, attitude to unhealthy habits are analyzed. Harmful production factors of respondents are considered precisely and its relationship with nosological structure of diseases.

Keywords: water transport, workplace factors, diseases.

INTRODUCTION

River transport has the great social and economic importance for the Republic Sakha (Yakutia). Lena River is the main thoroughfare of the North-East of Russia. It provides the delivery of cargos from the central part of the country to this region. Being one of the main type of transport of the republic, it provides the delivery of economic cargos of North-East of Russia: the Republic Sakha (Yakutia), Irkutsk region, Krasnoyarsk region, Chukotka Autonomous Area, and also it delivers cargos at the area of the North seaway from Khatanga bay to Peveka in arctic and western territories of republic. Water crafts of mixed navigation river-sea carry out the transfer of oil products. The existence of less accessible areas, where cargos are delivered only by river transport, and climate and geographical specifics of the region, which allows the short-term period of navigation, needs high productivity in short deadlines.

In accordance with the orders №206 dated under 11.04.2005 "About Federal medical and biological agency" and №95 dated under 26.06.2008 "About the working process of departments of FSI "FEDMC of Roszdrav" the medical service of water transport workers is transferred to Federal medical and biological agency of Russia (FMBA of Russia), Lensk Central Basin Hospital was renamed into Yakutsk hospital FSBIH "Far Eastern District Medical Center of Federal Medical and Biological Agency". Medical services of water transport workers are provided according the state task.

According the order of the Government of the Russian Federation №1156 dated under 21.08.2006 to Yakut hospital FSBIH "FEDMC FMBA" are added the following companies of water transport in the republic: " Lensk United River Shipping Company" JSC, FBI "Administration of Lensk Basin", Yakut and Kolymsk areas of water ways and navigation, "Kolymsk Navigation Company" LLC, "Navigation company "Yakutsk" LLC, "River Port "Yakutsk" LLC, North-Eastern Management of State Sea River Control, trade-union organization of workers of a water transport YRPO "Basin Committee of Fleet" and Yakut Institution of Water Transport. They are served under the following contracts "Passenger Regional Management" LLC and "River Taxi" LLC.

The problems of decreasing and preventing the professional diseases among the members of navigation team are the priority in activities of medical prophylactic institutions on water transport. The specific of work of navigation team on river-crafts has the strict requirements to the health of people working on river fleet. High influences on formation of diseases have the shortcomings of organization of the regime of labor, life, food, habitability on the craft etc. The leading factors in this are: the influence of professional damages- noise, vibration, high wetness, different climate, geographical and meteorological factors. Besides that, the workers of water transport have high psycho-emotional stress [2]. Successful economic development of the country directly depends on conditions of labor resources, quality of which is closely related with quantity and health level of the population, who is taking part in economic activity of the government, because the health of workers is the necessary condition to increase the productivity of labor and economic growth, as well as it determines the safety and welfare of society [1]. All mentioned above determines the necessity of modernization of the health service on the water transport and for improvement of health and prolongation of labor longevity of water transport workers.

The **aim** of research is the assessment of medical and social factors, which influence on health of water transport workers of the Republic Sakha (Yakutia).

MATERIAL AND METHODS OF RESEARCH

On the basis of the Yakut hospital FSBIH "FEDMC FMBA" it was conducted the medical examination with questioning of 367 people, aged from 18 to 78 (the average age 42,8 ± 13,1 years), man - 287 people (average age 42,5 ± 13,4), women - 60 people (average age 44,3 ± 1,5) (picture 1, a). People from 30 to 39 turned out to be the leading age group, and the leading ethnic

group turned out to be Russians (88,56%) (picture 1, b). The questioning was conducted according the requirements of Helsinki declaration (2000).

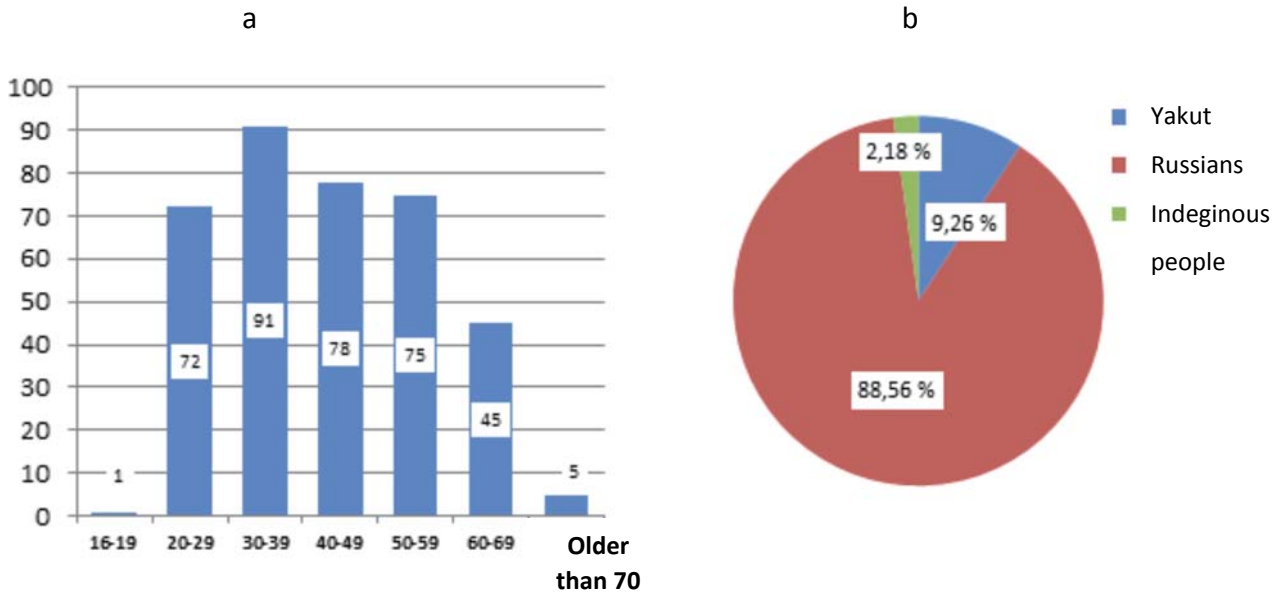


Figure 1. Differentitation of the questioned people in accordance with age (a) and ethnicity

RESULTS AND DISCUSSION

The questioning showed that natives of Yakutsk amounted 35,8% (131 people), other areas of the Republic Sakha (Yakutia) - 19,3 % (71 people). The rest part 44,8 % (164 people) turned out to be natives of other subjects of the Russian Federation.

The differentitation by the work position showed that among the examined people, the specialists of water transport (wheelmen, machinists, mechanics, cranemen, docker-skinners, conductors, craft cooks etc.) amounted 78,9% (289 people), managers (captains of crafts, managers of surveying parties, machine-shop managers) - 12 (44), workers-6,5 (24) and others 2,72% (10 people). Among specialists of water transport 27,8% have the work experience more than 20 years, 20,1 - 10-20, 27,8 - 5-10, 15,6 - to 5 yers, 8,68 - to 1 year, i.e. 75,7% of workers had the work experience more than 5 years. 54,5% of managers the work experience was more than 20 years.

Among the interviewed people (366 people) 62,02% are married, 22,95% are single, 9,5% are divorsed, and 5,46% are widowed. Single people are predominantly among specialists of

water transport (26,73%), and age group constitutes from 20-29 years (55,5%). Divorsed people are among of age group 40-49 years (16,9%).

Around 80,2% (292 people) of interviewed people gave the positive answer to the question "Are you satisfied with your state of health?"

The interview on the influence of harmful workplace factors on the workers of the water transport showed that 45,13% of the interviewed people deny its existence, 16,6% indicate one factor, 17,27% – two factors, 18,38% – three factors, 3,06% indicates from four to six factors (picture 2). More than third part of interviewed people (31,75%) have the duration of influence of professional harmfulness more than 25 years, 28,13% - to 5 years and 22,84% - to 10 years.

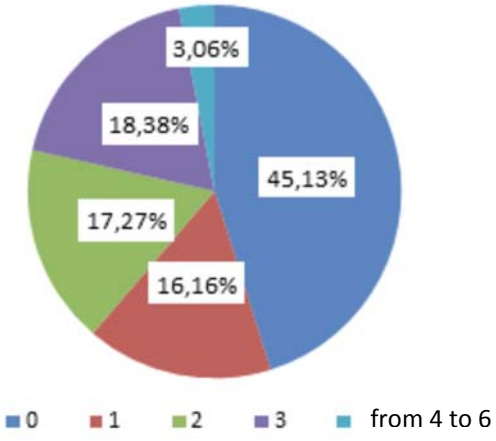


Figure 2. The quantity of factors of the working environment of the questioned people

The results of questioning showed that such production factors as noise (74,11%), vibration (72,59 %) are the most widespread among the workers of the water transport. Around 12,69 % of questioned people indicated the influence of the electromagnetic radiation, 11,7%- the dustiness of the work environment, 6,09% - the welding aerosols.

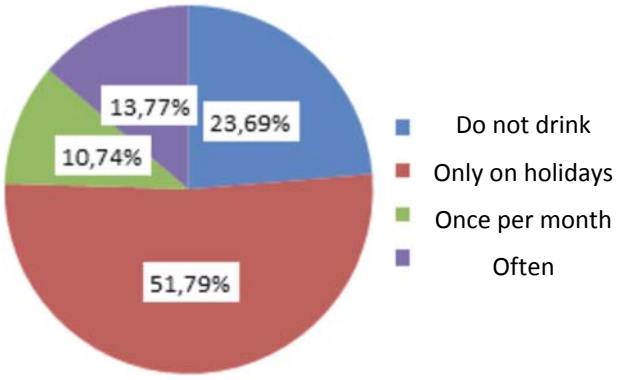
It should be noted, that 66,85% of the questioned people think that their work is stressful. The analysis showed the significant differences depending on the position (χ^2=19,26, p=0,000), thus 95,45% of managers , 63,41% specialists and 16,6 % workers indicate that the work on the occupied position is stressful.

To the question "Are you physically active?" - 74,04% of the questioned people gave the positive answer and 25,6% think that the physical activity for them is not enough. The insufficient

physical activity was indicated by 56,52% of people aged from 20 to 29, 46,77%- from 30 to 39, 22,22% from 40 to 49, 33,9% from 50 to 59, 9,7% from 60 to 69 years old.

The analysis of the answers to the questions, concerning the unhealthy habits, showed that 23.69% of questioned people do not drink alcohol, 32,51% do not smoke (picture 3, a, b). Thus, smokers constitute 58.20% and alcohol drinkers 13.77%.

a



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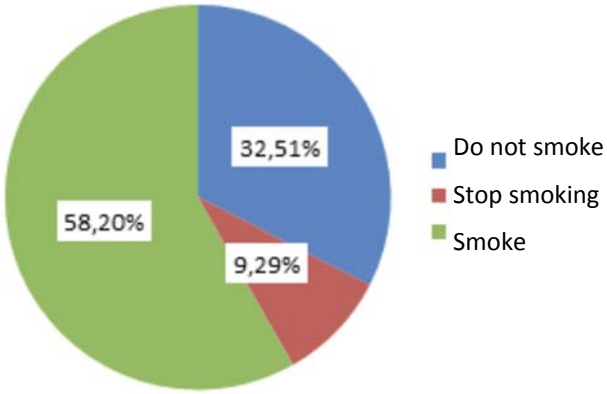

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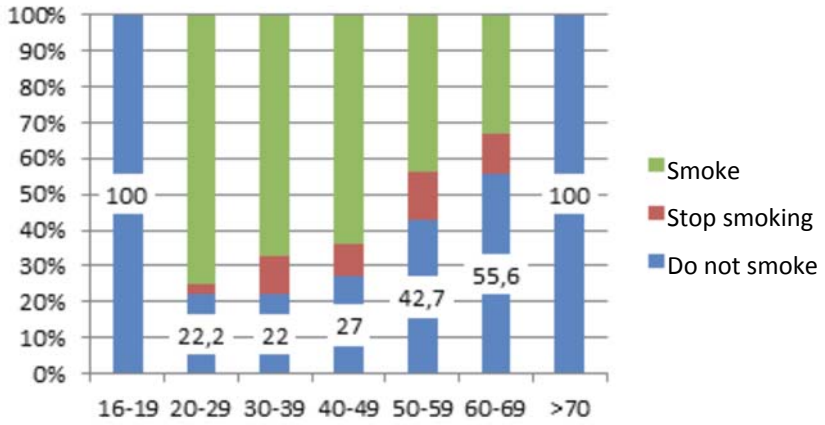

Figure 3. Prevalence of unhealthy habits (alcohol-a, smoking-b) and dependence of smoking on age (c)

It turned out that the percenage of the smokers depends only on the age of questioned people (χ^2=43,92, p=0,000), but not from the occupied position, labor stress, place of live, education and other factors. It is necessary to say, that the highest percentage of the smokers is in the age group 20-29 years (75%), with age the number of smokers decreases (picture 3, c).

The results of medical examination of workers of companies of water transport showed, that the cardiovascular diseases occurred more often (35,15%), than other diseases. From 129 people with cardiovascular pathology, around 104 (80,6%) have a diagnosis - essential hypertension, which appeared to be most depended on the age (χ^2=101,24; p=0,000) and from the occupied position (χ^2=15,2; p=0,019). More often this pathology is met among people in senior age groups 50-59 years (56%) and 60-69 years (68%) and 47% managers.

The pathology of endocrine system - 76 people (20,7%) appeared to be next according the frequency among the examined people. 82,8% suffer from fattiness (63 people). The frequecy of fattiness increases with age (χ^2=17,93; p=0,006). It should be mentioned that people, who chose from different variants of food ("milk", "vegetable", "meat" and "mixed") the variant "mixed" more often suffer from fattiness (χ^2=11,08; p=0,05). Diseases of nervous system are met at 15,5%, musculoskeletal system at 15,04%, urogential system at 11,99%, respiratory organs at 11,98%, digestion organs at 9,81 %.

It is necessary to mention that the frequency of sensorineural hearing loss of the examined people was high (12,9%). This pathology has the linear dependence (χ^2=53,28; p=0,000) on the age. Besides this, the dependences from the following factors of the production environmnet were identified: noise (χ^2=7,72; p=0,005) (picture 4,a) and vibration (χ^2=6,59; p=0,009). The results of the analysis show that, besides the mentioned above factors the frequency of sensorineural hearing loss depends on the quantity of the simultaneous combination of several factors of production environment (noise, vibration, dustiness etc) (χ^2=14,74; p=0,022) (picture 4,b).

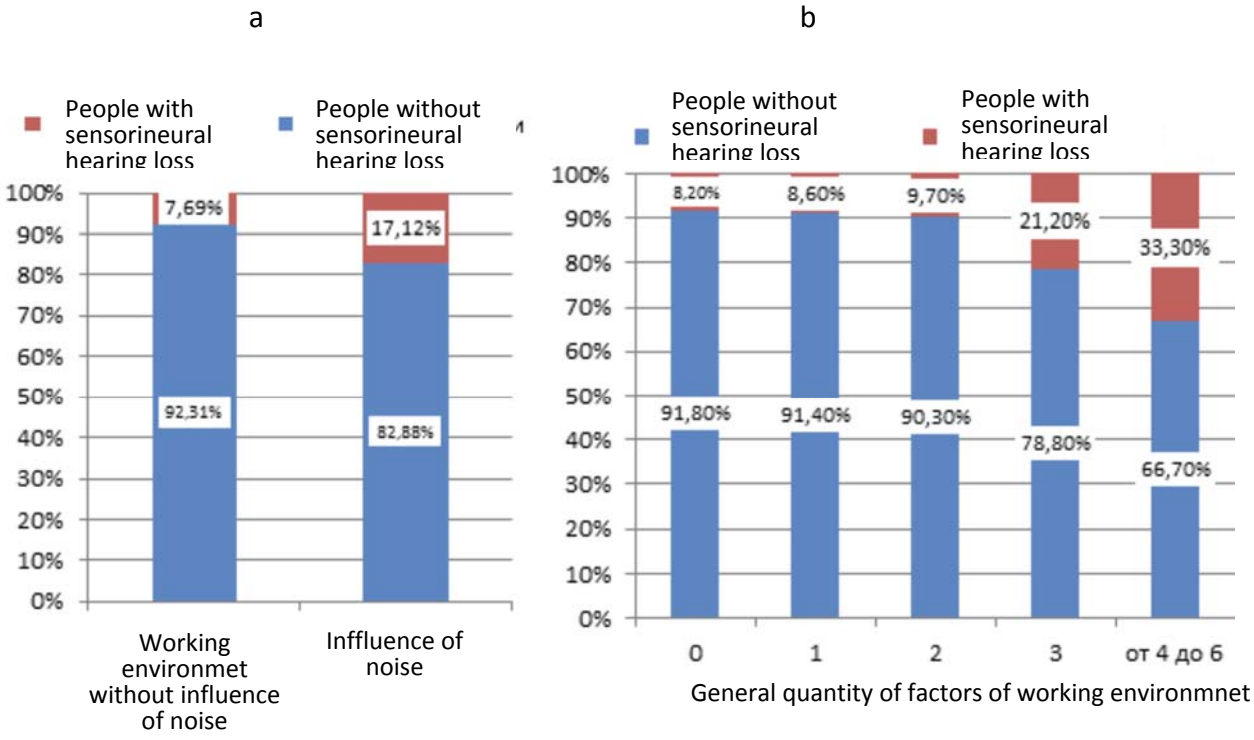

Figure 4. Dependence of sensorineural hearing loss on factors of working environment (a-influence of noise, b- quantity of factors)

CONCLUSION

Thus, the results of the questioning indicate to the need for the medical and prophylactic work on harm of the smoking and influence of physical activity among people of young age to 30 years, because in this age group the percentage of the smokers is much higher and the physical activity is not high enough in comparison with other groups. The results of medical examination show that as a person gets older the frequency of the cardiovascular diseases among the workers of the water transport increases, in particular essential hypertension and fattiness. It should be noted that among the examined people the frequency of sensorineural hearing loss depends not only on age, but also on factors such as noise, vibration and the quantity of complex production factors.

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Characteristics of Newly Identified Patients with Infiltrative Pulmonary Multidrug-Resistant Tuberculosis in the Sakha Republic (Yakutia)

ABSTRACT

This paper presents social and clinical data on newly identified patients with pulmonary infiltrative multidrug-resistant tuberculosis in the Sakha Republic (Yakutia) treated at the Therapy Department for Pulmonary Tuberculosis no.3, the Research & Practice Center for Tuberculosis. The majority of the patients were unemployed individuals of active working age, with the history of close family exposure to sputum-positive case. Most often, tuberculosis was detected on presentation to a doctor, and the detected cases were mostly cases with extensive destructive disease and high bacterial loads of multidrug-resistant *M.tuberculosis (MDR)*.

Keywords: *Mycobacterium tuberculosis*, infiltrative pulmonary tuberculosis, multidrug-resistance, chemotherapy regimen, primary drug resistance, antitubercular agents.

INTRODUCTION

Multidrug resistance (MDR) of *M.tuberculosis* (MTB) is currently one of the most urgent problems in the science of tuberculosis treatment and prevention. In the Sakha Republic (Yakutia), the incidence of MDR MTB is tending to grow: in 2013 MDR cases made 32.4% among the newly detected pulmonary tuberculosis (TB) cases, which is 4.4% percent higher than in 2011.

MATERIAL AND METHODS

We observed 91 patients with newly detected infiltrative pulmonary MDR TB, who were undergoing intensive phase treatment with chemotherapy regimen IV in the settings of tertiary therapy department for patients with MDR MTB, in the Research & Practice Center for Tuberculosis. All patients were HIV-negative; all had primary type of drug resistance.

RESULTS AND DISCUSSION

Observation group included more males (50; 54.9%) than females (41; 45.1%). Patient age ranged from 18 to 65; the majority (80.2%) was individuals of active working age (21 to 50 years). More than half of the patients were urban residents (59.3%; 54), while the rest (40.7%; 37) resided in rural settlements. Social and living conditions for the patients diagnosed with infiltrative pulmonary MDR TB are presented in Table 1.

Table 1

Social and living conditions of patients with infiltrative pulmonary tuberculosis caused by multidrug-resistant mycobacteria

Parameter	Total (n=91)	Urban residents (n=54)	Rural residents (n=37)
Gender			
Males	50 (54.9%)	29 (58%)	21 (42%)
Females	41 (45.1%)	25 (61%)	16 (39%)
Social status			
Unemployed, active working age	43 (47.3%)	23 (53.5%)	20 (46.5%)
Employed	31 (34.1%)	18 (58.1%)	13 (41.9%)
College/Higher education undergraduates	13 (14.3%)	10 (76.9%)	3 (23.1%)
Retirees	4 (4.3%)	3 (75%)	1 (25%)
Living conditions			
Housing with modern conveniences	27 (29.6%)	20(74.1%)	7 (25.9%)
Partly lacking conveniences	24(26.4%)	14(58.3%)	10(41.7%)
Private housing	23(25.3%)	3(13%)	20(87.0%)
Hostel	10 (11%)	10(100%)	-
Homeless	7 (7.7)	7(100%)	-

There were 43 (47.3%) unemployed patients of active working age, 31 (34.1%) patients with permanent employment, 13 (14.3%) undergraduate students of colleges/higher education institutions; and 4 (4.3%) retirees. Among the patients with permanent job, the majority had blue-collar occupation (27; 87.1%), and 4 (12.9%) were white collar workers. Educational background was as follows: completed or unfinished higher education (13; 14.3%); vocational secondary college or secondary general school (71; 78%); unfinished secondary school or elementary education (7; 7.7%). As for living conditions, 27 (29.6%) patients resided in houses

with modern conveniences, 24 (26.4 %) were living in houses partly lacking conveniences, 23 (25.3%) were living in private houses, 10 (11.0%) patients resided in hostels, and 7 (7.7 %) patients were Of No Fixed Abode.

There were 22 (24.2%) patients with alcohol addiction, 40 (43.9%) patients with nicotine addiction, and 1 patient with substance addiction. Number of patients with a history of previous detention was 6 (6.6%).

Analysis of the frequency and timeliness of preventive chest x-ray examinations underwent by the patients before the detection of TB showed that only 20 (21.9%) underwent their exams in time; 18 (19.8%), 39 (42.9%), and 14 (15.4%) patients had been x-rayed for more than 2, 3, or 5 years, respectively. Among the employed and undergraduate patients, 16 (36.4%) had been examined for 2 or more years.

Tuberculosis disease was detected more often on presentation to a physician (52 cases; 57.1%). On presentation, most patients complained of the symptoms typical for tuberculosis-induced intoxication: coughing for a long time (for more than 2 months), fever, fatigue, loss of weight, hemoptysis. 30 (33%) patients were found to be x-ray-positive during the scheduled preventive chest x-ray examination or else during job seeking; (9.9%) patients were detected after they were referred to TB Clinic for further examination due to exposure to contagious TB case.

Study of the epidemiological background showed that 39 (42.9%) patients had a recent contact with MDR TB case; of them, 21 (53.8%) were close family contacts, 18 (46.2%) were social contacts (i.e. with sick friends, relatives, or former prisoners, who had MDR MTB). Obviously, exogenous superinfection played a leading role in the development of TB disease in the lungs, as close contacts with pulmonary MDR TB cases were highly common in the epidemiological backgrounds of the patients.

Analysis of medical histories showed that before presenting to physician, patients with MDR TB had been considering themselves sick for a period ranging from 2 weeks to 2 months (54; 59.3%), from 3 to 4 months (16; 17.6%), or from 5 to 6 months (3; 3.3%). 18 (19.8%) patients thought they were not sick.

Patients with infiltrative pulmonary MDR TB commonly presented with symptoms of fatigue, fever, night sweats, and loss of weight. These symptoms were pronounced in 17 (18.3%)

patients and moderate in 59 (64.8%). Respiratory syndrome was observed in 77 (84.5%) patients. Of them, 92.2% had complaints of moist cough; 58 (63.8%) had shortness of breath on exertion; 33 (36.3%) admitted chest pain on breathing. 14 (15.4%) patients had hemoptysis as the reason to seek medical care. Half of the patients (52%) noticed loss of weight; average body mass index was less than 18; body weight deficit ranged from 5 to 10 kg.

Study of the immune status showed that B-cell activation was more common, with an increase in IgG levels from 20 to 380 mg/mL (5.3 to 16.5 mg/mL in health) in 90.5% of the cases; increase in IgM levels from 3 to 6.5 mg/mL (0.5 to 2 mg/mL in health) in 78.6% of the cases; and increase in IgA levels from 4.5 to 27.5 mg/mL (0.8 to 4 mg/mL in health) in 35.7% of the cases. These results confirmed the activation of secondary immune response typical for TB disease, and usually manifesting as increased Ig levels, especially IgG, a highly specific and one of the most important antibodies in terms of protection against infectious agents.

Radiological examinations, including chest x-ray and computed tomography, revealed that tuberculosis involved one lung in most cases (36.6%); in the rest of the cases, the disease involved one lobe (29.6%), or two segments of the one lung (18.3%), or both lungs (15.5%). All patients developed destructive TB; cavitations were sized <4 sm. in 71.8% of the cases; <2 sm. in 28.2% of the cases; multiple cavitations were observed in 41.8% of the cases; seeding to neighboring areas of the lung or to the opposite lung was found in the majority of the patients (73.6%).

Study of the respiratory function showed meaningfully decreased pulmonary ventilation and vital capacity of the lungs (60 %); of them, 20 (27.8%) patients had restrictive impairments; 40 (55.6%) had moderate decrease; in 12 (16.6 %) patients no impairments were detected.

Based on the fiberoptic bronchoscopy findings, the following conditions were diagnosed: draining purulent endobronchitis (22; 24.2%); diffuse cataral endobronchitis with the inflammation stage I or II (49; 53.8%); atrophic endobronchitis (10; 11%); no pathologic conditions (10; 11%).

Culture testing was performed using BACTEC MGIT-960 liquid medium system and absolute concentration method on Lowenstein-Jensen medium for drug sensitivity determination. Sputum culture tests were performed in all patients before the prescription of chemotherapy.

Most newly identified cases were started on standard chemotherapy regimen I (57.1%). Regimen IIB was prescribed in 42.9% of the cases who had been exposed to MDR TB.

Use of BACTEC MGIT-960 system for culture tests shortened time to determination of M.tuberculosis drug sensitivity. Determination of MDR required 1 to 1.5 months in 73 (80.2%) patients, and <3 months in 18 (19.8%) patients. Patients with confirmed MDR TB were started on chemotherapy regimen IV and transferred to the specialized department for MDR cases in 3 to 7 days, after the decision of the Centralized Medical Supervisory Committee.

Fluorescence microscopy of the sputums from patients with infiltrative pulmonary MDR TB performed on admission to hospital showed that mycobacterial counts were predominantly excessive (34; 47.9%), or moderate (19; 26.7%), or scarce (18; 25.4%).

Drug resistance profiles are presented in Table 2. As is seen from the table, there was a high incidence of DR to first and second line drugs (42.8%).

Table 2

Primary multidrug-resistance profiles (n=91)

Combination of anti-TB drugs	Number of cases
HR	3 (3.3%)
HR /S /E	49 (53.9%)
HRSKm / Cm /E /PAS /Et /Cs	31 (34%)
HRSOf /E /Et	8 (8.8%)

Notes: *H – Isoniazid; R – Rifampicin; S – Streptomycin; Km – Kanamycin; E – Ethambutol; Cm – Capreomycin; Et – Ethionamide; PAS – Para-aminosalicylic acid; Fq – Fluoroquinolone.

Fig. 1 shows that DR to isoniazid and rifampicin is most often associated with DR to streptomycin (88%), kanamycin (37.4%), or ethambutol (29.7%).

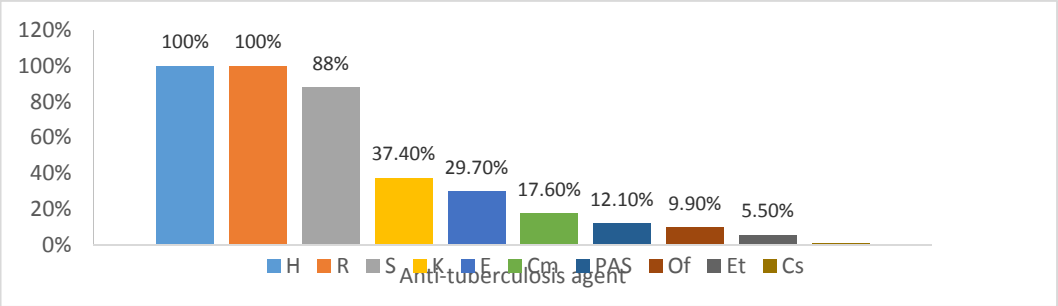

Fig.1. Incidence of drug resistance to individual anti-tuberculosis agents

CONCLUSIONS

In the Sakha Republic (Yakutia), patients who develop infiltrative pulmonary MDR TB were mostly urban residents, male, of active working age but unemployed, with nicotine and alcohol addiction. Commonly observed delays in regular preventive chest x-ray examinations coupled with late presentation to a physician stems from poor health education among the population.

Infiltrative pulmonary MDR TB was characterized by subacute onset, with moderate tubercular intoxication and a respiratory syndrome typical for TB (prolonged moist cough; shortness of breath on exertion; chest pains; coexistence of nonspecific endobronchitis; impaired respiratory function). As a rule, patients with pulmonary TB developed an extensive and destructive disease with seeding lesions and excessive mycobacterial sputum counts. This emphasizes once more the high epidemiological danger that drug-resistant cases present. It is important to stress out that the majority of patients with primary DR had high incidence of DR to the first- and second-line drugs, which suggests prolonged close contact with a sick person already harboring MDR M.tuberculosis.

In view of the stressed epidemiological situation for TB in the Sakha Republic, health education activities among the population and preventive medical examinations must be expanded, especially among the unemployed population, primary network health personnel must be educated to prevent and detect TB, and learn the correct patient referral during population examination for the presence of TB, to identify epidemiologically dangerous cases. The detection of DR forms of TB must be based on the use of up-to-date diagnostic culture

methods enabling fast determination of drug sensitivity, and initiation of adequate chemotherapy in the specialized TB facility.

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Rotavirus Incidence in Different Regions of the Russian Federation in the Pre-Vaccination Period

ABSTRACT

The article presents the results of a retrospective epidemiological analysis of the rotavirus incidence in the Russian Federation, Saint Petersburg, Novgorod Oblast and the Sakha Republic (Yakutia) in 2000-2013. It identifies regional variations in the epidemic process intensity in the pre-vaccination period, age groups of risk, and the role of the water factor in the infection transmission. The age group most susceptible to the disease is children under two years of age.

Keywords: rotavirus infection, incidence, virological testing, vaccination.

INTRODUCTION

According to the World Health Organization (WHO), every year they register about one billion cases of diarrhea worldwide, causing up to 4 million deaths, with 60-70% of the patients being children under the age of 14 years [13]. In the Russian Federation (RF), acute enteric infections (AEI) consistently rank third or fourth among the infectious diseases of childhood [1,2]. In recent years, we witness an increased role of viral gastroenteritis, which is alarming due to its widespread and high incidence in child population [9, 11]. Every year, from 50 to 80% cases of diarrhea in the world are caused by viruses, and mostly, by rotaviruses accounting for 25 to 60% of AEI [7]. Rotavirus infection (RVI) is a common highly contagious infection, and a global pressing problem. Annually, they register about 138 million RVI cases, with 454 to 705 thousand people dying of the infection [8,10,12]. The highest RVI incidence rates are found in children aged 6 to 24 months; by the age of five years, almost every child has had several episodes of rotavirus gastroenteritis [10,14]. In Russia, the mortality of RVI has increased over 22-fold (from 3.2 per 100,000 the population in 1993 to 71.6 in 2013), mainly due to the improved etiological deciphering of AEI [4]. For the Russian Federation as a whole, children hospitalized with RVI under 12 months make 28.0% of children under six years of age [5].

At present, there are three licensed live RVI vaccines in the world: monovalent one for genotype G1P rotavirus [8], monovalent one for genotype G9P rotavirus [11] and pentavalent one for rotaviruses of genotypes G1P [8], G2P [4], G3P [8] G4P [8] and G9P [8]; they have proven efficient and safe in practice. RVI vaccination is introduced in over 100 countries around the world; in 42 countries it is a part of the national immunization schedule. The rotavirus vaccines not only help to reduce the incidence, but also reduce the number of deaths, decrease the

number of hospitalizations and associated socio-economic losses. In October 2012, the Russian Federation registered the pentavalent vaccine; in 2013, a number of subjects began immunization of children under regional vaccination programs and on the paid basis, as well (Moscow, Saint Petersburg, Lipetsk, Yekaterinburg, Omsk, Novosibirsk, Krasnoyarsk, Yakutsk and others). In May 2014, the Ministry of Health included RVI immunization in the calendar of preventive vaccinations by epidemic indications [6].

Aim of the research: to determine the patterns and regional features of the rotavirus infection epidemic process in subjects of the Russian Federation before initiation of the rotavirus vaccination program.

MATERIALS AND METHODS

We have done a retrospective epidemiological analysis of RVI incidence in Saint Petersburg, Novgorod Oblast and the Sakha Republic (Yakutia) for the period 2000-2013. The materials are obtained from the forms of the federal statistical observation: No. 2 "Information on infectious and parasitic diseases", No. 2-13 "Information on the activities of sanitary-hygienic, microbiological and parasitological laboratories, the Center for Hygiene and Epidemiology in the Sakha Republic (Yakutia)", No. 23 "Information on outbreaks of infectious diseases." We used the data from the State reports on the sanitary-epidemiological welfare of the population in these regions for 2013; bulletins of statistics and analytical materials "Infectious diseases in the Russian Federation for 2012-2013." The Rotavirus-Antigen-IFA-Best test systems manufactured by JSC Vector-Best were used to detect the rotavirus antigen in water samples. We analyzed the results of testing samples of drinking water and wastewater in the Sakha Republic (Yakutia). We used conventional methods of statistics. The statistical analysis of the data and graphics are made using standard Microsoft Office software package (Excel, Word, 2010).

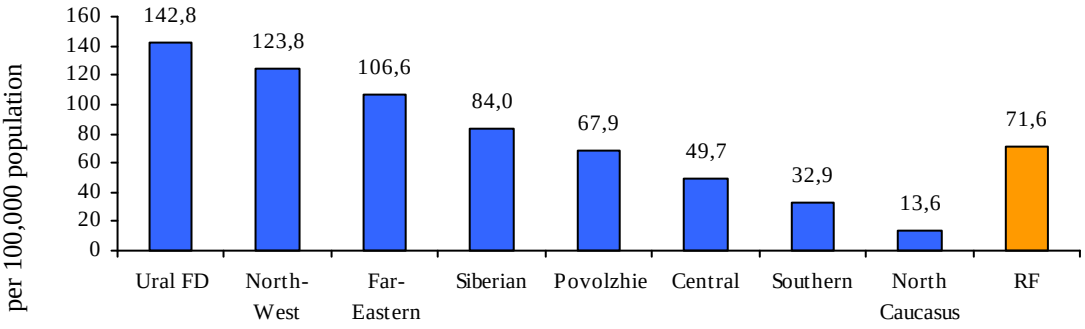

Figure 1. Rotavirus incidence in federal districts of the Russian Federation in 2013

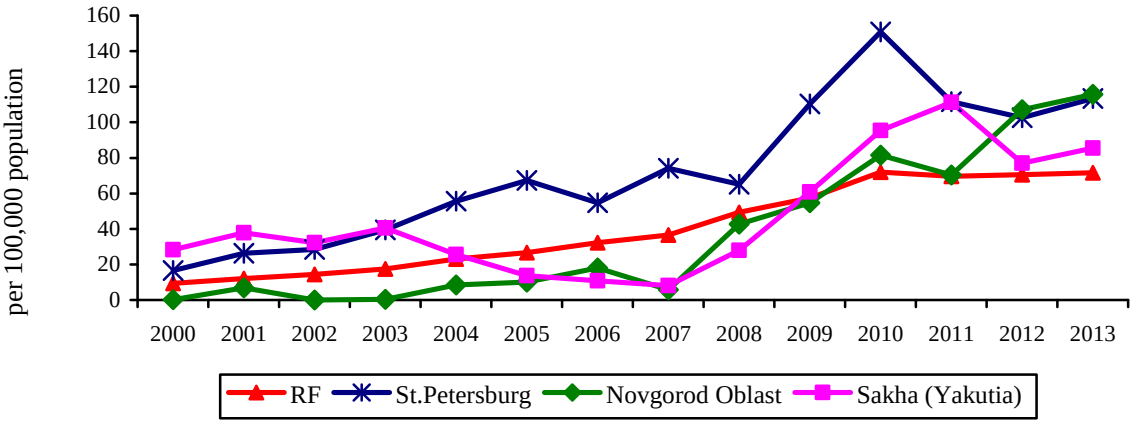

Figure 2. Rotavirus incidence trends in the Russian Federation, Saint Petersburg, Novgorod Oblast and Sakha Republic (Yakutia) in 2000 – 2013

RESULTS AND DISCUSSION

Rotavirus is registered in almost all subjects of the RF. When analyzing the data on the incidence in different federal district, we found out that in 2013, the figures varied from 13.6 in the North-Caucasian Federal District (NCFD) to 142.8 in the Ural Federal District (UFD) per 100,000 population, which depends on the level of laboratory diagnosis (Fig. 1). Four federal districts showed the incidence rate exceeding the average one by 1.2 to 2 times.

In the North-Western (NWFD) and Far-Eastern (FEFD) federal districts, in 2013, the RVI incidence was 123.8 and 106.6 per 100,000 population, respectively. Novgorod Oblast and Saint Petersburg rank 6th and 7th among 11 regions of the North-Western Federal District; the Sakha Republic (Yakutia) ranks 6th out of 9 regions of the FEFD. Saint Petersburg accounts for 30.4% of the diagnosed RVI, Novgorod Oblast - 4.2%, Sakha Republic (Yakutia) - 12.2% of the total

incidence of this infection in the North-Western and the Far-Eastern Federal Districts.

The analysis of the long-term trends of RVI incidence in Russia shows a constant improvement of laboratory diagnosis of the infection, as well as regional differences in the intensity of the epidemic process. In the past four years, before the initiation of the vaccination program, the RVI incidence in Russia had stabilized at 69.6 ± 0.2 – 72.1 ± 0.2 per 100,000 population. However, with this nationwide stabilization, the three regions in question are characterized by a constant upward trend (Fig. 2). In 2000-2013, Novgorod Oblast showed the greatest increase in the incidence, going up by 810 times. In Saint Petersburg, the incidence has increased by 7 times. In the Sakha Republic (Yakutia), the epidemic process is characterized by less RVI growth – by 3 times.

During the observation period, Saint Petersburg showed the incidence rate significantly higher than the average for the Russian Federation, and it varied between 16.6 ± 0.6 – 150.9 ± 18 per 100,000, with the 2013 figure at 113.4 ± 1.5. Novgorod Oblast initiated extensive laboratory diagnostics of RVI in 2008, which affected the incidence: over 14 years, the minimal RVI incidence was recorded in 2000 at 0.1 ± 0.1 per 100,000; the maximum one – in 2013 at 115.8 ± 4.3 per 100,000. As of 2013, the Sakha Republic (Yakutia) had the same figure at a significantly lower level – 85.4 ± 3.0 per 100,000 ($p < 0.05$).

The RVI epidemic process on the territory of these Russian subjects is predominantly sporadic. In 2013, the patients affected during outbreaks in Saint Petersburg made 0.3% (2 focal points with 18 affected people), in Novgorod Oblast - 3% (3 focal points with 22 affected people). The same year, there were no RVI outbreaks registered in the Sakha Republic (Yakutia).

The study of the RVI incidence in different population groups showed that the epidemic process in the compared regions of Russia involves mainly children under 2 years of age (Table 1).

In 2013, Novgorod Oblast and the Sakha Republic (Yakutia) had the incidence of children under the age of 1 year at 2055.5 ± 168.9 and 2278.3 ± 118.5 per 100,000 population, respectively ($p > 0.05$), with a significantly lower figure for the Russian Federation as a whole at 1215.2 ± 8.0 ($p < 0.001$). In the age group of 1-2 years, the highest incidence rate was registered in Novgorod Oblast – 2263.6 ± 127.1 ($p < 0.001$). The lowest rate of the epidemic process was observed in the Sakha Republic (Yakutia) – 1157.8 ± 61.5 ($p < 0.001$).

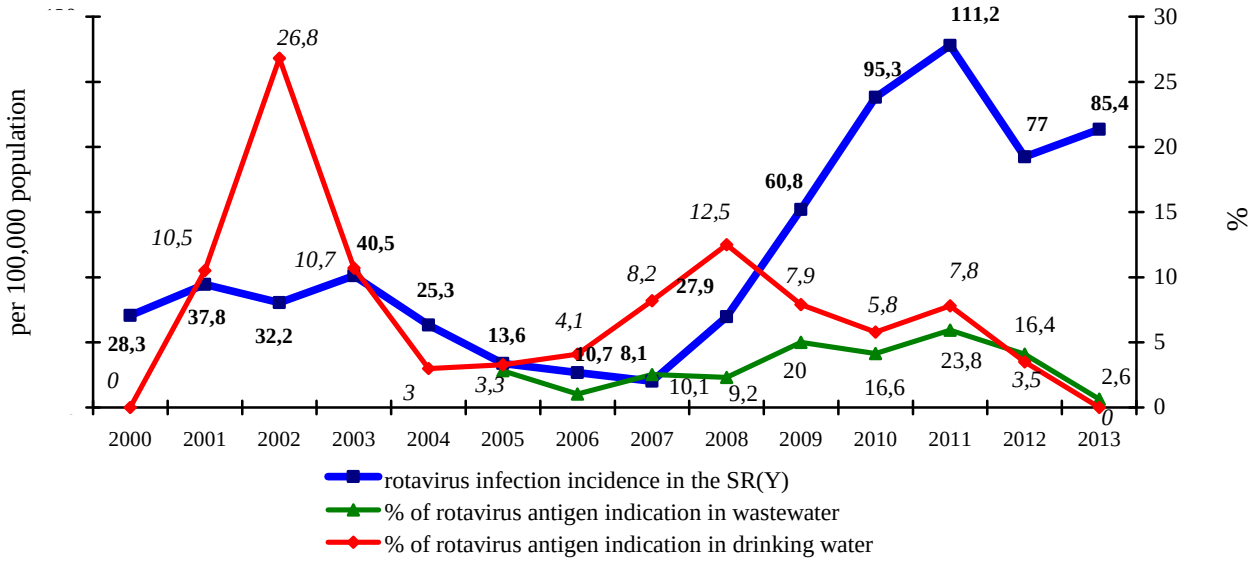

Figure 3. Rotavirus infection incidence in the Sakha Republic (Yakutia)

and the share of the rotavirus antigen detection in samples of drinking water and wastewater,

2000–2013

Table 1.

Rotavirus infection incidence in different population groups of the Russian Federation, Novgorod Oblast and the Sakha Republic (Yakutia) in 2013

No.	Subject	RVI morbidity, total	by the age groups (years):				
			under 1 year	1 - 2	3 - 6	7 - 14	15 - 17
		o/oooo±m	o/oooo±m	o/oooo±m	o/oooo±m	o/oooo±m	o/oooo±m
1	Russian Federation	71.6±0.2	1215.2±8.0	1321.4±6.2	329.4±2.3	49.8±0.7	16.2±0.6
2	Novgorod Oblast	115.8±4.3	2055.5±168.9	2263.6±127.1	425.5±40.6	99.9±15.0	30.7±13.4
3	Sakha Republic (Yakutia)	85.4±3.0	2278.3±118.5	1157.8±61.5	129.1±15.3	27.8±5.1	0

In Yakutia, the main risk group for RVI development are children of the first year of life, the incidence rate in which amounted to 2278.3 ± 118.5 ($p<0.001$) in 2013. In Novgorod Oblast, the incidence in the age groups under 1 year and 1-2 years was not statistically different – 2055.5 ± 168.9 and 2263.6 ± 127.1, respectively ($p>0.05$). In Russia as a whole, the greatest intensity of the epidemic process is observed in children of 1-2 years of age – 1321.4 ± 6.2 ($p<0.001$). Novgorod Oblast had high rates of rotavirus gastroenteritis in children of 3-6, 7-14 and teenagers of 15-17 years.

Monitoring of the pathogen circulation in the environment is an important part of the epidemiological surveillance of RVI, which is necessary for identifying risk factors for the disease. This purpose requires virological testing of drinking water from centralized water supply, as well as wastewater and open water. The study found out that, in contrast to Saint Petersburg and Novgorod Oblast, in the Sakha Republic (Yakutia) the rotavirus antigen was detected in samples of drinking water and wastewater almost every year. The analysis of how often the rotavirus antigen was found in drinking water showed that the first and most intense rise of the rotavirus antigen detection took place 2001-2002 (10.5 ± 3.3 and 26.8 ± 69%, respectively), due to the powerful effects of spring flooding on the Lena River in 2001 (Fig. 3). However, the RVI incidence remained at a relatively low level.

The second rise of the rotavirus antigen detection was recorded in 2008 (12.5 ± 2.9%), which preceded an increased morbidity. In 2011, with the maximum level of RVI incidence, there were relatively high detection rates of rotavirus antigen in drinking water (7.8 ± 3.4%). In 2012, along with the reducing incidence, there was registered a decrease in the frequency of antigen detection in drinking water to 3.5 ± 1.5%. [3]. However, in 2013, with an increase in RVI incidence, the virus antigen in samples of drinking water was not observed. The calculation revealed a direct weak correlation between the incidence and frequency of the rotavirus antigen detection in drinking water (Spearman's rank correlation coefficient $p=0.12$). Over the entire follow-up period, the average percentage of the rotavirus antigen detection in wastewater was 14.5 ± 1.0%, with the minimum rate in 2006 (4.1 ± 2.0%), and the highest in 2011 (23.8 ± 3.5%). These results indicate that the waterway RVI transmission has a certain impact, but it is not a risk factor, particularly in infants.

CONCLUSION

1. The results of the study showed that in the pre-vaccination period there were regional features of the RVI incidence, manifesting themselves in different intensity of the epidemiological process.

2. The age group of risk are children under 1 year and of 1-2 years of age, which corresponds to the data from statistics and literature on other regions and countries.

3. Water factor has a certain impact on RVI transmission in the Sakha Republic (Yakutia); however, its role has been decreasing lately.

4. The results of the study have proven the necessity of vaccination against RVI of children under 1 year of age.

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Life Quality of Patients with Viral Hepatitis and Cirrhosis

ABSTRACT

The WHO-100 questionnaire helps on researching the quality of life the of hepatitis and cirrhosis patients.

Research objective: to assess the quality of life (QoL) of chronic viral hepatitis (CHV) and cirrhosis (C) patients.

Due to the questionnaire there were examined 15 patients with CHV and C.

It is stated that chronic viral hepatitis reduces the quality of life on spiritual sphere, and the quality of life of cirrhosis patients were lower on all spheres (physical, mental, social and spiritual).

Therefore, rehabilitation activities must be not only medical, but also of psychological and sociocultural orientation. The "WHOQoL-100" questionnaire can be used as additional tool for estimating severity and also effectiveness of carried out medical and rehabilitation activities.

Keywords: quality of life, the WHOQoL-100 questionnaire, chronic viral hepatitis, cirrhosis.

INTRODUCTION

Quality of life is evaluation category of past, generally characterizing parameters of all components of its life: life opportunity, life-sustaining activity and standard of living (instruments, recourses and environment) – in relation to some objective or subjective standard [3]. The quality of life index takes into account the following rates: health and education situation, lifetime, local employment, its purchasing ability and access to politics [2]. In 2004 the President of the Russian Federation defined the quality of life as objective criterion of social and economic development of the Russian Federation. After years the top public officials made a speech repeatedly emphasizing the importance of targeting social and economic politics to improve the quality of life. The quality of life is determined first of all by opportunities of a human being (or society) to realize the life processes by life potentials. The second factor is process-productive characteristics of life in relation to people's needs, interests, values and goals. The third factor of quality of life is external opportunities, that is, environment, objects and subjects properties. It must be a kind of the vital functions of the first direction could certainly be carried out, and functions of the second would have a significant probability of achieving purposes for people

who want to do it and are willing to make for it essential efforts [4].

Research objective: to assess the quality of life (QoL) of chronic hepatitis viruses (CHV) and cirrhosis (C) patients.

MATERIAL AND METHODS

There was used the "WHOQL-100"questionnaire – multidimensional tool allowing to get both the respondent's assessment of quality of life in general and private estimates on certain spheres and subspheres of its life as a method of research.

Due to the questionnaire there were examined 15 patients with CHV and C. Diagnose of CHV was confirmed by discovering HBsAg, a-HBcor IgG, a-HDV, a-HCV and polymerase chain reaction method. Disease duration from the moment of diagnosis identification ranged from 6 months to 6 years. Diagnose of cirrhosis was confirmed by EGDS and Abdominal ultrasound. There were used nonparametric test of Manna-Whitney for comparison of mean score between groups. Distinction were considered statistically significant at $p<0.05$.

RESULTS AND DISCUSSIONS

It is stated due to the following research that the quality of life the patients with cirrhosis was lower than the patients with hepatitis viruses according to both dimensions of spheres of the WHOQoL-100 questionnaire and total integral estimation. Subjective assessment and quality of life of cirrhosis patients were lower than the patients with hepatitis viruses by 4 point ($p<0,05$).

As it shown in Fig.1, decrease dimensions of quality of life was recorded at the level of physical wellbeing which includes misery and discomfort, vitality, energy and weariness, sleep and relaxation ($p<0,05$). The decrease dimensions of QoL in this sphere are caused by weight of a current and existence of complications which considerably deteriorate physical condition of the patients.

Accentuated decrease dimensions of QL was recorded at the level of physiological weightiness the patients with cirrhosis which includes good vibes, thinking, educability, recollection, concentration, self-concept, appearance estimation, bad emotions (Fig.2). Such decrease is caused by an acute organism intoxication which occurs by lack of blood purification. Thereby the patient's vital potential decreases.

Decrease dimensions of QoL was observed at the level of the independence of CDLD patients, which includes degree of movement, capability to carry out daily routine, dependence on medicine and capability for work (Fig.3).

Differences were also observed in dimensions of sphere of social relationship of

respondents, including internal assessment of personal relationship and practical social support, and sexual activity (Fig.4). Diagnosis of cirrhosis, informing the patient and his relatives about disease severity and its outcome impact on character of personal relations, leading to emotional alienation of patients, incomprehension and support of relatives, but sometimes to making the break.

Dimensions of spiritual sphere (relation to religion and private persuasion) of QoL of cirrhosis patients were higher by 1.4 points than those GV and AG patients (Fig.5). We think that the higher patient's severity the more they turn to religion.

Total integral estimation of QoL of cirrhosis patients was lower by 1.7 points than the patients with GV ($p<0,05$).

We figure out the mean group estimation of QoL of cirrhosis and hepatitis viruses patients. Especially the lower group estimation of QoL of hepatitis viruses patients were by the following subspheres as vitality, energy, weariness, appearance estimation, dependence on medicine, capability for work, spirituality, religion, personal persuasion (Tab. 2).

The patients with cirrhosis have the lowest group estimation ("the worst" score) in sphere of dependence on drugs. Rating scale "worse" was by the following subspheres: misery and discomfort, vitality, energy, weariness, good vibes, thinking, learning, memory and concentration , self-estimation, appearance estimation, capability for carrying out daily routine, capability for work, personal relations, sexual activity, environment, medical and social support, possibilities for getting new information, transport, spiritual, religion, personal persuasion.

CONCLUSION

The chronic viral hepatitis and cirrhosis significantly reduce the quality of life of patients not only in physical and physiological well-being and social relations, relations to environment and independence level. Therefore, rehabilitation activities must be not only medical, but also psychological and sociocultural orientation. The "WHOQoL-100" questionnaire can be used as additional tool for estimating severity and also effectiveness of carried out medical and rehabilitation activities.

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Prerequisites of Ecological Safety of Animal Husbandry Products

ABSTRACT

This article presents the results about influence of motor transport on accumulation of heavy metals (HM) of lead, zinc, copper and cadmium in the soil and in fodder plants of pasturable grounds of the Khangalassky region. Results of our researches testify that the pasture of cattle in close proximity to a highway can be the prerequisite of impurity of animal husbandry products by heavy metals. As a result of analyses of samples of the soils selected in the Khangalassky region showed that concentration of Pb, Cd, Cu, Zn in a soil cover of pasturable grounds of the village of Tekhtyur and village Nemyugyu don't exceed the established sanitary and hygienic standards. It is revealed that the maintenance of Pb, Cd, Zn, Cu in fodder herbs of pastures of the village of Tekhtyur and village Nemyugyu depended on their concentration in the soil. Thus the level of cadmium and lead in plants isn't exceeded by maximum concentration limit, and concentration of zinc and copper in 5 m of a highway exceeded maximum concentration limit.

Keywords: heavy metals, fodder herbs, soil, highway, motor transport.

INTRODUCTION

Nowadays environmental pollution by chemical compounds, including heavy metals is one of the main problems. In nature plants are affected by many stressors of both a natural, and anthropogenic origin. Having got to the soil, heavy metals can then collect in plants and make negative impact on processes of a metabolism that as a result leads to reduction of a crop and pollution by toxicum of the subsequent links of a food chain. The main sources of pollution by heavy metals are: road and transport complex, industrial enterprises, unutilized industrial and household wastes [14, 15, 16].

The significant contribution to pollution of environment is made by motor transport. Intensive receipt in environment of heavy metals which are emitted with exhaust gases is connected with its operation. Combustion of ethylated fuel is accompanied by release of lead. At combustion of lubricant oils emitted is cadmium. A large number of this element is formed as a result of attrition of tires about asphalt concrete [9].

The problem of providing the population with ecologically safe agricultural production is the priority direction of development of economy of our republic. Within a problem the important place is allocated for questions of development of animal husbandry in densely

populated areas of the Republic of Sakha (Yakutia). However, in areas with anthropogenic load in ecosystem the solution is impossible without professional knowledge on migration and accumulation of heavy metals in the soil, sterns and livestock production.

Natural pasturable grounds in the Central Yakutia, namely in Khangalassky district are located along the highway of republican importance. Toxic connections from the fodder plants eaten by animals on a trophic chain passes into an organism of cattle, then into animal husbandry products (meat, milk) which are consumed by local population.

The aim to define the influence of motor transport on accumulation of heavy metals of lead, zinc, copper and cadmium in the soil and in fodder plants of pasturable grounds of the Khangalassky region.

MATERIAL AND METHODS

Researches were conducted in the Khangalassky region of the village of Tekhtyur and the village Nemyugyu (Oi village), in pasturable meadows of the emissions of the motor transport located in a zone of influence.

Tekhtyursky district is located (village of Tekhtyur) on the left coast of the Lena River, in upper courses of small rivers Bestyakh, Suon, Urekh, and small rivers of Kenkeme, from the center of the district of Pokrovsk on 47 km, distance from Yakutsk of 27 km. The spread of the republican highway passing through the territory of the village of Tekhtyur is 2.15 km, including with a hard coating of 2.15 km. Transport connection is all the year round.

Nemyugyunsky district (Oi village) it is located on the left coast of the Lena River and there is in 7 km from the center of the district of Pokrovsk, a distance from Yakutsk to Oi village is 67 km. The transport connection with Yakutsk and Pokrovsk is carried out all the year round on the republican importance highway "Umnas" with a hard coating. Total length the insight districts of roads makes 35 km, including with a hard coating of 7 km, from them is covered with asphalt of 3 km.

The selection and preparation of tests of the soil and fodder herbs carried out in accordance with GOST 28168-89, 26929-94 ("Soils Sampling", "Raw materials and foodstuff"). The Concentration of lead, cadmium, copper and zinc was determined by method of the nuclear and absorbing spectral analysis (AAS MGA-915) in the accredited laboratories of State Budgetary Institution Republic of Sakha (Yakutia) and State Budgetary Institution Republic of Sakha (Yakutia) "Yakut republican veterinary and test laboratory" (GOST 30178-96, GOST 28168-89), determined

the maintenance of a humus by Tyurin's (State standard specification 26213-84) method, pH in a water extract of the soil defined in accordance with GOST 26423-85 [3, 4, 5, 6, 7].

Fodder herbs collected during blossoming (July) in a dry sunny weather, according to the standard rules [4].

The concentration of Pb, Cd, Cu, Zn in samples of soils and herbs determined by a nuclear and absorbing method in a flame acetylene-air on the MGA spectrophotometer – 915. For extraction HM from soils we used acetate ammonium the buffer with Ph-4,8 at a ratio soil/solution – 1/10, extraction time 24 hours. Sample preparation of vegetable raw materials is carried out by method of a dry combustion with the subsequent extraction by the nitric acid diluted (1:1) extraction time 24 hours. Analyses made in triple frequency, results statistically processed with application of the Excel program – 2013.

RESULTS AND DISCUSSION

The contents of HM in soils of pasturable grounds of Khangalassky region

The special place among manifestations of anthropogenic impact on soils belongs to pollution of the territory heavy metals as fast self-cleaning of soils in the conditions of permafrost from metal pollution to the level demanded on hygienic and ecological safety is complicated [21].

According to the generalized scheme of soil geographical zoning (the Soils of the USSR, 1979), the zone of island and continuous distribution of permafrost within the North West - the Siberian lowland belongs to the West Siberian province gley weak-calx and undercalx and illuvial-humus soils of the Central taiga and forest region [10, 11].

Khangalassky region (the Central Yakutia) is generally located in a distribution zone of Permafrost cespitose and meadow types of soils on which grows the meadow vegetation [22].

The results of our researches showed that in pasturable meadows of Tekhtur village the maintenance of a humus varied from 3,2% to 10,2%, acidity of soils fluctuated from 6,5 – 7,5 (the subacidic and alkaline environment). Lead level in the soil fluctuated from 0,02mkg/g to 0,15 mkg/g, cadmium - 0,005 mkg/g to 0,02 mkg/g, zinc - 0,24 mkg/g to 0,45 mkg/g and copper - 0,10 mkg/g to 0,25 mkg/g.

In accordance with the data in table 1, in soils of pasturable grounds of Tekhtur village is the greatest accumulation of mobile connections zinc, the smallest cadmium. (tabl. 1)

Table 1

Concentration of HM in the soil of pasturable meadows of the Hangalassky region of the village of Tekhtyur

Heavy metals	MPC	Distance from a highway				
		Tekhtyur	5 m leftside	5 m rightside	200 m rightside	250m leftside
Pb, mgk/g	6	0,08±0,01	0,15*±0,03	0,14±0,02	0,10±0,03	0,02*±0,01
Cd, mgk/g	-	0,01±0,001	0,02±0,001	0,02±0,001	0,01±0,001	0,005±0,003
Zn, mgk/g	23	0,32±0,03	0,45*±0,05	0,42±0,03	0,37±0,03	0,24*±0,02
Cu, mgk/g	3	0,10±0,01	0,25±0,02	0,23±0,01	0,15±0,02	0,10*±0,01

Note: in Tables 1 and 2 * $p < 0.05$ in comparison of 5 m from a highway

Concentration of HM depended on distance from a highway. In 5 m from a highway of concentration of all four elements were higher, than at distance of 200-250 m. Thus the TM level in the soil was distributed in decreasing order of Zn >Cu>Pb> Cd.

However, bioaccumulation of HM and their mobility is defined by size pH and the maintenance of a humus in the alkalescent environment with decrease pH ion-exchange absorption of cationic forms of the pollutants getting to the soil considerably accrues; at anion forms inverse relationship is shown - their main weight is occluded in the alkalescent environment in which anions in a two-charging form prevail [16].

Possibly, high concentration of zinc in the soil, is connected by that zinc is an essentially microcell for soils, plants and the person. Besides, he treats elements kindly soluble in the soil. With a humus this element forms steady connections. Zinc adsorption by the soil depends from pH. In the alkaline environment zinc is adsorbed on the hemosorbtion mechanism, and in the sour environment there is a kationo-exchange absorption. At the increased acidity the share of mobile zinc. Most fully zinc is absorbed by iron oxides [12, 18].

Rather high concentration of copper it is also connected with pH. As in alkalescent and even to the neutral environment copper for a long time is late in the soil. However at the raised contents copper makes toxic impact, both on plants, and on the subsequent components of a food chain, including the person, and can be the cause of various chronic diseases [20].

In soils of pasturable meadows of the village Nemyugyu the humus varied from 1,8% to 3,6%, acidity of soils fluctuated from 7,5 to 8,5.

Accumulation and distribution of the elements determined by soils of the village Nemyugyu had the same regularity, as well as in soils of the village of Tekhtyur (tabl. 2).

Table 2

Concentration of HM in the soil of pasturable meadows of the Hangalassky region of the village Nemyugyu

Heavy metals	MPC	Distance from a highway				
		Nemyugyu	5 m leftside	5 m rightside	80 m rightside	300 m leftside
Pb, mgk/g	6	0,14±0,01	0,28*±0,02	0,25±0,01	0,15±0,02	0,04*±0,01
Cd, mgk/g	-	0,02±0,01	0,04±0,01	0,05±0,02	0,02±0,01	0,01±0,001
Zn, mgk/g	23	0,94±0,05	1,95*±0,10	1,90±0,11	0,52±0,05	0,44*±0,06
Cu,mgk/g	3	0,16±0,02	0,43*±0,03	0,42±0,03	0,19±0,01	0,15*±0,02

Data presented in table 2 testify that the HM level on pastures of the village Nemyugyu was statistically authentically higher, than in pastures of the village of Tekhtyur. Zinc was more in the soil in Nemyugyu 2,9 times, copper – 1,6 times, cadmium – 2 time, lead – 1,7 times.

Higher content of heavy metals in pasturable meadows in Nemyugyu village can be connected with populous (population of the village Nemyugyu 3,6 times higher, than the village of Tekhtyur) and with a close arrangement with Pokrovsk (7 km). On this interval of the republican road loading is raised a transport stream.

Results of our researches testify that the pasture of cattle in close proximity to a highway can be the prerequisite of impurity of animal husbandry products by heavy metals.

As a result of analyses of samples of the soils selected in the Khangalassky region showed that concentration of Pb, Cd, Cu, Zn in a soil cover of pasturable grounds of the village of Tekhtyur and village Nemyugyu don't exceed the established sanitary and hygienic standards [1, 2, 19].

The maintenance of HM in fodder herbs of pasturable grounds of the Khangalassky region. Plants are the second important factor on the way of movement of heavy metals on a food chain in a human body. Root systems are capable to keep rather big quantity of ions that is connected with cumulative action of morphological structures and chemical reactions of the nonspecific nature which treat the exchange capacity of roots, concentration of metals in vacuoles, a chemical inactivation of specific connections [17].

Vegetable forages are the important power supply for animals, both in summer, and in winter time, and impurity of forages of HM is reflected not only in animals, but also in human health. It is already proved that such elements as cadmium and lead are carcinogens. According to medical statistics of Republic of the Sakha (Yakutia) mortality from oncological diseases for the last five years increased more, than twice [8].

In tables 3 and 4 presented a data about the contents of HM in fodder herbs of pastures of the village of Tekhtyur and village Nemyugyu. Concentration of lead in meadow herbs fluctuated from 0,10 mg/kg to 0,15 mg/kg, zinc from 31,34 mg/kg to 42,70 mg/kg, copper from 7,80 to 15,23 mg/kg, and cadmium was found only in the item Tekhtyur (tabl. 3).

Table 3

Concentration of HM in fodder herbs of pasturable meadows of the Hangalassky region of the village of Tekhtyur

Heavy metals	MPC	Distance from a highway				
		Tekhtyur	5 m left side	5 m right side	200 m right side	250 m left side
Pb, mg/kg	5,0	0,15±0,02	0,11±0,05	0,10±0,03	0,21±0,03	0,10±0,02
Cd, mg/kg	0,5	0,01±0,00	0	0	0	0
Zn, mg/kg	10-50,0*	31,34±0,11	34,49±0,18	42,70±0,20	39,46±0,23	31,98±0,17
Cu, mg/kg	1,0-10*	10,55±0,15	7,80±0,10	15,23±0,12	11,18±0,12	8,16±0,11

The greatest accumulation of heavy metals in fodder herbs was revealed in 5 m from a highway, the smallest - in 250 m. In the herbs growing in the item Tekhtyur and in 200 m from the road on the right side the level of copper corresponded to the upper bound of maximum concentration limit. The results received that do not contradict literary data [20, 21].

Table 4

Concentration of HM in fodder herbs of pasturable meadows of the Hangalassky region of the village of Nemyugyu

Heavy metals	MPC	Distance from a highway				
		Nemyugyu	5 m left side	5 m right side	80 m right side	300 m left side
Pb, mg/kg	5,0	0,26±0,05	0,35±0,08	0,22±0,05	0,25±0,06	0,38±0,03
Cd, mg/kg	0,5	0,01±0,00	0,01±0,00	-	0,01±0,00	0,02±0,00
Zn, mg/kg	10-50,0*	50,83±0,18	85,84±0,21	61,86±0,40	47,87±0,24	36,16±0,23
Cu, mg/kg	1,0-10*	13,50±0,11	19,23±0,14	16,64±0,13	26,12±0,15	25,39±0,17

High concentration of lead in 300 m of the left side from a village Nemyugyu highway, it is possibly caused by anthropogenic factors: motor transport of local population. Unlike the village of Tekhtyur in herbs of pastures of the village Nemyugyu cadmium was found. However it is concentration were much lower than maximum concentration limit (tabl. 4).

Distribution of concentration of HM in vegetable sterns of the village Nemyugyu and Tekhtyur had the same character, as well as in soils of pastures: Zn>Cu>Pb>Cd. That is the level of microcells in plants directly depends on their contents in the soil in which they grow. This fact shows that the prerequisite of ecological safety of animal husbandry products is monitoring of element structure of soils.

High levels of zinc and copper in plants are caused to their physiological meaning. Copper in plants plays an important role in oxidation-reduction processes, improves intensity of photosynthesis, and promotes formation of chlorophyll. Zinc in a vegetable organism activates 30 fermental systems in a cell. In plants, along with participation in breath, proteinaceous, carbohydrate and nucleinic exchanges, zinc regulates growth, influences formation of amino acid of tryptophane and raises the maintenance of phytohormones. Zinc is necessary for normal development of an ovum and a germ of plants. It raises hot-, warm- and cold constancy of plants, and a physiological role of copper in a vegetable organism is closely connected with its participation in the fermentativnykh processes directly as catalyst or as a part of cupriferous enzymes. It increases intensity of breath, catalyzes oxidation of ascorbic acid, provides assimilation of nitrate nitrogen and fixing of nitrogen of the atmosphere. Copper is necessary to plants for formation of chlorophyll, participates in a metabolism of proteins and carbohydrates [1, 2, 21].

Excess of maximum concentration limit of copper and zinc in fodder herbs leads to increase in their contents in an organism of pets. High concentration of copper and zinc in muscular tissue and in bodies of cattle can debalance metabolic balance of other metals that can break activity of many enzymes and a metabolism, leading to pathology not only animals, but also the person. Disbalance of the relation copper/zinc is the main causal factor in development of coronary heart disease. At increase in level of copper in a human body there is growth stop, гемолиз, and decrease in the content of hemoglobin, degradation of tissues of liver, kidneys and a brain [21].

Thus, determination of level of heavy metals in the soil and fodder plants is necessary for environmental monitoring of environment. As heavy metals on a food chain get to a human body and there can be the reason do not adaptation of violations and pathological conditions of the person in the north.

CONCLUSIONS

1. It is established that in soils of pasturable grounds of the village of Tekhtyur and the village Nemyugyu of the Khangalassky region concentration of Pb, Cd, Zn and Cu don't exceed maximum concentration limit.

2. Concentration of heavy metals depends on distance from a highway: in 5 m of concentration of all four elements were higher, than at distance of 200 - 300 m.

3. It is revealed that contents of Pb, Cd, Zn, Cu in fodder herbs of pastures of the village of Tekhtyur and village Nemyugyu depended on their concentration in the soil. This level of cadmium and lead in plants isn't exceeded by maximum concentration limit, and concentration of zinc and copper in 5 m of a highway exceeded maximum concentration limit.

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Contributions

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Mortality of Population in Northern and Arctic Regions of the Republic of Sakha (Yakutia) in the Aspect of Demographic Security

ABSTRACT

There are some problems in maintaining the demographic safety in the Republic of Sakha (Yakutia). Such integral indicators as life expectancy, depopulation index and total fertility rate can be applied as indicators of demographic safety. In aggregated form they characterize reproduction of the population, the basic concept that lies in demographic safety entity.

The Arctic is a region of prospective industrial development of natural resources. It is important to have demographic potential with the necessary quantitative and qualitative parameters.

Mortality processes are the most important in terms of demographic safety for the Arctic and Northern regions of the Republic. Current state of population mortality is estimated as representing a certain threat to the demographic security. There were positive signs for the 2009-2014 years: the number of deaths and the overall death rate were decreased. However, mortality rates are significantly higher than the average for the Republic.

The infant mortality rate, which is estimated in the world community as an indicator of social welfare society, has extremely uneven dynamics that due to the presence of demographically small aggregates. Over the years, the infant mortality rate is higher than the average for the Republic.

High mortality due to external causes of death remains the essential point in the characterization of mortality in the Arctic regions of Yakutia. In most of the Arctic and Northern regions of the Republic, the absolute number of deaths from external causes was decreased. However, stable high indicators compared with average coefficients for the Republic are marked there. For example, in the Allaihovskiy district in 2012 year mortality from suicide was above the national average of 7.75 times and in 2014 year in Anabarskiy district –7.8 times.

Elevated levels of population losses as a result of external causes of death requires special measures to preserve the demographic potential of Arctic regions, having a special geopolitical importance and representing the main resettlement area of the small-numbered indigenous peoples of the North.

Keywords: mortality, infant mortality, external causes of mortality, demographic security, the indigenous peoples of the North.

INTRODUCTION

Intensification of public attention to demographic problems is not least caused by national geopolitical interests. The Russian Federation with its vast poorly developed spaces is in a geopolitically dangerous situation being contiguous with demographically redundant states. Geopolitical security largely depends on a degree of development and population of border territories. Meanwhile, strategically important territories of the Far East lose its population. These moments make actual attention to problems of demographic security of Far Eastern regions.

The demographic security implies such a state of demographic processes, which is sufficient for reproduction of population without a significant influence of external factor and provision by human resources of geopolitical interests of state [6,22]. To assess the demographic security threshold values are applied, achievement of which means violation of normal course of development of various elements of reproduction and leads to formation of negative destructive tendencies in the provision of security [1,45]. In our opinion, as indicators of demographic security only integral indicators can be applied, which in an aggregated form characterize the reproduction of population – that main concept that is laid in the main point of demographic security. This is a lifespan, and a conditional depopulation coefficient and a total fertility rate, which are formed according to processes of mortality of population, population dynamics, and processes of fertility [3].

In an analysis of demographic security for arctic and northern regions of the Republic from the demographic processes are the most significant processes of mortality. The Arctic is a region of promising industrial development of natural resource potential, for which it is important to have demographic potential with necessary quantitative and qualitative parameters. Provision of demographic reproduction, without which it is impossible to have necessary labor potential of region, can be considered as one of factors of sustainable development of the Arctic. Another fact making actual the attention to the processes of mortality of population of this region is a fact that the main area of settlement of indigenous small-numbered peoples of the North is in the

Arctic. These peoples according to international criteria are classified as endangered ethnic groups, which causes special attention to the demographic reproduction of population.

The objective of research: to analyze the processes of mortality of population in the arctic and northern regions of the Republic of Sakha (Yakutia)

MATERIALS AND METHODS

In an analysis there were used statistical data on the mortality of population – a crude death rate, an infant mortality rate, mortality according to causes of death, including from external causes of death (murders, suicides, injuries, poisonings, etc.). Indicators of demographic security have been calculated on the basis of indicators of depopulation of population, the total fertility rate and life expectancy.

RESULTS AND DISCUSSION

In general for the Republic of Sakha (Yakutia) in preservation of demographic security there are quite definite problems, as evidenced by the dynamics of indicators of demographic security (table 1).

Table 1

Dynamics of indicators of demographic security in the Republic of Sakha (Yakutia)

Indicators	Threshold value	1990	2000	2005	2009	2010	2014
Depopulation coefficient	1	0.345	0.709	0.708	0.586	0.583	0.483
Total fertility rate	2.15	2.46	1.77	1.74	2.00	2.01	2.25
Life expectancy, number of years	75	66.24	63.66	64.68	66.42	66.75	69.81
Deviation of actual indicator from threshold value, %							
Depopulation coefficient	100	34.5	70.9	70.8	58.6	58.3	0.483
Total fertility rate	100	114.4	82.3	80.9	93.0	93.5	104.7
Life expectancy, number of years	100	88.3	84.9	86.3	88.7	88.9	93.08

The problems of demographic security are particularly relevant for the arctic and northern regions of the Republic having particular importance in a geopolitical sense for the Republic, and for the entire Russian Federation. Practice shows that the demographic problems for the northern territories not only retain their significance, but also worsen [2].

Unlike a birth rate, where the situation is sufficiently safe, the processes of mortality of population are the biggest threat for the demographic reproduction. In the dynamics for 2009-2014 there are positive changes, namely a decrease of number of the deceased and the crude death rate. But a level of mortality considerably exceeds an average level in the Republic; and in certain regions an excess is very significant. For example, in 2013 the death rate in Eveno-Bytantaysky District was almost 80% higher than the regional average, in Allaikhovsky District - by 68%. In 2012 in the same district the excess amounted to 55.9%. As a result the high mortality rate determines a lag of the arctic regions in a level of natural increase: in general in the Republic it was 8.8‰, in the arctic regions it was only 7.3‰. This situation is typical for the arctic regions over a sufficiently long period of time [4, 32].

An ambiguous situation is observed in a sphere of infant mortality, which in the world community is regarded as an indicator of social well-being of society. The dynamics of this indicator in certain areas is extremely uneven, which is associated in some way with presense of demographically small aggregates. But over the years the mortality rate of children under the age of 1 year was higher than the average in the Republic (table 2).

Table 2

Dynamics of infant mortality rate in arctic districts of the Republic of Sakha (Yakutia), 2010-2014

	2010	2011	2012	2013	2014
Abyysky	14.9	13.2	0.0	14.3	0.0
Allaikhovsky	0.0	18.5	0.0	20.0	18.0
Anabarsky	18.2	14.7	15.6	12.7	13.0
Bulunsky	16.0	20.0	14.0	7.0	0.0
Verkhnekolymsky	0.0	0.0	14.5	0.0	0.0
Verkhoyansky	12.5	5.0	4.7	9.1	12.3
Zhigansky	20.8	0.0	11.4	0.0	0.0
Momsky	12.0	0.0	29.4	11.5	10.1
Nizhnekolymsky	41.5	12.8	13.3	12.2	0.0
Olenyoksky	20.2	0.0	9.9	20.2	0.0
Srednekolymsky	7.2	13.8	6.9	0.0	0.0
Ust-Yansky	20.8	19.2	31.5	16.1	7.3
Eveno-Bytantaysky	0.0	35.7	0.0	31.2	16.4
On average for group	14.2	11.8	11.6	11.9	5.9
Total for the Republic of Sakha (Yakutia)	7.2	6.3	9.6	9.6	7.9

As an essential point in a characteristic of mortality in the arctic regions of Yakutia high mortality due to the external causes of death remains. During 2010-2014 the mortality indicators due to these reasons per 100,000 people in all regions of the Arctic (with few exceptions) were higher than the average for the Republic (table 3). Moreover, in some regions this excess was exceptionally high: in 2012 in Allaikhovsky District the mortality from the external causes was higher than the average republican level by a factor of 3.63, in 2014 by a factor of 3.02.

Table 3

Dynamics of death rates of population in northern and arctic districts of the Republic of Sakha (Yakutia) due to external causes of death for 2010-2014 (per 100,000 people)

Districts	2010	2011	2012	2013	2014	2014/2010
Abyysky	225.1	205.1	323.4	164.7	376.4	1.67
Allaikhovsky	261.4	302.1	621.3	391.2	462.3	1.77
Anabarsky	370.2	433.9	205.3	440.7	323.2	0.87
Bulunsky	448.4	388.0	327.0	149.1	195.0	0.43
Verkhnekolymsky	210.2	151.2	177.9	160.0	205.7	0.98
Verkhoyansky	334.6	302.1	245.5	210.9	244.7	0.73
Zhigansky	256.9	303.5	93.4	234.3	210.9	0.82
Momsky	268.8	317.0	160.3	139.9	256.4	0.95
Nizhnekolymsky	512.8	239.5	177.9	338.2	202.9	0.40
Olenyoksky	389.0	486.9	516.2	349.4	299.5	0.77
Srednekolymsky	341.9	204.0	271.2	341.5	91.9	0.27
Ust-Yansky	284.4	340.4	260.1	509.2	254.6	0.90
Eveno-Bytantaysky	349.9	351.9	284.7	71.5	250.3	0.72
On average for group	327.2	309.7	281.9	269.3	259.5	0.79
Total for the Republic of Sakha (Yakutia)	195.4	181.8	171.3	160.5	152.9	0.78

Although in most arctic and northern regions of the Republic the mortality due to the external causes decreased, nevertheless consistently high indicators during 2010-2014 were

registered in Abyysky, Allaikhovsky, Anabarsky, Verkhoyansky, Nizhnekolymsky, Olenyoksky and Ust-Yansky Districts. In 2 regions an increase of mortality from the external causes was noted – Abyysky and Allaikhovsky Districts.

In a structure of mortality from the external causes in the Republic of Sakha (Yakutia) the suicides and murders take up a major share (in 2014, respectively, approximately 22% and 16%). In the arctic and northern group of regions this indicator is even higher: the suicides are on average 24%, the murders are 18%.

In the dynamics the share of the arctic and northern regions in the total number of the deceased from the suicides decreased from 17.6% to 12.3% of all deaths from the suicides in the Republic of Sakha (Yakutia). Although the overall dynamics is positive, but the mortality of population from suicides in the arctic regions consistently higher compared to the average level in the Republic with only very few exceptions (Table 4).

Table 4

Mortality of population of northern and arctic districts from suicides for 2010-2014 (per 100,000 people)

Districts	2010	2011	2012	2013	2014	2014 / 2010
Abyysky	67.5	45.6	46.2	47.0	70.6	1.046
Allaikhovsky	0.0	33.6	310.7	71.1	106.7	3.176*
Anabarsky	142.4	173.6	88.0	88.1	264.4	1.857
Bulunsky	145.7	107.8	130.8	34.4	80.3	0.551
Verkhnekolymsky	0.0	21.6	44.5	22.9	22.9	1.060*
Verkhoyansky	93.4	23.8	16.4	59.1	25.3	0.271
Zhigansky	93.4	140.1	23.3	23.4	46.9	0.502
Momsky	67.2	45.2	0.0	0.0	23.3	0.347
Nizhnekolymsky	21.4	43.5	22.2	45.1	0.0	2.107**
Olenyoksky	46.8	121.7	196.7	99.8	124.8	2.667
Srednekolymsky	151.9	12.7	90.4	78.8	13.1	0.086
Ust-Yansky	111.3	113.5	91.1	53.6	40.2	0.361
Eveno-Bytantaysky	174.9	70.4	35.6	35.8	71.5	0.409
On average for group	85.8	73.3	84.3	50.7	68.5	0.798
Total for the Republic of Sakha (Yakutia)	40.8	39.7	40.1	35.8	33.9	0.831

*2014/2011

**2013/2010

And in individual districts and in particular years, as in the case of infant mortality, the excess is very considerable. For example, in 2012 the death rate due to the suicides in Allaikhovsky District was above the average republican coefficient by a factor of 7.75, in 2014 in Anabarsky District - by a factor of 7.8. A decrease of mortality indicator from the suicides in 2014 compared with 2010 was registered in most regions of arctic and northern groups.

Another significant cause of population deaths from the external causes are the murders. A relative share of arctic and northern regions in the total number of the deceased from the

murders in the Republic of Sakha (Yakutia), unfortunately, rose from 11.2% in 2013 to 16.7% in 2014. In general in the Republic the mortality as a result of murders constantly decreases from 34.3 per 100,000 population in 2010 to 21.9 in 2014, i.e., by 36.2%. In the arctic and the northern districts the dynamics is very uneven (table 5).

Table 5

Mortality of population of northern and arctic districts from murders for 2010-2014 (per 100,000 people)

Districts	2010	2011	2012	2013	2014	2014 /2010
Abyysky	67.5	22.8	23.1	47.0	141.1	2.090
Allaikhovsky	130.7	33.6	69.0	35.6	71.1	0.544
Anabarsky	0.0	57.9	29.3	88.1	0.0	1.522*
Bulunsky	89.7	64.7	98.1	34.4	22.9	0.255
Verkhnekolymsky	21	21.6	66.7	45.7	91.4	4.352
Verkhoyansky	54.5	55.6	73.7	25.3	33.8	0.620
Zhigansky	70.1	46.7	46.7	46.9	0.0	0.669**
Momsky	67.2	67.8	22.9	46.6	69.9	1.040
Nizhnekolymsky	42.7	65.3	44.5	22.5	90.2	2.112
Olenyoksky	24.3	73.0	0.0	49.9	25.0	1.029
Srednekolymsky	63.3	25.5	51.7	13.1	26.3	0.415
Ust-Yansky	49.5	12.6	39.0	80.4	67.0	1.354
Eveno-Bytantaysky	35.0	70.4	142.3	0.0	71.5	2.043
On average for group	55.0	47.5	54.4	41.2	54.6	0.993
Total for the Republic of Sakha (Yakutia)	34.3	27.9	28.0	26.2	21.9	0.638

*2013/2011

**2013/2010

Despite the decline of indicator on the whole in the Republic, in most regions of arctic and northern group the mortality due to the murders increased and in some areas very considerably.

For example, in Nizhnekolymsky District by a factor of 2.112, in Abyysky District – by a factor of 2.090, Eveno-Bytantaysky District – by a factor of 2.043.

The mortality of population of northern and arctic districts from accidental alcohol poisonings does not have a sufficiently large contribution to the total number of the deceased. On the whole in the Republic the share of the deceased for this reason amounted to 4% of the total number of the deceased from the external causes, and in the arctic and northern regions – 2%. The mortality due to this cause of death in the arctic and northern regions is not recorded every year: in 2010 in 6 regions out of 13, in 2011 - in 3, in 2012-2014 – 3 regions. But during 2010-2014 the death rates due to this cause of death were higher than the average for the Republic of Sakha (Yakutia).

Likewise episodically as the mortality from accidental alcohol poisonings, the mortality due to transport injuries is registered. In the structure of external causes in the arctic and northern regions a share of death cases of population from all types of transport injuries is on average 5% (for comparison, the Republic of Sakha (Yakutia) – 10%), which is completely explainable by a low level of transport development in the North. During 2010-2014 individual death cases due to transport reasons were registered and not in all regions (only in 9 of 13 northern and arctic districts). As in the mortality from alcohol poisonings, in case of registration of mortality from transport injuries in the arctic and northern regions its level was higher than on the average in the Republic. But in our opinion this is explainable to a greater extent by a paucity of these regions, specificity of demographically small aggregates.

The attention to questions of demographic security of the Arctic is made actual by the fact that it is inhabited by the indigenous small-numbered peoples of the North, which by international standards are classified as the endangered ethnic groups with a population of no more than 50,000 people. The increased mortality, especially from the external causes of death, should cause a chain of other actions in a population policy – a development of individual measures on preservation of demographic potential of indigenous small-numbered peoples of the North, creation of socio-economic conditions of increased comfort, etc. However, the places of compact living of these peoples not only lack a higher quality of life, but, on the contrary, are more disadvantaged in terms of social infrastructure [5]. Meanwhile, the places of compact living of peoples of the North originally had a goal to create special conditions for a recovery of

demographic well-being of these peoples. There is no doubt that a lag of social infrastructure exerts a quite definite influence on a course of demographic processes.

CONCLUSIONS

In the Republic of Sakha (Yakutia) there are quite definite problems in the preservation demographic security. The present state of processes of mortality in the northern and arctic regions can be assessed as representing certain threats for the demographic security. The arctic and northern regions are characterized by higher indicators of population mortality especially due to the external causes of death. An increased level of population losses as a result of external causes of death requires adoption of special measures on the preservation of demographic potential of the arctic regions having the particular geopolitical significance and representing the main area of settlement of indigenous small-numbered peoples of the North.

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Physical Efficiency and Lipid Peroxidation in the Sportsmen in the Far North

ABSTRACT

The article presents results of studies of physical capacity and lipid peroxidation in the highly skilled sportsmen - single combat wrestlers in the Far North. It was shown that the level of physical capacity of sportsmen - single combat wrestlers was depended on the cardiorespiratory system indices, which was manifested in a significant predominance of the effects of the parasympathetic system on the cardiovascular system and the greater lability of regulatory mechanisms. The intensity of lipid peroxidation and antioxidant system state affect the physical capacity of the sportsmen - single combat wrestlers.

Keywords: physical capacity, Kerdo vegetative index, cardiorespiratory system, lipid peroxidation, antioxidant system.

INTRODUCTION

The physical working capacity of sportsmen is an integral indicator of the final outcome of adaptive changes in the body of his physical abilities and the ability to withstand intense exercise and largely determines sporting achievements [2]. Physical activities increase level of consumption of oxygen that conducts to acceleration of oxidizing processes; therefore one of criteria of an objective assessment of level of special readiness of the athlete is studying of intensity of lipid peroxidation.

Physical activity increases the level of oxygen consumption, which leads to an acceleration of oxidation processes, in this regard, one of the criteria for an objective assessment of the level of special readiness of sportsman consider is the study of intensity of lipid peroxidation.

It is known that physical working capacity dependent on the morphological and functional condition of all systems of the organism and on the various factors, which role differs depending on sports specialization, age, etc.. The main functional system of limiting physical capacity of sportsmen is the cardiorespiratory system [7].

MATERIAL AND METHODS

The study was conducted on 29 sportsmen-single combat wrestlers of high qualifications (candidates for the master of sports (cms) and the master of sports (ms)), aged 17-21 years.

For establishment of interrelation of physical working capacity with oxidative processes in an organism of athletes we determined intensity of lipid peroxidation (LPO) by accumulation of TBA - reactive product (TBA-AP) [9]. The condition of antioxidant system was determined by the total content of low molecular weight antioxidants (LMAO) in erythrocytes membranes by spectrophotometric methods prior to the test load [6].

To determine the vegetative support the adaptation process in sportsmen, we considered: frequency of heartbeat, arteriotony, the pressure pulse (PP), a Kerdo vegetative index (KerdoVI) not only at rest, but also under the influence the dosed physical load bicycle [3]. Measurement of cardiovascular held at rest in a sitting position after 5 minutes of taking this position. Heart rate per of minute measured by palpation in the projection of the radial artery. Measurement of systolic and diastolic blood pressure was carried out on the left hand on the standard method of S. V. Korotkov.

The general physical operability of PWC170 was defined, on the Neyrosoft stationary bicycle (Ivanovo), thus registered the maximum consumption of oxygen (MCO). Examinees carried out on the stationary bicycle two burdens of moderate intensity with a frequency of 60 rev / min shared 3 – a minute interval of rest. Each load lasted 5 minutes. As a result, all the sportsmen were divided into four groups: the first group consisted of sportsmen with a low capacity for work, the second - with the capacity below average, the third - with an average capacity for work and the fourth - with the capacity above average.

In the quiescent state (before loading) and in the first minutes of recovery (after to loading) for during 30 seconds measured the heart rate (HR) and arteriotony. After each of physical exercise was counted pulse recovery time (in minutes) [1].

The material for investigations heparinized blood. Blood sampling was perfomed in the morning on an empty stomach from the cubital vein.

The study was approved by the decision of the local Ethics Committee at FGBNU "Yakut Scientific Center of complex medical problems."

Statistical processing of received data was performed using statistical software application package STATISTICA 6.0. Applied standard methods of variation statics was used: Calculation of mean values, standard deviations, 95% of a trusting interval. The significance of differences between mean values was evaluated by nonparametric method «Kolmogorov-Smirnov». Data in tables are presented as M ± m, where M - average, m - an error average. Probability of the null hypothesis accepted at $p < 0.05$.

RESULTS AND DISCUSSION

Studies of the functional state of athletes have shown that 31% of those surveyed have a low physical working capacity, 26% – below an average, 26% – average and only 17% – above an average, results of PWC170 are presented in table 1. According to literary data, at healthy young men of the meaning PWC170 fluctuate ranging from 850 to 1100 mkg/min., and at the sportsmen who are engaged in single combats, the general physical working capacity fluctuates ranging from 1370 to 1594 кгм / mines (approximately on 30 - 40% surpass data not of coaching men) [1]. The research results show that the indicators of of the cardiorespiratory system in sportsmen are within of norms age, but there are some differences in the study groups (Table 1).

So, in the group of sportsmen with a low capacity the level of Pulse pressure is more high as compared to other groups, but the level of Maximal Consumption of oxygen is mionectic on 32%, what in the group of sportsmen with a good capacity (tabl.1), that testifies to the low aerobic productivity which isn't satisfying oxygen inquiry at intensive loadings.

Distinctive feature of sportsmen with low working capacity is that the blood circulatory system at them is under control of sympathetic system, KerdoVI – positive (table 1). It is known that excessive sympathetic influence leads to deterioration of a metabolism of skeletal muscles, in particular, to decrease of the activity of LDG in them, and, therefore, and to violation of processes of utilization of a lactate. Decrease in working capacity can be also a consequence of violations of a power exchange, first of all reduction of efficiency of aerobic oxidation, transition of power supply to more "expensive" anaerobic way, and, therefore, and increases in need for oxygen which were found.

Table 1

Indicators of a functional condition of athletes with various working capacity to behavior of the testing load (M±m)

Indices	working capacity			
	low	Beneath low	medium	Higher than medium
PWC kgm/min	870±41	1160±31	1305±22	1614,00±82**
HRF, beats / min	76,24±2,89	79,66±6,80	67,62±2,98	66,00±4,08*
ADs, mmHg	118,12±2,91	109,00±5,09	110,00±2,67	108±8,36*
ADd, mmHg	76,56±3,17	74,00±4,00	73,75±2,63	74,00±5,09
PD, mmHg	41,56±3,70	35,00±2,23	36,25±1,82	34,00±2,44*
VIK, CU	1,78	-1,14	-4,96	-18,18
Δ VIK, CU	+40,86	+50,14	+55,70	+67,72
MO**C,** l/min	2,75±0,23	3,26±0,35	3,57±0,31	3,99±0,37*
t HRFR, min.	4,31±0,69	2,83±0,60	2,62±0,49	1,8±0,20**
t ADR, min.	3,86±0,41	3,33±0,55	3,00±0,50	2,88±0,66*

Note: ** p<0.01 in comparison with the I group, * p<0.05 in comparison with the I group

In group of athletes with good working capacity, KerdoVI in an intact state was equal – 18.18 conventional units (table 1) that is characteristic for a "sports" vegetative profile of athletes of high qualification [8,4]. In athletes with a good capacity for work at intensive loads mechanisms of rapid mobilization of metabolism were developed due to significant activity of the sympathetic system, Kerdo ΔVI was on 40% higher than in the group of athletes with a low capacity for work.

In groups of athletes with average working capacity above average is noted reduction frequency of heartbeat at rest that is one of the most important effects of an ekonomization of hearted activity. The increase in duration of a phase of relaxation (diastole) provides a bigger blood-groove and the best supply of a cardiac muscle with oxygen. High physical performance is characterized by the greatest reduction of a myocardium. The athlete's myocardium with high physical performance spends the smaller effort to propulsive action of the heart, than the athlete's myocardium with low working capacity at similar loadings is considerable. At any average the HELL and the minute volume of blood, higher frequency of heartbeat is followed by big consumption of oxygen, and consequently, smaller efficiency of functioning of a myocardium.

After performance work of veloergometer in all groups of athletes the sharp increase in sympathetic influences which is possibly caused by activation of simpathicus adrenalovy system at physical activities was observed.

At athletes with low working capacity after performance of the submaximum veloergometric work, time of restoration of frequency of heartbeat and HELL passed more long in 2.4 ($p<0.01$) and 1.3 ($p<0.05$) time respectively, than in group of athletes with working capacity above average (tab. 2). Between physical working capacity and time of restoration of frequency of heartbeat negative correlation communication is noted ($p<0.01$). Between restoration time the HELL and a vegetative index of Kerdo positive correlation communication is revealed ($p<0.05$).

It is known that activation of LPO is a universal response to numerous factors. Intense physical activity, excessive activating PAUL, increase the permeability of the membrane of the nerve fibers and the sarcoplasmic reticulum myocytes, which hinders the transfer of motor nerve impulses and reduces the possibility of contractile muscle. Damaging effects on lipid peroxidation tanks containing calcium ions, inevitably leads to the dysfunction of the calcium pump and deterioration of muscle relaxation properties, moreover when damaged mitochondrial membranes decreases the efficiency of oxidative phosphorylation, which leads to a reduction in energy supply aerobic muscular work. These data indicate that our results are consistent with the literature data [5].

A comparative analysis of the level of lipid peroxidation products alone, prior to the test load showed that the first group of athletes with low performance of athletes, and the second - with the performance below the average concentration of TBA - AP was 1.87 times higher ($p<0.01$) and 1.96 times ($p<0.01$) compared with the fourth group of athletes with the performance above average (Figure 1).

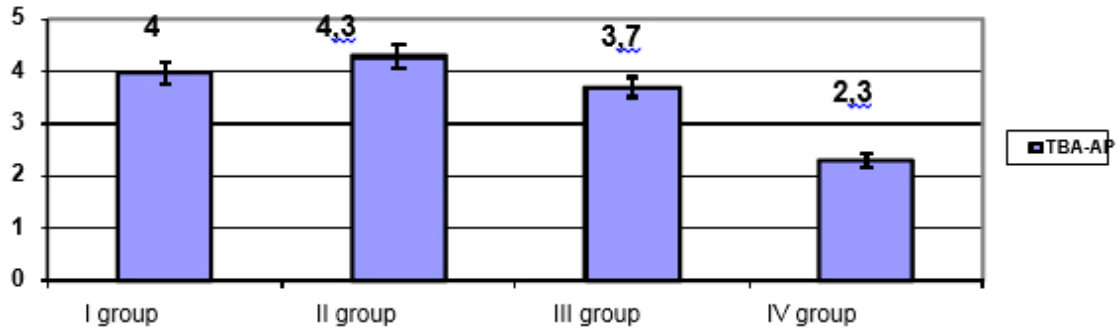

Fig. 1. TBA-AP level (mkmol/ml) in the erythrocytes membranes in the sportsmen with various physical capacity

In turn speed the lipid peroxidation depends on a condition of AOS. Determination of Lmao in erythrocyte membranes revealed that the athletes first, second and third groups Lmao content was reduced, compared with the athletes of the fourth group (Figure 2).

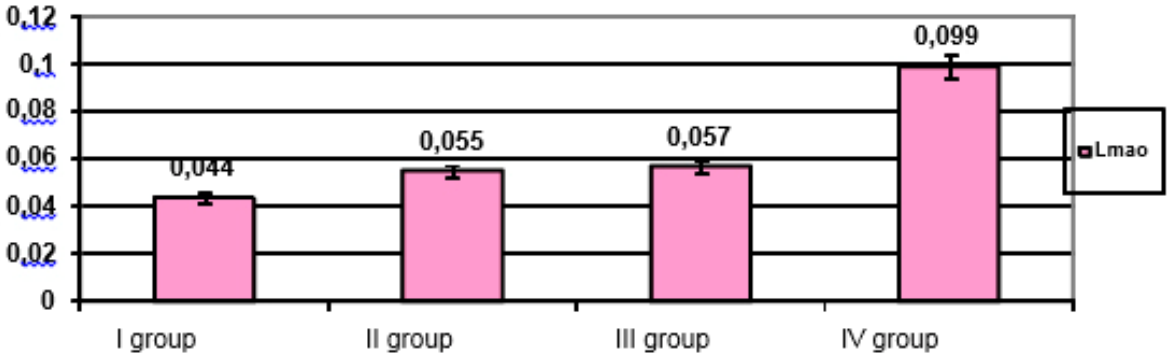

Fig. 2. The sum content Lmao (mgequ/ml*er) of the low-molecular oxidants in the erythrocytes membranes in the sportsmen with various physical capacity

Athletes first group by 56% in the second group of athletes by 45% and the third group of athletes by 43%.

Correlation analysis showed that the concentration of TBA-AP has a negative correlation with RWC170 ($p < 0.05$). Content Lmao has a positive correlation with RWC170 $r = 0,645$ ($p < 0.05$). The highest rates were observed physical performance in athletes with low tiobarbiturat-active products and high content of low molecular weight antioxidants.

CONCLUSIONS

1. The level of physical performance of athletes, martial artists and their adaptive potential depends on the parameters of the cardiorespiratory system, which manifests significant prevalence of parasympathetic influences on the cardio vascular system and the greater stability of regulatory mechanisms.
2. The intensity of lipid peroxidation and condition of antionsidant system affects the physical performance of athletes, martial artists.

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Food Preference Reflects Adaptation to the Living Conditions in the North

ABSTRACT

The article presents the materials of the leading researchers on the issue of the traditional food of indigenous residents of Yakutia in the extreme conditions of the North.

Keywords: nutrition, tradition, the North, adaptation, indigenous population.

INTRODUCTION

The tradition of eating is one of the markers of national identity in the eyes of members of the ethnic group and the fellows. People, whose eating habits are largely urbanized and "westernized", are at increased risk of serious imbalance of eating [38]. Asit shows from the experience of other countries and regions, underestimating the influence of traditionalism in food would be a serious mistake [27] and it’s increasingly becoming a significant force [19, 35].

In the scientific literature, there are explanations of the different prevalence of cardiovascular disease, including hypertension and atherosclerosis (as the most important risk factors for stroke) among representatives of different ethnic groups influenced by the nature of eating, and above all the salt regime, employment, indigenous traditional activities, migration, urbanization [43, 44].

In the literature there are researches of a wide range and high content in food of people from regions with high longevity, whose ration includes high amount of antioxidants, well known “geroprotectors” [47].

Note that some features of the eating of the Arctic and Subarctic Aboriginals depends not only on social and cultural, but genetic factors. In particular, it was shown by us high prevalence of hypolactasia in different subsets of the Saami in Finland and Russia [38]. According to our observations, people with high longevity, have a distinct way of life, which features moderation in eating, varied diet with the inclusion of a sufficient amount of fish, dairy products, which helps to survive in rough environment, and it therefore has geroprotective properties [9].

Particular importance for the health, performance and longevity in the North is full and regular meals, high in micronutrients, vitamins and minerals [6]. M.V.Lomonosov (1761), observing the life of aborigines, noted the exceptional role of meat in their diet [12]. Arctic explorers Fridtjof Nansen (1895, 1896), Stefansson (1913-1919), Soviet polar A.I.Mikheev (1924 - 1934) who experienced life in the conditions of North, noted that the diet of only meat is not

associated with substantial harm to health [13]. According to Lvov, who studied high longevity of inhabitants of North, a crucial role in the prevention of diseases among Northerners played by correct (efficient) nutrition [14].

It is generally accepted, that good nutritionis the foundation ofhealth, which means a set of processes associated with the consumption of nutrients and their digestion, thus ensuring the normal functioning of the body and maintain health [5, 26, 45].

The indigenous people of the North have consumption of proteins and fats in the daily more than the inhabitants of the European part of Russia, Siberia and the Central highlands of Kyrgyzstan [38]. A large intake of dietary cholesterol in indigenous population is not accompanied by a significant hypercholesterolemia [39]. Patients with coronary heart disease consume high amount of fats and carbohydrates more than the healthy inhabitants of the North [3]. Daily consumption of proteins and fats of the indigenous people of Chukotka is more than the residents of Novosibirsk, but less carbohydrates [32]. In Buryatia ethnic eating habits areidentified: Buryat population consumes the same energy value rations, but high in total fat, more than non-Buryat indigenous and alien population [18]. Indigenous rural population of Yakutia is characterized by a high intake of protein; the residents of Novosibirsk and Buryatia consume it less. The consumption of proteins in the indigenous rural population of the Republic of Sakha (Yakutia) is higher than the inhabitants of Novosibirsk, Buryatia, Chukotka, [17, 18].

According to Gabyshev M.F., the fundamental importance of balanced diet is Yakut horse milk [38]. Some studies have shown the healing properties of the Yakut breed young horse [27]. Young Yakut horse meat has higher content of essential amino acids than in meat of other cultural meat breeds, including cattle. Specialists of the Nutrition Institute of the Russian Academy of Medical Sciences conducted the study in which they made the following conclusion: " Yakut horse meat has high content of polyunsaturated fatty acid (18: 2, 18: 3, 20: 5, 22: 6) and especially the omega-3 family, as well as vitamin E "[8,9]. Omega-3 lowers triglycerides, reduces the risk of blood clots, prostaglandins helps to control and influence the immune system and is essential for normal functioning of the endocrine glands, for the prevention of cancer [27]. The high content of fatty acids, especially omega-3, omega-6 fat in the meat of Yakut horses and cattle is a biochemical adaptive trait acquired during the evolution [40]. Thus, for the residents of Yakutia is their staple food, which stood for centuries in barren diet - meat and dairy products aboriginal Yakut cattle and horse, is a determining factor in the longevity of northerners [32].

Protein-fat type of food of indigenous population of the North has a clear difference [38].

If the base product of traditional Yakut cuisine is meat, especially young horsemeat, then for the minorities of the North is the venison [40]. When comparing the emission spectrum of fatty acids contained in the young horsemeatwith beef there was a significant difference in the composition of saturated and unsaturated fatty acids [27]. Thus, young horse had most valuable and mobile fractions, such as linolenic and linoleic acids [20]. The beef fat had only 1% linoleic acid [27]. Saturated fat was predominant in beef, which prevented it from detaching from the vessel wall, gradually clogging the lumen of vital organs [30].

The most typical Arctic diet is characteristic for coastal sea hunters (Inuit, Eskimos and Aleuts) [39]. The level of fat in their diet is 50% dietary energy, whereas the carbohydrate fraction may be less than 10%. According to Kaznacheev V.P., Panin G.E., food of the Far North, which is mostly protein-lipid, is a balanced or nearly balanced diet[39]. The proportion of carbohydrates in the diet of living in the coastal villages of the Chukchi and Eskimos lower than that of the alien population that can be attributed primarily to differences in the consumption of refined sugar [Stepanov, Babin, Klochkova, 1987]. In reindeer herders - Nenets - carbohydrates account for about one third of the total caloric intake [Atsushi Yoshida, 1997] [21, 35].

According to some authors, the main diet of Evens is meat and fish, which is due to their traditional occupations - reindeer herding, hunting and fishing [27]. Consumption of these products, which is high in calories, is very essential for the human body living in harsh climatic conditions of the North and the hard work of reindeer herders and hunters [27]. The energy supply of northern indigenous peoples, including Evens, is closely linked with the outside world - nature [41]. Eating foods taken from nature, they nevertheless tried to keep the balance between man and nature [36, 37]. Despite the extremely difficult conditions of life, nine month arctic cold and low varied food with the basic ration of meat and milk, the Yakut people are famous for their longevity [8, 9].

Some authors point out that the type of food the Arctic has emerged as an adaptive response to seasonal hunting. High fat intake allowed storing energy in fat "depot", based on its expenditure in the period of the decline of fishing and the emergence of malnutrition [42]. However, the protein-lipid type of food is appropriate for populations engaged in traditional industries with a long stay in the cold [35]. Thus, the organization of proper nutrition in the North must take into account the evolution of human diet [1, 2.4, 10].

As result of continuous adaptation to specific food, human body creates a stable system of exchange processes [35]. There is speculation that individuals who had departed from the

traditional way of life and consuming mostly western food products has a lower rate of metabolism [22, 35]. This was confirmed by the results of studies conducted in recent years in North America [7, 16]. Natives of the North are experiencing increased demand for fat-soluble vitamins (Panin, 1987), but in the northern communities, preserving traditional protein-lipid diet, hypovitaminosis is rare [30].

Some studies have revealed differences in the diet depending on the climatic and geographical conditions of residence and to establish the so called types of eating [11, 15, 25, 31, 34]. A significant use of dairy products, fish, and less sugar, vegetable oil, low salt researchers explain the mechanism of heat at a high temperature and high humidity, since in this case the inclusion of heat transfer is difficult, so the primary load heat decreases [27] .If a high level of energy consumption of the organism of northerners, particularly long-lived, can be explained by a significant consumption of protein and fat [28]. Thus, the nutrition of the indigenous population in high longevity populations can be regarded as an active factor involved in the formation of an adequate adaptation to the environment [30]. National type of food, spontaneously formed for centuries long process and the necessary adaptation to the climatic conditions of residence, characterized by favoritesof meat and fatty foods and foods with a high temperature, it is described by a number of researchers of the North [27]. They noted the high proportion of protein in the diet and fat at relatively low carbohydrate content [27].

Some authors support the preferential use of hot dishes and especially the hot tea in cold regions [27]. It should be noted that the hot meal is one of the most effective methods of warming the body by convective heat transferred from blood to other organs and tissues [27]. It is known that small vessels such as arterioles, capillaries and venules are ideal coils [27]. Nutrition features and diet of the northern type are biologically caused, as over time the population of visitors gradually within 20 years of living in the region, goes to Arctic feeding behavior [27]. These reactions help to survive in conditions of low temperatures and maintaining the functions of the body in extreme climatic conditions [27].

It is believed that basal metabolic rate is increased in northern people when compared to populations of tropical and temperate zones of the twentieth century in Canada and Alaska [46]. Other researchers have found similar relationships of basal metabolism with the region of residence [47].

Current literature suggests that people who came to the North, activated lipid metabolism steadily increased the content of free fatty acids and total cholesterol levels, energy

metabolism switches from the "carbohydrate" to "fat" type [48]. According to some reports, nutrition of inhabitants of northern regions of Russia also has certain features and characterized by over-eating, the prevalence of protein-fat food, along with a lack of vitamins and some trace elements that may contribute to lipid metabolism disorders, enhanced deposition of cholesterol and β-lipoproteins in the intima of vessels, followed by the development of atherosclerosis [49]. Other authors who have studied mainly the actual nutrition of older people, say that there is a relationship of food with longevity, depending on the ambient temperature [27].

CONCLUSION

Thus, today usage of the traditional food of the North is very important in the sense that the ethnic food of these people (ecologically clean) is closely related to human health and the nation's gene pool. All this leads to the preservation of traditional food and culture of the ethnic group as a whole.

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Working-Age Population Mortality in the Republic of Sakha (Yakutia): Regional Characteristics

ABSTRACT

The purpose of this study is to examine the regional characteristics of the working-age population mortality in the Republic of Sakha (Yakutia). With the use of the continuous statistical method and the method of mathematical analysis, there was done a retrospective analysis of the official data from mortality reports by the Territorial Office of the Federal State Statistics Service (FSSS) and demographic yearbooks of the Republic of Sakha (Yakutia) for the period of 1990-2014. It was found out that the distinguishing feature of the mortality in the republic is a high level of human losses in the younger age groups from preventable causes. As of 2013 data, the mortality rate of the working-age population exceeded the Russian Federation average by 5%, in particular, cardiovascular diseases – by 10.3%, external causes – by 26.7%. At the same time, Yakutia demonstrates a decreasing trend of the working - age population mortality from all the major classes of the causes, which determined the 2014 decrease in crude mortality rate in this age group by 5.1% (down to 5.7 per 1,000 population of the corresponding age). In the structure of causes of death in working-age population of the Russian Federation as a whole, the ranking places were successively occupied by cardiovascular diseases (170.3 per 100 thousand people of working age), external causes (158.3), and neoplasms (81.9). In Yakutia, the leading position went to external causes (216.1), followed by cardiovascular diseases (189.9), and neoplasms (67.1).

The study of the level, structure and trends of the working-age population mortality in the republic in the context of different health-economic groups of regions (Arctic, industrial, rural) reveals significant intra-regional variations in the data. In the period 1990-2014, all the groups of regions showed significant increase in the working-age population mortality rate. It should be noted that the rural group rate was remaining relatively stable, as there was no increase in the mortality of working-age women; still, it was higher than the average republic's indicator by 7.0%. Since 2000, the Arctic regions showed the highest mortality rates in the working-age group in the republic, with the excess being observed in both men and women. Over the entire study period, the group of industrial regions demonstrated a relatively prosperous situation, despite a growing trend.

Differences were also identified in the structure of the main causes of mortality of the working-age people in different groups of regions. The Arctic group experienced the highest numbers of deaths from cardiovascular diseases (345.7 per 100 thousand people of working age), digestive diseases (56.4), external causes (404.5), whereas the industrial group – from infectious diseases (20.0) and neoplasms (75.0). The rural group, with the average numbers for all the major causes, showed an upward trend in mortality from cardiovascular diseases and external causes.

Premature mortality of working-age people in the republic results in economic cost for the society, which annually makes the average of 0.4% of the gross regional product.

Keywords: population mortality, working age, economic cost.

BACKGROUND

Mortality is one of the main indicators characterizing the level of socio-economic development and welfare of certain areas, public health, accessibility and quality of the services [5]. Regions of the Russian Federation, so different in various living conditions of people, differ in the rate of mortality, as well. [3] A distinctive feature of health in the Republic of Sakha (Yakutia) is the problem of premature mortality with a high birth rate and positive natural growth of the population. The high share of human losses in the younger age groups has a negative impact on the formation of human resources, as well as on the demographic situation in the area as a whole. [1] As of 2012 data, the mortality rate of the working-age population exceeded the Russian Federation average by 12.0% (649.4 and 575.7 per 100 thousand population, respectively). The year 2014 witnessed positive dynamics, and the analyzed parameter decreased to the national average – 5.7 ‰; still, it exceeds the 1990 figure by 14.0%.

The different groups of regions of the republic demonstrate significant differentiation of mortality parameters due to the socio-economic conditions in which people live, territorial differences in resources supply, and performance of the therapeutic and preventive care system.[2]

Aim: to study regional characteristics of the working-age population mortality in the Republic of Sakha (Yakutia).

MATERIAL AND METHODS

The main sources of information were the reports on the age and sex composition by regions of the Republic of Sakha (Yakutia), published by the Territorial Unit of the Federal State Statistics Service in 1994-2014; demographic yearbooks of the Republic of Sakha (Yakutia); reports on mortality in 2000-2014. The continuous method was used to characterize the level,

structure and trends of mortality in the working-age population in the republic as a whole, as well as in the context of different medical-economic groups: Arctic, industrial, and rural. The groups of regions were formed basing on the medical-economic zoning of administrative-territorial units of the Republic of Sakha (Yakutia) (L.F. Timofeev, V.G. Krivoshapkin, 2006). [4] The calculation of the economic cost caused by the working-age population mortality is made according to the methodology approved by orders of the Ministry of Economic Development of Russia No. 192, Russian Health Ministry No. 323н, Ministry of Finance of Russia No. 45н, and Federal State Statistics Service No. 113 of 10.04.2012 "On approving the methodology for calculating the economic cost of mortality, morbidity and disability of the population." Under the method of calculating, the economic cost of mortality was considered as losses associated with the underproduction of gross regional product (GRP) due to the disposal of an individual from labor activity because of death.

RESULTS

The annual loss of the working-age population in the republic make over 40% of all deaths: in 1990 – 44.2%, in 2010 – 46.9%, in 2013 – 40.2%. The dynamics of the index was characterized by undulating course and experienced two growth periods, the first of which fell on 1990-1995, when the mortality rate for both genders rose by 63.0%, with the mortality of working-age men increasing by 71.0% (from 7.5 to 12.8 ‰), which was four times higher than the figure for women; the increase in the mortality rate of women was 60%. Starting from 1996, there was a deceasing trend in the analyzed indicators, which was replaced by another rise in male mortality up to 12.0 ‰ in 1999-2004, which led to worse general indicators for both genders. Later, since 2010, there has been a tendency for reduced annual loss of life in the working-age population however; the 2014 level was still higher than that of 1990 by 12.5% for both genders.

Since 1996, the mortality rate of the working-age population in the republic consistently exceeds the Russian Federation average, and it amounted to 5.9‰ in 2013 (in the Russian Federation - 5.6). With the mortality rate of working-age people decreased by 32% in the Russian Federation in 2005-2013, Yakutia had a lower rate of reduction (16%). (Table 1)

Table 1

Dynamics of the working-age population mortality rate in the Republic of Sakha (Yakutia) (per 1,000 people of the relevant age)

Years	Republic of Sakha (Yakutia)			Russian Federation
	Both genders	Men	Women	Both genders
1990	4.9	7.5	2.0	4.9
1991	5.0	7.4	2.3	5.0
1992	6.2	9.5	2.5	5.8
1993	7.1	11.0	2.8	7.4
1994	8.0	12.3	3.1	8.4
1995	8.0	12.8	3.2	8.0
1996	7.4	11.2	3.2	7.1
1997	6.7	10.2	2.9	6.3
1998	6.6	9.9	3.0	6.1
1999	7.2	10.9	3.3	6.8
2000	7.3	11.3	3.2	7.3
2001	7.9	12.2	3.4	7.5
2002	7.8	12.1	3.5	6.8
2003	7.7	12.0	3.4	7.2
2004	7.7	12.0	3.4	7.2
2005	7.0	11.0	3.2	8.3
2006	7.2	11.1	3.3	7.5
2007	6.8	10.6	2.9	7.0
2008	7.2	11.2	3.1	6.9
2009	7.3	11.1	3.2	6.4
2010	7.2	11.2	3.1	6.3
2011	6.8	10.3	3.0	6.0
2012	6.5	10.0	2.7	5.7
2013	5.9	9.1	2.4	5.6

In the structure of causes of death of the working-age population during the study period, accidents, poisonings and injuries ranked first, followed by cardiovascular diseases and neoplasms, except the year 2010, when the mortality rate from cardiovascular diseases exceeded all other indicators. In respect of individual classes of causes, the period of 1990-2012 saw an

increase in deaths from certain infectious and parasitic diseases – by 35.6%, from cardiovascular diseases – by 2 times, respiratory diseases – by 53.3%, from digestive diseases – more than 2 times, and from external causes – 1.8%. In the following period of 2013-2014, because of large-scale measures to reduce mortality, there were marked positive changes in the medical and demographic situation of the area. Mortality indices went down significantly, including those for infectious diseases and cardiovascular diseases decreasing by 13.0%, respiratory diseases – 26.6%, digestive diseases – 23.9%, external causes – 8.9% (Table 2).

Table 2

Mortality indices for the working-age population by main and particular causes in the Republic of Sakha (Yakutia)

(per 100,000 of working-age people)

Cause of death	1990	1995	2000	2005	2010	2011	2012	2013	2014
All causes	487.5	818.3	737.9	773.6	725.5	679.0	649.4	590.6	559.0
Infectious and parasite diseases	11.8	20.9	18.6	17.5	12.5	16.9	16.0	13.2	13.9
Neoplasms	78.6	87.2	78.4	79.0	64.2	67.1	73.9	67.1	62.8
Cardiovascular diseases	108.4	206.0	193.2	264.2	260.3	231.0	218.9	189.9	190.0
Respiratory diseases	15.2	27.1	28.4	30.5	23.4	24.6	23.3	18.8	17.1
Digestive diseases	18.7	56.0	40.9	43.9	55.9	46.7	42.7	39.8	32.5
External causes, including:	221.3	350.1	324.2	291.7	252.9	240.1	225.2	216.1	205.1
- road accidents			24.0	28.6	19.6	26.3	23.8	28.2	21.2
- suicides			68.9	67.0	56.1	56.0	55.0	50.9	50.6
- homicides			74.8	70.5	47.7	39.7	40.0	37.2	30.3

The breakdown of the main causes of mortality of the working-age population in Yakutia in 2011-2014 was as follows: external causes – 36.0%, cardiovascular diseases –33.5%, neoplasms – 11.0%.

Ranking of the main causes in the Russian Federation was different during the entire study period, with the leading position going to cardiovascular diseases (170.3 per 100 thousand population), followed by external causes (158.3), and neoplasms (81.9).

The gender differences are so that the mortality rate among working-age men is 4 times higher than the mortality rate of women in the same age category. In 2014, men accounted for 79.8% of the total number of deaths in working age (four out of every five deaths). External causes led to the death of almost every second deceased man of working age (42.1%) and every third deceased woman (28.7%). To a large extent, this disadvantage stems from the spread of alcohol abuse and alcoholism, with a worse crime situation in the country as a whole, and the republic, as well.

In terms of specific causes of death, the proportion of working-age people is the dominant value. For example, among the dead from tuberculosis, working-age people accounted for 73%, mental disorders – 50%, accidents – 82.5%, suicides – 87.1%. (Table 3)

Table 3

Share of the working-age people dying of individual causes (in %)

Cause of death	Working-age population share
Tuberculosis	73.0
Mental disorders	50.0
Chronic alcoholism	62.5
Alcoholic liver diseases	70.6
Accidents and poisoning	82.5
Alcohol poisoning	77.4
Suicides	87.1

A retrospective analysis of mortality of the working-age population in the Arctic, rural and industrial groups of regions of the republic revealed significant variations of indicators. By 2012, the total mortality of the working-age population, against 1990, increased in all the compared groups: in the rural group – by 29.6%, industrial – by 18.4%, the Arctic – by 2.5 times.

Of particular note is a significant growth in the Arctic regions, where, since 2000, the level of human losses of working age is almost 1.5 times higher than that of the rural and industrial groups and the republic as a whole. The subsequent declines in 2013-2014 took place in the Arctic regions, where the rate of decline made 18.3%, in the industrial – 4.0%, whereas the rural group experienced certain stagnation. (Table 4)

Table 4

Working-age mortality rate in different groups of regions of the Republic of Sakha (Yakutia) (per 1,000 people of the relevant age and gender)

Groups of regions	1990	1995	2000	2005	2006	2007	2008	2009	2010	2012	2013	2014
Rural	5.4	7.3	6.9	7.9	6.8	7.2	7.4	7.9	7.5	7.0	6.4	6.4
Arctic	4.0	8.3	**8.9**	**11.3**	**9.9**	**10.2**	**11.3**	**11.0**	**11.8**	**10.1**	**10.4**	**8.5**
Industrial	4.9	8.3	6.8	7.0	6.9	6.1	6.5	6.4	6.6	5.8	5.2	5.0
Sakha Republic (Yakutia)	4.9	8.0	7.3	7.8	7.2	6.8	7.2	7.3	7.2	6.5	5.9	5.6

It should be noted that the Arctic regions demonstrate the highest mortality rates in the republic for both men and women of working age (Table 5). As of 2012 data, the mortality rate of working-age men in the Arctic regions was 26.2% higher than in the rural group, and 37.9% than in the industrial one; the mortality rate of women was higher by 44.2 and 55.8%, respectively.

Table 5

Mortality indices of men and women of the working age in different groups of regions in 1990-2012 (per 1,000 people of the relevant gender and age)

Groups of regions	1990		1995		2000		2005		2010		2012	
	Men	Women	M	W	M	W	M	W	M	W	M	W
Rural	8.0	2.8	10.9	3.3	11.3	3.2	12.2	3.3	11.4	3.2	10.7	2.9
Arctic	7.0	2.4	12.3	3.7	12.6	4.4	17.1	4.8	17.2	5.7	14.5	5.2
Industrial	7.3	2.2	12.8	3.2	10.4	3.0	11.0	2.9	10.5	2.7	9.0	2.3
SR(Y)	7.4	2.3	12.2	3.3	10.4	3.2	12.2	3.2	11.2	3	10.0	2.7

In the beginning of the study, the rural group showed the highest mortality rate of working-age men (8.0 per 100 thousand population) among the three groups, but later, the figure did not change much, and in 2012 it became lower than the Arctic group figure by 35.5 % (10.7 and 14.5, respectively). The mortality rate of working-age women in 1990-2012 remained

virtually unchanged (2.8 and 2.9 per 100 thousand of the working population), but was higher than the republic's average by 6.9%.

Throughout the study period, the industrial group demonstrated the lowest mortality rates of the working-age population for both genders and a relatively slow growth rate (by 18.0%); since 2000, these regions enjoy the most prosperous situation with mortality of working-age men and women. The proportion of deaths in working age is 41.8%; (in rural - 42.8%, in the Arctic - 53.6%).

The analysis of the main causes of mortality of the working-age population in the compared groups also showed differences. For example, in the Arctic regions, the situation remains serious for cardiovascular diseases, digestive diseases, and external causes (Table 6). The mortality rate from cardiovascular diseases exceeds that of the rural and industrial groups by 1.6 times, from digestive diseases – by 1.5 and 1.3 times, external causes – by 1.4 and 2.3 times.

Table 6

Mortality indices of the working-age population of certain main causes in different groups of regions (per 100,000 people of the relevant gender and age)

Groups of regions	Infectious diseases	Neoplasms	Cardiovascular diseases	Respiratory diseases	Digestive diseases	External causes	All causes
Rural	10.0	70.3	216.0	20.6	37.7	284.0	696.5
Arctic	7.0	71.1	**345.7**	14.7	**56.4**	**404.5**	1012.6
Industrial	**20.0**	**75.0**	204.2	27.0	43.0	176.4	581.4
SR(Y)	16.0	73.9	218.9	23.3	42.7	225.2	649.4

Mortality rates of the working-age population in the rural group from the main causes are quite comparable with the republic's average, except for external causes, the figure for which is 20.7% higher than in the republic, and 37.9% than in the industrial regions. The industrial group has relatively high mortality rates from infectious diseases, neoplasms, and respiratory diseases.

In the structure of the economic cost, the greatest share of losses in all classes of diseases in the context of age groups was observed in the older working men aged 49-54 years, women in the age groups 49-56 and 58-59 years. Cardiovascular diseases (38.2%) and external causes of death (30.0%) make the largest contribution to the economic losses. The third place in the

structure of the economic cost goes to neoplasms (12.2%). The mortality rate of the working-age population of the three main causes accounts for 79.5% of the economic cost. They are followed by mortality from digestive (6.6%) and respiratory (3.4%) diseases.

In the cardiovascular diseases class, women account for more economic losses from mortality by 3.2% (40.5%), whereas in the class of injuries, poisoning and certain other external causes – men by 1.8 times (34.1 %). The economic cost for men is almost 3 times higher than the losses among women and average annually to 74% of all losses.

Overall, the economic cost of premature mortality in the Republic of Sakha (Yakutia) in the study period increased by 17.7%, and in 2012, it amounted to 2,166.7 million rubles, or 0.4% of the gross regional product of the republic.

CONCLUSION

Thus, the Republic of Sakha (Yakutia) still faces a problem of high mortality of the working-age population of both genders from preventable causes (external causes, cardiovascular, digestive, respiratory, and infectious diseases), which, given a growing trend in the proportion of retirement-age people and continuing migration loss of working-age people, has a negative impact on the formation of labor resources in the republic. The use of the zoning method revealed intra-regional differences in both the level and the structure of human losses. Understanding of mortality characteristics in certain regions is necessary to develop a set of measures to reduce premature mortality from specific causes.

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Chronic Pancreatitis at Children of the Republic of Sakha (Yakutia)

ABSTRACT

This article is devoted to the study of the immune status in children with pathology of the pancreas. In the analysis of changes of immune status in children with chronic pancreatitis we revealed the greatest decline in T-cell level and components of complement, a decrease level of immunoglobulin A. In patients there is a reduced content of IFN-γ and FNO-ά.

Keywords: immune system, pancreatitis, lymphocyte subpopulations, interferons, tumor necrosis factor, cytokines, interleukins.

INTRODUCTION

The relevance of the problem of pathology of the gastrointestinal tract in children is determined by a number of circumstances. In structure of the general morbidity in children one of the first places belongs to digestive tract pathology [2,3].

Chronic pancreatitis in the structure of diseases of the digestive system in children is, due to the opinion of various scholars, from 5% to 25% of patients with gastroenterological diseases and 0.1 to 0.5% of the total number of children admitted to the children's surgical Department [1- 5].

The study of patterns and risk factors for the formation, diagnosis and tactics of treatment of pancreatic diseases in children in the Far North appears to be relevant because of the high prevalence of this disease, as well as the dietary habits of children in the Far North. [1-5].

The purpose of the study to investigate the immune and cytokine system states in children with chronic pancreatitis, living in different regions of the Republic Sakha (Yakutia).

MATERIALS AND METHODS: the study included 100 children with reactive pancreatitis aged 7 to 14 years (Table), and 2000 healthy children control group. The standards are developed by the staff of Immunological laboratory Diagnostic center of the Ministry of Health of the RS (Y) together with the Institute of Health of the RS (Y). All studies were conducted in the period of low temperatures (winter).

Determination of subpopulations of T - and B-lymphocytes was performed by ELISA using monoclonal antibodies.

Determination of immunoglobulins was carried out turbodimetrical method by measuring the rate of light scattering in the formation of immune complexes in the kinetic measurement at multiscale.

Level FNO, IFN in serum were determined using ELISA method, according to the instructions supplied with the kits antibodies. Kits for the determination of interleukins by ELISA kits reagents "Pro Con IL-1", "Pro Con IF gamma" (LLC "Protein contour" St. Petersburg). Principles of solid-phase ELISA based on the fact that the enzyme horseradish peroxidase, covalently attached to antibodies, while maintaining the biological activity (the ability to interact with the substrate by binding with immobilized immune complex formed on "sensitized" wells, which were incubated your samples and standard reagents.

Statistical calculations made on the basis of applied programs "SAS" and "SPSS" In the analysis of contingency tables (estimates of the correlation of the characteristic and evaluation of significance of differences between groups) used the criterion ^{2} (Pearson and likelihood ratio) and Fisher's exact test. Comparison of mean values was performed univariate analysis of variance using T-student criterion for assessing the equality of mean F-Fisher test to assess equality of variance.

The results of the study: due to the results of the analysis for the last 5 years there has been an increase in pathology of the gastrointestinal tract. Gastrointestinal diseases take the second place in the structure of infant pathology.

In children of school age there has been an increase of diseases of the pancreas, diseases of gallbladder, biliary tract, and functional disorders of the stomach, gastritis and gastroduodenitis. A high prevalence of diseases of the gastrointestinal tract in children of the Republic of Sakha (Yakutia) was revealed In the analysis of changes of immune status in children with chronic pancreatitis in comparison with the group of healthy children we revealed the greatest decline in T-cell-mediated (CD3+, CD4+, CD16+), components of complement C3 and C4, the decline In-cell link CD22+. These changes show antigenic stimulation and decreased immune resistance in children with chronic pancreatitis. According to the literature, during exacerbation of chronic pancreatitis, the content of T-lymphocytes decreases (table), in remission of their value increases [1]. Currently there is no consensus about the pathogenetic role of b lymphocytes in chronic pancreatitis. Thus, some researchers point to the increase in the number of b-lymphocytes [2], some researchers indicated the decrease in the content of b-lymphocytes in reactive pancreatitis [1], which coincides with the results of this study. The complementary reduction of activity a number of authors consider due to the presence of antipancreas antibodies [1, 2] and their involvement in immune responses to consumption of complement.

The results of our study coincide with the literature data [1,2], these changes are explained by the formation of immune complexes with identified antibodies to trypsin, insulin.

Table

Indicators of immune status in children with pancreatitis of Sakha (Yakutia) Republic

Indicators	The performance standards indicators of Sakha (Yakutia) for children(n = 300), M ± M	Children with pancreatitis (n = 100), M ± M
CD3+	52,6 ± 1,7	20,1 ± 1,02*
CD4+	26,3 ± 0,7	11,2 ± 0,7*
CD8+	22,5 ± 0,23	16,2 ± 1,0
CD16+	23,2 ± 0,54	4,6 ± 1,1*
IRI	1,18 ± 0,64	0,7 ± 0,02
IgA	2,34 ± 0,69	1,3 ± 0,3*
IgG	13,3 ± 0,16	9,2 ± 0,7
IgM	1,6 ± 0,03	0,9 ± 0,09
CD22+	19,8 ± 0,16	9,9 ± 1,9
C3	0,67 ± 0,12	0,20 ± 0,02*
C4	0,34 ± 0,05	0,11 ± 0,02*
ЦИК	96,8 ± 0,132	194,2 ± 1,5*

*p< 0.05 between the standards and indicators obtained in each group.

In children with chronic pancreatitis significantly elevated level of the CEC and reduced content of IFN-γ, FNO-α in comparison with the group of healthy children are noted. The changes indicate a decrease in antiviral defense in children with chronic pancreatitis.

The results of the study indicate a need for further study with the aim of developing effective schemes of immunomodulation.

CONCLUSIONS:

1. The high incidence of gastrointestinal tract in children of the Far North associated with living in an extreme climate and geographical conditions, the changing nature of supply and the reduction of socio-economic standard of living of the population, which requires the introduction of programs of disease prevention and health improvement of the children's population of the Northern districts.

2. In children with chronic pancreatitis there are reduced cellular immunity (BG3+, CD4+, CD8+, CD+, DM 22+), the decrease in T-cell level and components of complement.

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The Analysis of the Patient's Condition after Liver Transplantation in the Republic of Sakha (Yakutia)

ABSTRACT

Clinical records of 21 patients aged 27-57 years who were on hospital treatment after liver transplantation in Therapy Department of the "No.1 Republican Hospital - National Centre of Medicine" State-Financed Institution of the Republic of Sakha (Yakutia) in 2004-2015 are analyzed. Transplantation is carried out in stages of decompensation of cirrhosis of non-viral and viral etiology. Early performed surgery increases life time of patients and improves the quality of their life.

Keywords: cirrhosis, liver transplantation, immunoreduction therapy, preventive care

INTRODUCTION

In the Republic of Sakha (Yakutia) according to Goskomstat the prevalence of liver and gall bladder diseases in general exceed similar indicators of the Far East Federal District and the Russian Federation. The high level of the crude incidence of the population of Yakutia of liver diseases, exceeding almost twice the indicators of the Far East Federal District and Russian Federation, steadily reserves in 2005-2009 years. Steadily high rates are observed in Allaikhovsky, Abyisky, Eveno-Bytantaysky, Tattinsky, Nyurbinsky regions. In 2009 in comparison with 2005 primary incidence of liver diseases sharply increased: in 9,5 times in Allaikhovsky, in 5 – in Tattinsky, in 4 in Anabarsky and in 3,6 times in Kobiaysky regions. [3].

Liver transplantation (LT) is the most effective and often the only radical and perspective method of treatment of patients with a terminal stage of the chronic liver diseases, acute hepatic failure, cancerous and benign liver tumor. Patients with cirrhosis (C) are the basis quota of the persons needing transplantation. For the last decades the number of the patients with cirrhosis of various etiologies needing liver transplantation [5] increased noteworthily.

Aim of the research is analysis of patient's condition after allotransplantation of cadaveric liver and live relative donor for cirrhosis.

MATERIALS AND METHODS

Clinical records of 21 patients aged 27-57 years who were on hospital treatment after LT in Therapy Department of "No.1 Republican Hospital - National Centre of Medicine" State-Financed Institution of the Republic of Sakha (Yakutia) in 2004-2015 are analyzed. The cause of the decompensated C of non-viral etiology was primary biliary cirrhosis (PBC) at 5 patients, 1 patient had primary sclerosing cholangitis and 15 patients - C of viral etiology, and one of them had hepatitis B and also transformation to hepatocellular carcinoma. All patients having coexistent diseases were examined by the therapist and specialized doctors: a cardiologist, a gastroenterologist, a physiotherapist, a surgeon, etc. All general clinical trials (clinical blood and urine analysis), biochemical blood count (hepatic tests, immunoassays, etc.), functional and tool methods of research, fibrogastroduodenoscopy, Abdominal ultrasonography, Computed Tomography (CT), etc. were conducted on all patients. Informed consent of patients to participation in investigation and conduction of additional diacritical interventions was an express condition.

RESULTS AND DISCUSSION

The first surgery on liver transplantation in No.1 Republican Hospital (Yakutsk) was performed in 2013, two surgeries – in 2014, 4 surgeries were performed current 2015. Middle age of patients is 40 years - 4 men and 3 women with cirrhosis of a viral etiology, and one of them is a patient with hepatocellular carcinoma. After liver transplantation the analysis indicators of this patient on cancer-specific marker were normalized (carcino-embryonic antigen – 2,70; alpha fetoprotein – 3,10). One patient died in the early postoperative period; multiple organ failure was cause of death of one patient.

The Sakha Republic (Yakutia) is endemic zone of prevalence of viral hepatitis B, C, and D. Hepatitis D virus (HDV) is infection often damaging young people able to work and it provides to chronization and enlargement of cirrhosis which quickly progressing to decompensated stage with expansion of portal hypertension, invalidization and high mortality [1].

Decompensation sets in cirrhosis at certain moment and blood flows through the veins of the esophagus. Therefore till 2005 in No.1 Republican Hospital the Therapy Department in common with doctors of Endoscopy Department conducted endoscopic sclerosing of varicosity

of esophagus and stomach by the specimen "etosklerol" and deligation of esophagus varicosity by ligatures that allowed to prevent recidivation of bleedings and to extend longevity of patients.

From 2004 Clinical centre of No.1 Republican Hospital - National Centre of Medicine is the branch of V.I. Shumakov Research Centre of Transplantology and Artificial Organs (Moscow). In 2004 we sent 4 patients for liver transplantation. The first 3 patients with cirrhosis of nonviral etiology (Hanot's cirrhosis, primary cirrhosis cholangitis) successfully underwent allotransplantation of cadaveric liver. In the course of the treatment the condition of patients was satisfactory [4].

From 2010 we investigated and sent 13 patients to V.I. Shumakov Research Centre of Transplantology and Artificial Organs, and also to A.I. Burnasyan Federal Medical Biophysical Centre (Moscow) – 5 of them with cirrhosis of non-viral etiology (4 with primary biliary cirrhosis and 1 with secondary biliary cirrhosis), 7 patients with cirrhosis of viral etiology and 1 with non verified cirrhosis. All patients underwent liver allotransplantation from live relative donor. In the early postoperative period 1 patient with primary biliary cirrhosis and 2 patients with hepatitis D virus died. In both cases the heavy reject phenomena developed. In 2010 cirrhosis occurs again at one patient's transplant, so she was returned to Research Centre of Transplantology and Artificial Organs, where she successfully underwent retransplantation of cadaveric liver with satisfactory function.

The condition of all patients after liver transplantation was evaluated as satisfactory in the course of the immunosuppressive treatment: Prograf, Medrol, Myfortic. After ternary immunosuppressive therapy the recrudescence of smoldering chronic inflammatory conditions of gastro-intestinal tract, urinoexcretory path, and cardiovascular system [2,6]. Also antibacterial, antiviral, hepato- and gastroprotective agents and semiologic therapy were assigned to patients for recrudescence of coexistent diseases. The degree of disability is determined to all patients; vocational rehabilitation noted in two patients.

CONCLUSION

The main etiologic factors of enlargement of decompensated cirrhosis are nonviral diseases such as primary biliary cirrhosis, primary sclerosing cholangitis and viral liver diseases – chronic viral hepatitis B, C, D. The conduction of vaccinal prevention and educative activities, genetic consultation among the population decrease liver diseases. It should be noted that early conducted surgery increases longevity of patients, improves the quality of their life.

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The Cytokine Profile at Children with Juvenile Forms of Arthritis

ABSTRACT

Research of cytokine profile at 76 children with various forms of juvenile arthritis aged from 0 till 16 years is conducted. Average values of levels of pro-inflammatory cytokine (TNF-α, IFN-γ and IL-6) is ten times exceed the limit of the normal range. High level of pro-inflammatory cytokine of IL-1β significantly correlates with a hereditary loading of patients, and high levels of anti-inflammatory cytokine of IL-10 are observed at patients with the juvenile ankylosing spondylitis (JAS).

Keywords: cytokine, juvenile forms of arthritises

INTRODUCTION

Juvenile arthritis (JA) is one of the most common and most debilitating rheumatic diseases at children. JA disease ranges from 2 to 16 per 100 thousand of children's population under the age of 16 years. Prevalence of JA in different countries ranges from 0.05 to 0.6%. The prevalence of JA in children under 18 years reached 62.3 in Russia. The primary disease - 16,2 per 100 thousand including teenagers - 116.4 and 28.3 and children under the age of 14 - 45 8 and 12.6 [2].

The juvenile rheumatoid arthritis is the multifactory constitutional inveteratephlogotic immune autoaggressive disease with the primary affect of supporting-motor apparatus. The main **aim** of the pathogenesis of JRA is the activation of cellular and humoral parts of immune autoaggressive process.

It is expected that entheticor changed self-antigen is understood and processed by macrophage which present as T-lymphocytes. The interaction of antigen-presenting cells with T-lymphocyte stimulates the cytokine synthesis, causing a cascade of pathogenic changes with the development of systemic manifestations of the disease and progressive inflammation in joint cavity. In this case systemic appearances of JRA (fever, rash, lymphadenopathy, weight loss, etc.) are associated with increased synthesis and the activity of tumor necrosis factor (TNF-α) and interleukin (IL-6, IL-1) [4]. Early diagnosis and treatment of juvenile idiopathic arthritis in children is one of the most urgent problems of pediatrics, the etiological factors of development which

has not been established till nowadays. Among the possible reasons underlying pathological process, discusses the infectious nature of the disease, trauma, stress, immunogenetic predisposition. The aim of our research is the evaluation of cytokine profile in patients with different forms of juvenile arthritis.

METHODS AND MATERIALS

We studied 76 children (aged 1 to 16 years) with juvenile seronegative arthritis (reactive arthritis, spondylitis, juvenile arthritis, etc.), passing stationary inspection treatment in cardiorheumatological unit of the republican hospital No. 1 in national center of medicine. The average age of children was 9.88 ± 4.25 years. Among the examined children: Yakut nationality was 66, Russians - 11, Evenks – 3.The age structure of the children examined by us strongly varied, however 18.8% from them appeared 13-years, 10,0% - 7 years etc. Note that, this pathology in 42.5% of cases was found in children of 12-16 years, i.e. during adolescence. The distribution by sex showed the predominance of boys (60%) of girls (40%), which corresponded to the literary data [3].

A B C

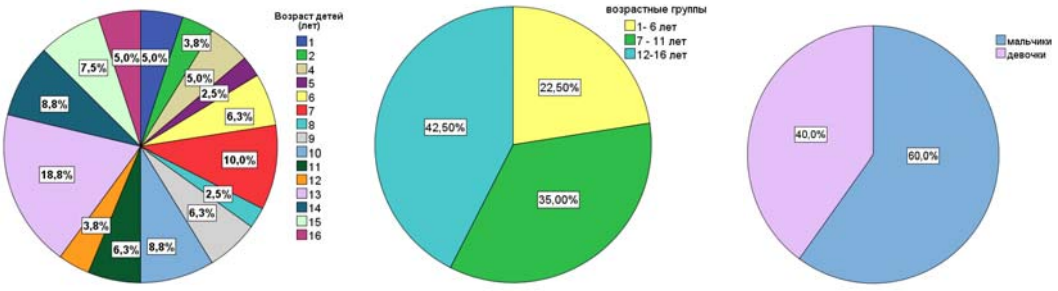

Figure 1.Distribution of the studied children on age (A), age groups (B) and a sex (C).

Concentration of anti-inflammatory (IL-4, IL-10) and pro-inflammatory cytokines (IL-6, IL-1β, IFN-γ and TNF-α) in blood serum determined by method of an enzyme immunoassay with application of sets of the reagents released by JSC Vektor-Best (Novosibirsk, Russia) by the enclosed instructions, results expressed in pg/ml.

All sick children were conditionally divided by diagnosis into 3 groups: 1 group consisted of children with psoriatic arthritis (PA) (n=1), juvenile rheumatoid arthritis (JRA) (n=14); 2 group consisted of the children with reactive arthritits (RA) (n=24), juvenile idiopathic arthritis (JIA) (n=2), the last group – children with the juvenile ankylosing spondylitis (JAS) (n=16).All of the received quantitative results are subjected to statistical analysis using the package «SPSS.17.0"company StatSoftInc (USA) 2001. The equality of sample means was tested by the parametric Student t-test (in the case of a normal distribution) and non-parametric U-Mann-Whitney test for independent samples (if different from the normal distribution).Data are expressed as M (average mean) ± m (standard error of the mean). The method of correlation analysis of the data with the calculation of coefficients and Spearman rank correlation was used for identifying the relationship between the studied parameters. For the threshold significance we took size p with a value <0.05.

RESULTS

The average values of the investigated cytokines indicate a different character of changes (Table 1). In carrying out the average mean of children and cytokines to normal values of healthy individuals, the greatest degree of improvement observed in the level of pro-inflammatory cytokines TNF-α (12.42 in time), IFN-γ (in time 11.17), IL-6 (a 9.41-fold) and IL-1β (1.73 times).

Table 1

Average value of concentrations of cytokine at sick children in comparison with the normal values of conditionally healthy persons (JSC Vektor Best)

Cytokine (pg/ml)	Indicators of the studied group				Indicatorsofhealthyperson	
	Minimum	Maximum	Averagevalue	Standarddeviation	Rangesofnorms	Averagevalue
IL-4	1,06	11,94	**2,44**	2,21	0-13	0
IL-6	3,44	252,7	**18,82**	34,78	0-16	2
IL-10	1,54	11,58	**3,61**	1,57	0-31	5
IL-1β	1,26	70,70	**2,78**	7,96	0-11	1,6
TNF-α	2,09	71,93	**6,21**	8,66	0-6	0,5
IFN-γ	14,63	90,63	**22,34**	10,83	0-10	2

Level shift of anti-inflammatory cytokines is characterized by increasing of IL-4 and decreasing of IL-10B 1.38 times. Thus, in children with juvenile forms of arthritis increased average proinflammatoryof cytokines TNF-α, IFN-γ and IL-6 as well as reduced levels of anti-IL-10.

Table 2

Cytokine level in the age groups of children with juvenile forms of arthritis

Cytokine (pg/ml)	Age groups		
	1 1-6 years (n=17)	2 7-11 years (n=28)	3 12-16 years (n=31)
IL-4	2,4 ± 0,37	2,01 ± 0,16	2,83 ±0,55
IL-6	**16,1 ± 4,0**	**12,79 ± 2,99**	**25,16 ± 8,80**
IL-10	3,9 ± 0,4	3,82 ± 0,37	3,25 ± 0,21 (p^{1-3}=0,089)
IL-1β	**1,78 ± 0,05**	**1,95± 0,11**	**3,99 ±2,15**
TNF-α	5,32 ± 0,45	7,17 ± 2,5	5,91 ± 1,03
IFN-γ	22,32 ± 1,87	25,16 ± 3,02	20,05±0,98

There was comparative analysis of the level of cytokines in different age groups, which have not identified any statistically significant differences between groups (Table 2).According to the

level of anti-inflammatory cytokine IL-10 decreasing tendency (p = 0.089) observed in the age group (12-16 years) compared with the first group (1-6 years) children. It should be noted that the average value of pro-inflammatory cytokines IL-6, IL-1β has the maximum level in the same third age group (12-16 years).Perhaps such obvious changes may be associated with features of puberty, when the immune system becomes vulnerable due to hormonal imbalance and disruption of regulatory functions of the hypothalamic-pituitary-adrenal system. The imbalance between the overproduction of pro-inflammatory cytokines mainly macrophage nature, such as TNF-α, IL-1β, IL-6 and anti-inflammatory cytokines IL-4 induces a chronic inflammatory process [5].

Correlation analysis was performed in a total sample of patients between levels of cytokines in serum and by range parameters as personal data, the diagnosis, the number of affected joints, positive for HLA-B27, duration of disease, articular syndrome, limitation of motion of the joints, the nature of disease onset (gradual, sharp) factors (respiratory infections, hypothermia, trauma, vaccinations, allergies), the presence of family history, swelling and pain.

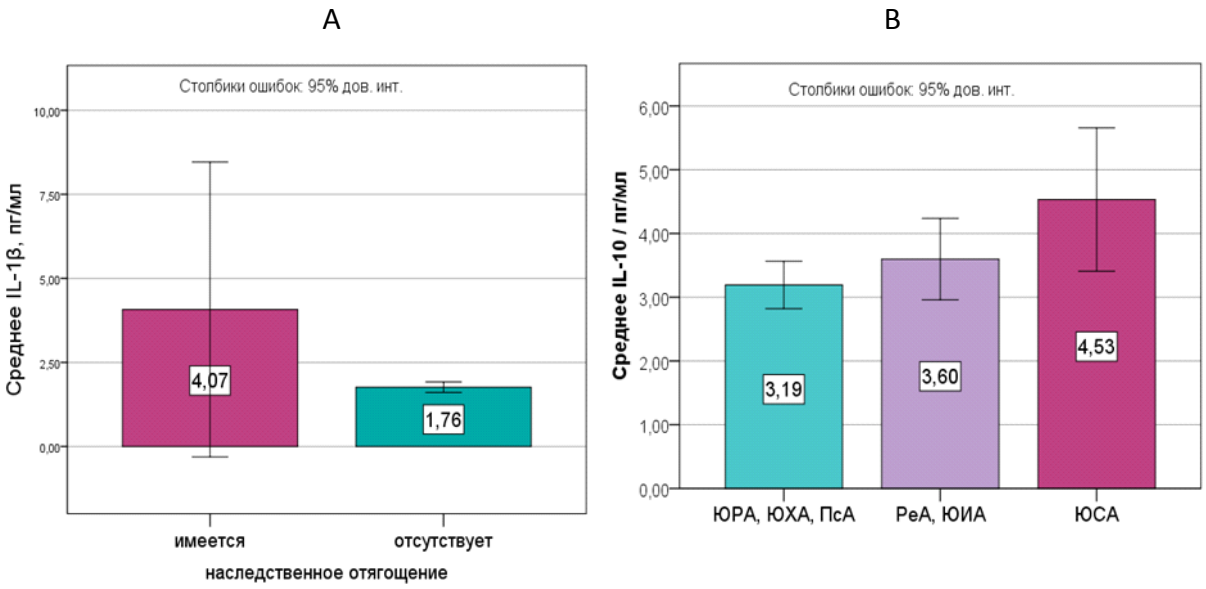

Figure 2.The dependence of the levels of IL-1βfrom hereditary loading (A) and IL-10 from the juvenile form of arthritis (B)

The results showed a correlation of the pro-inflammatory cytokine IL-1β (r = - 0,408; p = 0,000) with the presence of hereditary loading (Figure 2A). At children with hereditary loading of rheumatic diseases (parent questionnaire covering 3 generations), the level of this cytokine (2.15 ± 4.07 pg / ml) was significantly higher (p = 0.000) compared with children without burdeness (1.76 ± 1.76 pg / ml).Another correlation was established between the level of anti-inflammatory cytokine IL-10 (r = 0,314; p = 0,006) and conventional groups, ranked by diagnosis. The minimum value of the average level of IL-10 has been installed in one group (3,19 ± 0.18 pg / ml). In group 2, it was (3.60 ± 0.31 pg / ml), and the maximum level observed in group of patients 3 (4.53 ± 0.52 pg / ml). A statistically significant difference (p = 0.027) observed while comparing the groups 1 and 3. It's known that the main function of IL-10 - inhibition of cytokine production by T-helpers of the first type (TNF-β, IFN-γ), and activated macrophages (TNF-α, IL-1, IL-12). Most likely, rising of this cytokine has protective-compensatory mechanism to suppress inflammation.

Thus, the preliminary results of the analysis of the cytokine profile of children with juvenile forms of arthritis indicate rising of pro-inflammatory cytokines, more of TNF-α, IFN-γ and IL-6. High levels of the pro-inflammatory cytokine IL-1β significantly correlates with hereditary loading of patients, and high levels of anti-inflammatory cytokine IL-10 are observed at patients with juvenile ankylosing spondylitis (JAS).

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Modern Aspects of the Problems of Dental Diseases in Children with Connective Tissue Dysplasia

ABSTRACT

The present review of modern problems of dysplasia of connective tissue (DCT) has analyzed its manifestations of cardio-vascular system, musculoskeletal system, diseases of inner organs, vision organs, organs and tissues of the oral cavity and maxillofacial area. Thus it was noted that the DCT syndrome forms had a high medical-social importance as they often led to the disability of patients at the young age, which, as a rule, reduced quality of life and its duration. It is important to note that organs and tissues of the oral cavity, also as well as other organs and systems of organism have a connective-tissue origin where their compound components determine the level of protective processes in various diseases. Frequent manifestation of the phenotypic signs of DCT in the oral cavity are anomalies of tooth alignments, a vestibular inclination of anterior teeth of the upper jaw, deep cross bite, distal occlusion, high Gothic palate, dystopia and teeth overcrowding and also deviation of the nasal septum.

Thus multiple damage of DCT can affect the frequency of dysfunction of temporal-mandibular joint (TMJ) developing caries and non-carious damages, diseases of paradontium, damages in teeth development, parafunctions of chewing muscles. There is a direct interrelation of back posture disorders at the DCT phenotypic signs connected with the musculoskeletal system, formation and development of the dentoalveolar anomalies among children. There are deep crossbite and distal occlusion in the structure of dentoalveolar anomalies. Thus the main forms of scoliosis are characterized as the main manifestations of bone connective dysplasia (except idiopathic scoliosis). Also there is the interrelation of TMJ dysfunction syndrome and condition of the backbone which characterize that pathogenetic mechanisms of their formation are connected with the musculoskeletal disorders, bite anomalies leading to TMJ dysfunction. The dentoalveolar anomalies and deformations are major factors of defects of occlusion, area of occlusive contacts, emergence of supercontacts,

which create prerequisites to the development of discoordination of chewing group of muscles where the functional TMJ disorders appear. But, at the same time, the predominating role of the deep bite to the developing of TMJ dysfunction has been determined due to the expressed disorder of occlusive surface where the development of the expressed functional changes of chewing group of muscles were connected with the disorder of relative positioning of elements of the joint caused by shift of articulate head and meniscus due to articulate pole and articulate eminence.

In this regard the assessment of individual risk of children with different degrees of DCT expressiveness will promote searching of new means and methods which will interfere with the development of dental diseases and characterize the health prophylaxis of the children's population in a certain degree.

Keywords: dysplasia of connective tissue, collagenopathy, phenotypic signs, dentoalveolar anomalies, occlusion, dysfunctions of temporal and mandibular joint, caries of teeth, diseases of paradontium.

INTRODUCTION

Nowadays problems of dysplasia of connective tissue (DCT) where its basis is a hereditary collagenopathy [6, 25, 43] are widely studied. It should be noted that morphological and functional feature of organs and systems of organism depends on "maturity" of connective tissue [30]. Thus morphohistological feature of connective tissue are universality, plasticity, polymorphism of cellular systems which define a wide range of functionality and high level of adaptation by the influence of aggressive factors of the external and internal environment [24,38].

It should be noted that the classification developed by V.V. Serov, A.B. Shekhter (1981) who allocated 3 main types of connective tissue has been applied in medical practice: actually connective tissue; blood cells and hematogenic tissue; cartilaginous bone tissue. The connective tissue is divided into fibrous (quaggy and dense) and connective tissue with special properties (reticular, fat, pigmentary, mucous). The prevalence of collagenic fibers are characterized by dense connective tissue, the division of tissue to the formed (ligaments, sinews, cartilages, bones) and non-formed depends on orientation in the space (aponeuroses, reticular derma, capsules and covers of organs). Friable connective tissue consists of intercellular substance and cells (fibroblast, macrophages, corpulent, endothelial, adventitial, adipcytes, plasmocytes) [2, 20]. The research has established that connective tissue of smorphologic and structural points

in organs and systems of organism is the main and occupies 50% of the body weight of the person [20, 24, 36. 40]. Thus it equally carries out a basic and exchange-physiological role and as a functional element unites integrity of organs and systems[3].

It should be noted that the system component of connective tissue is controlled by genes and can have genetic damage as congenital and hereditary anomalies create a wide range of clinical syndromes far from each other [32, 52]. Besides, a genetic factor with multifactorial origin is in the basis of the differentiated defects of connective tissue [1, 39]. Also the connective-tissue defects localized only in one organ and DCT which shown external phenotypic signs of dysplasia are known as syndromes.

Today it has been established that aggressive factors of the external and internal environment, where their pathogenic influences take place in ontogenesis, which are connected with environment, food habits, psycho-emotional stress, etc. [5, 25] take part in the development of DCT. Nevertheless, the set the phenotypic DCT signs and microanomalies with external manifestations which are found at the physical examination [46, 53] has been revealed. So, characteristic external phenotypic signs of DCT are cranial and eye signs, changes in oral cavity and auricles, skin and its derivatives and also respiratory organs, urinary system, digestive tract, blood system, disorders of reproductive system, extremities, bones, joints, backbone and cardiovascular system [44]. Thus these disorders make negative impact on functional condition of organs and systems of organism which definitely reduce the quality of life of children [34].

Nowadays, despite broad studying of DCT, there are various opinions about its origin. So, some authors characterize that DCT has the monofactorial character connected with the developing diseases of the established and unspecified gene defect and also with diseases of connective tissue of the multifactorial nature [54]. But, at the same time, disorders connected with congenital and acquired, differentiated (syndrome) and undifferentiated (non syndrome) disorders in ontogenesis is most widely used among experts classification of the connective tissue [46]. In their structure the DCT undifferentiated forms which consist of stigma of dysembryogenesis (phenotypic manifestations), locomotory manifestations and locomotory-visceral manifestations [45] are mostly revealed. Thus Marfan's syndrome, Ehlers-Danlos syndrome, imperfect osteogenesis, pseudoxanthoma elasticum, etc. belong to the differentiated DCT [7, 17].It was established that DCT was developed at the gene level and level of disbalance of ferment and protein exchange with hyperactivity of lysyl oxidase and transglutaminase, RNA disorders and also disorders at the level of macro - and microelements

disbalance [2]. Thus it was established in the pathogenetic plan that deficiency of magnesium in connective tissue led to synthesis delay of all structural molecules, including proteoglycans, glucosaminoglycans, collagens and elastin [14]. It is known that system of DCT defeat is connected with the structural feature of connective tissue of organs and systems of organism. It also characterizes the multiorgan defect connected with disorders of bone and cartilage tissue, change of skin, vascular and valve formations of heart, urinary, digestive systems, etc. [12].

It defines the relevance of DCT problems which has medical-social aspects.It should be noted that the DCT hereditary syndrome forms, as a rule, lead to disability of patients at young age who reduce quality of life and its duration that defines its medical-social importance [11, 48].

Thus the DCT prevalence of undifferentiated forms in Russia fluctuates ranging from 2-30% [21]. Meanwhile, it was established that humans with DCT have features of clinical current of the postoperative period and outcome of surgical interventions which are connected with more expressed and long hypostasis of soft tissues, as a rule, followed by hemorrhages and hematomas and also complications in the form of development of fibrosis or a necrosis of soft tissues [27, 32].

It should be noted that today DCT problems connected with changes in the musculoskeletal and cardiovascular systems [10] are most widely studied. Thus actually there is no standard algorithm of diagnostics of DCT, reflecting requirements of various medical experts in their practice. Also, today, there is no consensus on "stigmatization thresholds". The concept "threshold level" was for the first time entered by A.A. Lazarus (1989) where the ability of various people to transfer negative incentives at excess of which there comes further deterioration of state with sharp and, perhaps, irreversible changes of negative character was characterized. Thus some authors approve absence or existence of DCT signs by four and five external signs among females and males [21]. According to V.N. Gorbunov (2010), identification of DCT syndrome requires existence of 6-8 signs of dysplasia where disorders of two-three organs of genetic factor were revealed. The revealed phenotypic signs of DCT, as a rule, were confirmed by the laboratory researches testifying the disorders of connective tissue exchange.

It should be mentioned that there is no their accurate gradation in the frequency and structure of these or those external signs with visceral pathology and small anomalies of development [53]. But, at the same time, the DCT symptom complexes connected with bone and muscular, copular and articulate, skin, and cardiac changes were revealed. Thus organs and

tissues of oral cavity of TMJ dysfunction were revealed in 55%, disorders of back posture – 51%, skin manifestations – 57%, bone and muscular changes – 52%, and also cardiac manifestations in 28% cases. According to B.V. Golovskaya with others (2002) it was noted that the expressed disorders of health were observed with combination of three of the listed symptom complexes.

It should be noted that the diagnostics is important for time identification and prevention of various DCT complications [47]. Today there is a wide range of methods of diagnostics. So, the diagnosis can be made for patient identification of 6-8 and more clinical diagnostic DCT signs in undifferentiated DCT, besides, involvement not less than 2-3 organs in pathological process and laboratory confirmation of disorders of exchange of connective tissue (increase of level of a daily excretion of glizaminoglican and oxyproline with urine is found), and also fact identification of the family accumulation of DCT signs. Thus an innovative and perspective method of diagnostics is the molecular and genetic way of research. But, despite it, today pathogenetic mechanisms of DCT development as underestimation of the DCT importance, as a rule, makes negative impact which leads to the defective organization of preventive actions, untimely diagnostics of multiorgan disorders and incorrect choice of tactics of maintaining patients. They are not described and studied.

It is known that DCT makes negative impact on the functional condition of organs and tissues of the oral cavity, and also maxillofacial area. In structural morphological components the connective-tissue origin, including maxillofacial area [44] have many organs and systems of organism. Thus, such phenotypic signs of DCT as anomalies of dentition (64,8%), disoclussion (35,4%) are mostly often revealed. Vestibular inclination of anterior teeth of the upper jaw, descending occlusion, distal occlusion (71%), high Gothic palate (44,4%), dystopia and overcrowding of teeth (55,6%), deflection of nasal septum (16,7%) [21, 29].

Besides, there are data confirming influence of undifferentiated DCT on the processes of reduction of dentoalveolar system which are followed by changes of structure and sizes of maxillary bones and hard tissues of teeth. Thus it was established that reduction processes make negative impact on tooth tissue to a lesser extent as they possess bigger stability. In this regard its maximum values can reach 8,5% which often are followed by formation of teeth contrusion to 63%, and also some anomalies of position of separate teeth where the indicator can reach 40% [37].

Nowadays there are data of interrelation of back posture disorders of the phenotypic signs of DCT connected with the musculoskeletal system, with formation and development of

the dentoalveolar anomalies in children where their frequency varies within digital values from 70 to 96% in some literature [9]. In structure of the dentoalveolar anomalies, deep crossbite and distal occlusion are mostly often revealed [37]. Thus the main forms of scoliosis are characterized as the main manifestations of bone connective-tissue dysplasia (except for idiopathic scoliosis) [48, 50].

At the same time, some researchers have established the interrelation of syndrome of TMJ dysfunction and condition of backbone which characterize that pathogenetic mechanisms of their formation are connected with dysfunction of the musculoskeletal system, anomalies of bite leading to TMJ dysfunction [8]. During the last period in the literature there were data that the dentoalveolar anomalies and deformations were major factors of occlusion defects, occlusive contacts, emergence of supercontacts, which, in turn, create prerequisites to the development of incoordination of chewing group of muscles where there are functional TMJ dysfunctions with the reliable importance. But, at the same time, the predominating role of deep bite to the development of TMJ dysfunction due to the expressed disorder of occlusive surface was defined [33]. According to their data of development of the expressed functional changes of chewing group of muscles are connected with the disorder of relative positioning of elements of joint caused by deviation of articulate head and meniscus of articulate pole and articulate eminence.

According to some authors there is a direct interrelation of underdevelopment of front part of the lower jaw or distal position of the lower jaw among children with scoliosis [21, 47]. Thus F.Ya.Khoroshilkina (2002) noted that children with scoliosis had a high level of prevalence of dentoalveolar anomalies. Besides, the interrelation of TMJ dysfunction with generalized hypermobility of joints and defect of the mitral valve [18] was established. Meanwhile, some authors specify the high level of prevalence of inflammatory processes in the gingival margin among the children having scoliosis [21].

It should be noted that the range of the DCT abnormality are the factors contributing to formation and development of diseases of paradontium which are connected with defects of bite, haemodynamic deviation in system of microcirculation and defect of tissue immunity [32]. Thus there are authentically significant indicators of prevalence of diseases of paradontium among children with DCT, than among somatic healthy children [28]. Meanwhile, there are data that children with DCT have certain diagnostic stomatological markers which are connected with a small threshold of the oral cavity, deep bite, prognathia, congenital shortening of

frenulum of tongue, narrowing of the lower jaw, upper palate, crossbite in frontal part of the lower jaw, diastema, a gum recession in the literature [32, 41].

Nowadays broader studying of dental manifestations of the differentiated DCT forms has been carried out. So, the main phenotypic signs of Marfan's syndrome are the extended and narrow face, various pathologies of auricles up to their absence, deep cavernous eyes and hypertelorism due to the increased ethmoidal labyrinth, frontal eminence which are sharply acting forward, pressed and expanded root of nose,micrognathia, Gothic palate, partially edentulous connected with defects of follicular development of teeth [26]. Thus Ehlers-Danlos syndrome is characterized by existence of cheilitisexfoliativa (dry and exudative form), and also prominent chin, underdeveloped wings and bones of nose, upper jaw, Gothic palate, clefts of hard and soft palate, anomaly of bite, generalized periodontal disease, high prevalence of caries, lack of some teeth or formation of supercontacts are possible [42].

It is necessary to emphasize that the main phenotypic signs of undifferentiated DCT are craniofacial anomalies of development: dolichocephalia, anomalies of development of ears, microgenia, micrognathia, Gothic palate, defects of growth of teeth, anomalies of bite, narrowing of tooth alignments, dense position of teeth of the upper and lower jaw, anomaly of position of separate teeth, pathologies of parodontium of dystrophic and inflammatory character, displastic-dependent form of TMJ defect, increase in excretion of metabolites of connective tissue with urine and saliva [22]. Besides, TMJ dysfunction of syndrome type of connective tissue dysplasia were defined [31].

It should be noted that heavy clinical symptom of TMJ dysfunction is the miofacial pain syndrome that in some references is expressed as Costen's syndrome and maxillofacial dyskinesia. Thus there can be a number of neurodental symptoms which are connected with irradiation of pain in various parts of the face and neck, and usually it is followed with emergence of trigger points in muscles[16]. Besides, similar symptoms in the form of musculo-tonic manifestations are revealed in osteochondrosis of muscles of cervical part of backbone [48]. During the last period the accurate interrelation of influence of the psychoemotional sphere of the patient with expressiveness of the painful symptom in TMJ pathologies [48] was established.

It is necessary to emphasize that the multiorgan DCT defects in a certain degree promotes the development of chronic all-somatic diseases [35]. Development of these diseases promotes decrease in immunobiological reactivity of organism in children and often leads to the

development of secondary immunological insufficiency which are followed with activation of parodontium pathogenic microflora [19]. In this regard the modern concept of etiology and pathogenesis of inflammatory diseases of tissues of parodontium provides, as a key factor decrease in children's immunity [51]. Thus the activated parodontium pathogenic microorganisms promote development of anti-inflammatory cytokines which damage tissues of parodontium [13]. Besides, cytokines which affect the biochemical messengers regulating stimulation and braking of inflammatory reactions which initiate the immune answer and indicate interaction between systems, cells in general [23]. Meanwhile, some authors characterize that IL-1 and TNF, in particular IL-1β and TNF-α have the greatest damaging effect in inflammatory and destructive processes of paradontium tissues. Besides, there are data that pro-inflammatory cytokines define expressiveness of inflammatory process and resorption of bone tissue, especially in generalized defects of parodonium tissues [4]. It should be noted that one of key links of the pathogenetic mechanism of development of chronic inflammatory process in paradontium is the condition of immune system of organism (humoral and cellular) [13].

It is necessary to emphasize that environment and its ecology has important value for certain etiologic and pathogenetic factors of development of inflammation of marginous gum. So, continuous influence of a complex of climatic and ecological factors causes tension of functional activity of organs and systems of organism where "favorable" conditions for emergence and development of pathological processes of organs and tissues of the oral cavity [32, 49] in inhabitants of the North. Among children of school age of 7-14 years of Yakutia the prevalence of diseases of paradontium fluctuates from 39,60 to 84,25% and among teenagers of 15 years this indicator makes 89,36%. Thus the intensification of the peroxidation of lipids (POL) in response to influence of extreme factors is one of pathogenetic mechanisms of development of inflammatory diseases of paradontium. Besides, among the children's population of the North the high level of frequency of congenital cleft of upper lip and palate 1 was noted: 765±68,16 (1,42±0,17%0) where nearly a half (41,21%) of anomalies was presented by one - and bilateral clefts of upper lip, dental arch, hard and soft palate demanding more long-term and difficult treatment. Meanwhile, in this group of children the pH deviation of the mixed saliva to the sour one which leads to decrease of the activity of alkaline phosphatase was noted. Thus concentration of calcium in oral liquid in children with congenital defects was

characterized as the low level which, as a rule, reduces the remineralizing potential of the mixed saliva [15].

It is necessary to emphasize that there is a wide range of various systems of treatment, rehabilitation of patients with DCT. So, T.I. Kadurina (2000) recommends physiotherapy exercises, massage, dietotherapy, vitamins, physical therapy, microcells and metabolites treatment for complex treatment and dispensary supervision of hereditary diseases of connective tissue. These actions, according to the author, stimulate collagen formation and correction of disorders of synthesis of glycosaminoglycan.

For normalization of connective tissue exchange, some authors recommend the use of collagen stabilizing complex with vitamins E, B2, B6 and C for DCT. Thus vitamin E increases antioxidant protection, improves tissue respiration, proliferation of cells, and B6 vitamin improves synthesis of collagen and stabilizes collagenic structures, vitamin C improves synthesis of collagen and pro-collagen. The collagen stabilizing complex is used in pre-and the post-natal periods [32].

It is known that decrease of regenerator potential of connective tissue and hemorrhagic syndrome is one of the brightest manifestations of DCT. In this regard, when carrying out early surgical correction concerning a frenektomy of upper lip (after eruption of the first permanent incisors) and lower lip, tongue (from 2-year age) and difficult removal of teeth, a number of authors recommend the three-day courses "ASCORUTIN", potassium orotat, "CALCIUM-D3 NYCOMED" in combination with "DICYNONE" and SUMAMED" (250 mg) for the purpose of increase of extent of regeneration of connective tissue, and also prevention intra-and post-operational bleedings and inflammatory complications [54].

It should be noted that organized system of medical care has important value in improvement of specialized dental help for children and teenagers with DCT. In this regard a certain algorithm (stage-by-stage solution) which includes definition of the accompanying pathology, symptoms of illness, hidden manifestations, including small and big signs, search of diagnostic reference point, preliminary scheme of examination, preliminary diagnosis, additional researches, specified diagnosis, individual plan of dental treatment and dispensary supervision was developed. Thus E.E. Statovskaya and T.I. Kadurin (2013) recommend considering advanced diagnostics which is connected with the dental functional analysis and examination by experts (cardiologist, orthopedist-vertebrologist, oculist, endocrinologist, neurologist, psychotherapist, gastroenterologist, therapeutist, pediatrician, etc.) that will allow early identification and treatment of the diseases associated with DCT.

CONCLUSION

Thus, prevention of diseases of pathological processes of organs and tissues of the oral cavity and also maxillofacial area among children with DCT has certain features. Thus similar researches in the conditions of the Republic of Sakha (Yakutia) haven't been studied yet earlier that dictates need of complex researches taking into account specific regional biological and environmental risk factors of formation and development of dental diseases in children with DCT.

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The Cholelithiasis Pathogenesis

The paper is dedicated to the memory of my teacher, MD, Professor, Honored Scientist of Russia, and Honorary Professor of the Sechenov First Moscow State Medical University

Vsevolod Alexandrovich Galkin

ABSTRACT

The author reports his search for scientific papers in the open databases Pubmed, Europa Pubmed Central, eLIBRARY using the search terms «gallstones and pathogenesis», as well as Russian equivalents for "cholelithiasis". For the analysis articles on the cholelithiasis pathogenesis with a high citation level were selected.

So far, the mechanisms of formation of stable nuclei of crystallization of cholesterol stones are not fully elucidated. Recently, there are many facts proving essential Galkin - Chechulin effect in the formation of cholesterol stones crystal nuclei and the role of the bacteria and inflammation.

Thus, in the pathogenesis of gallstone disease, the Galkin-Chechulin effect plays a significant role in the formation of stable crystallization nuclei (embryos). Such bilirubin containing microlites do not spontaneously dissolve and there may be no symptoms for decades, and in the event of the conditions, described by W.H. Admirand and D.M. Small they become nuclei of crystallization of cholesterol stones of macroscopic dimensions.

Keywords: cholelithiasis, pathogenesis, lithogenesis, cholesterol stones, biliary sludge, the Galkin - Chechulin effect.

INTRODUCTION

Cholelithiasis (CL) in recent years has become one of the most common diseases of the digestive system in the world. Outstanding domestic gastroenterologist, author of the discovery of the phenomenon of bilirubin crystallization in the unsaturated solution of bile, MD, professor, honored scientist of Russia, V.A. Galkin writes about CL: "Like a cloud of locusts, cholelithiasis is coming upon the mankind - this is truly a scourge hanging over people. By the simplest estimations, every tenth inhabitant of the Earth is experiencing suffering from gallstones "[4]. The highest prevalence of gallstone disease is observed among American Indians - from 59.5 to

68.2% among women and to 45% among men [40, 35, 45]. The lowest morbidity is observed among the Masai of East Africa, until recently they have not been detected with cholelithiasis [44]. In the world the CL prevalence among the adult population is 10% on average. In recent years, its incidence is increasing rapidly, including in our country.

It should be noted that so far the CL pathogenesis is not fully studied out. Every year in the world hundreds of articles dealing with different aspects of cholelithiasis are published. Knowledge of the disease pathogenesis intricacies is the key to the development of effective prevention and treatment.

The current stage of the CL pathogenesis study begins in the second half of the last century. To the beginning of XX century for 300 years of CL studying two concepts of the pathogenesis of gallstones formation have been formed [5]. They were presented by German scientists: inflammatory - B. Naunyn [34], and metabolic - L. Aschoff [11]. Microbial nature of the gallstone formation the well - known Russian therapist S.P. Botkin suspected, long before the appearance of B. Naunin famous work he assumed that "... life [of the microorganisms] gives in a result such chemical compounds which make substances that are usually in the bile in solution - insoluble, and because of this shortfall ... [precipitate]" [1]. In the first half of XX century good results were achieved in the study of chemical compounds that are the part of gallstones: cholesterol, bile acids [25, 33]. Up to the 50-ies of the last century, the major lipoproteins were identified; their plasma concentration and the role in the metabolism and transport of lipids were also defined [36]. These achievements became the basis for the further development of the scientific study of the pathogenesis of gallstone disease and the search for new effective methods of disease prevention and treatment.

The discovery of the laws of crystallization of bilirubin and bile cholesterol is an important milestone in the study of the pathogenesis of stone formation in the gall bladder. V.A. Galkin and A.S. Chechulin in 1957 experimentally established previously unknown phenomenon of bilirubin crystallization in the bile unsaturated solution in terms of bacterial catarrh inflammation of the gall bladder, which was associated with a decrease in the pH of the colloidal solution of bile [6]. In 1968, an article of W.H. Admirand and D.M. Small (Boston University) about the laws of crystallization of cholesterol and bile was published; for the first time built a model schedule of cholesterol crystallization, depending on the concentration of cholesterol, lecithin and bile acids

in the triangular coordinate system [10]. The current stage of the study of the gallstone disease pathogenesis began with in-depth research around these two scientific problems.

Composition of gallstones. At studying the composition of gallstones and its crystal structure as a result of use of X-ray analysis in the 60-s of the last century new data were obtained. Thus, it was found out, that the in vivo cholesterol is crystallized into monohydrate crystals of cholesterol, bilirubin into - biliribunate crystals of calcium, and calcium carbonate - vaterite, aragonite and calcite [29]. Later, it was noted that gallstones were distinguished for their diversity. As part of the stones such minerals as apatite, struvite, whitlokite and et al were discovered. Most of the researchers have identified two large groups of stones: cholesterol and pigment. In turn, pigment stones are divided into black and brown [51]. Subdivision of gallstones into types is very conditional because in clinical practice there are no absolutely "pure" stones. The stones are composed of a main component and impurities. Stones, in the dry residue of which, cholesterol is more than 50% are Cholesterol ones [20, 37]. Cholesterol stones are the most common in Western countries; they make up to 75-80% of gallstones. It should be noted that the frequency of the stones with cholesterol content in dry residue 90% (the so-called "pure" cholesterol stones) is not so high, only up to 10% of the gallstones' structure.

Scientists at the head of T. Qiao from the laboratory for the study of cholelithiasis (Guangzhou, China), based on the analysis of cholelitomy 807 cases identified 8 types of gallstones: cholesterol, pigment, calcium carbonate, phosphate, calcium stearate, protein, cystine and mixed [50]. In turn mixed stones were divided into more than 10 subtypes. Earlier, German researchers based on analysis of 1025 gallstones identified 6 types of stones: cholesterol, bilirubin, calcium, magnesium, palmitate-stearate, and polysaccharide. Calcium stones are composed of apatite, aragonite, calcite and uncertain calcium minerals, and magnesium – of struvite [39]. The mineral composition of gallstones has wide variability not only among the inhabitants of different countries, ethnic, age and gender groups, but also in one and the same patient. Type of the postponed for gallstone crystal layers may vary throughout one's life.

The microstructure of gallstones by scanning electron microscope allows understanding some aspects of lithogenesis [50]. Thus, it was found that the cholesterol monohydrate crystals in the form of rhomboid blocks are packaged as packs of a linear or radial character [28], and the crystals of calcium salts bilirubinate, often in the form of bizarre and globular formations, - chaotic. Primary elements of cholesterol monogidrite crystals and bilirubinate calcium in the

form of a separate rhomboid and globular crystals scientists find at microscopic examination of bile in patients with biliary sludge [31].

Biliary sludge. The term "biliary sludge" was introduced in the 70 -s of the last century in connection with the broad introduction of ultrasound [27]. It should be noted that in 1957, V.A. Galkin and A.S. Chechulin determined the conversion of bile into the gel state [6], but only in the late 60-s American scientists have found out the conditions of the crystallization of cholesterol and its precipitation [10] .

Biliary sludge - a state of bile with increased echogenicity with or without microcrystalline suspended or precipitated particles, diagnosed by transabdominal ultrasonography and clinical research methods. In 2002, the Russian Gastroenterological Association adopted a classification of gallstones, in which biliary sludge has been recognized as its initial or pre-stone stage [7]. Some researchers abroad have come to this conclusion earlier. [19, 43]. In Russia, V.A. Galkin, professor at the Setchenov Moscow Medical Academy was the first to study CL pre-stone stage [2 - 4].

The mechanism of formation of pigment stones is studied in detail enough. Black and brown pigment stones mainly consist of dicalcium bilirubinate (Ca (HUCB) 2), which polymerized and oxidized, turns into black stones, and those that remain unpolymerized, turn into brown ones. The formation of brown stones is caused by a bacterial infection, and black stones are formed by the crystallization of calcium bilirubinate at relatively sterile bile [53].

The formation of cholesterol stones. Some stages of crystallization of cholesterol gallstones are not entirely clear. Cholesterol in the bile because of its insolubility in water forms mixed micelles with phospholipids and cholate, which merging form vesicles at the fullness of bile with cholesterol and changes of cholates and phospholipids ratio. Subsequently unilamellar vesicles fuse to multilamellar forming liquid crystals, and then, through the intermediate forms, - into rhomboid crystals of monohydrate cholesterol [54]. These crystals merging must form embryos (tiny crystalline particles), which growing, must reach macroscopic dimensions. That embryo formation of cholesterol stones until now has not been sufficiently studied. This initial stage of formation of gallstones is indicated by a number of authors as nucleation stage or nucleation followed by growth stage or crystallization. The generation stage begins with the appearance of the first crystals, and ends with the formation of the embryo. According to some authors, the formation of "pure" cholesterol nucleation is impossible. Spontaneous crystals

nucleation requires highly supersaturated solutions. It is considered that cholesterol may spontaneously crystallize in a solution, supersaturated with cholesterol on 300%. For a human such a concentration of cholesterol in bile is not possible. Therefore, the formation of nuclei of cholesterol crystalline stones occurs in a result of heterogeneous crystallization [41] with participation of salts of calcium, phosphate, bilirubin, etc.

The nucleus or embryo of gallstones' crystallization is detected as small stones smaller than 3 mm. In current clinical practice, the detection of stones with a diameter of less than 3 mm is treated as a diagnostic criterion for gallbladder microlithiasis [42]. It should be noted that so far there is no clear definition of the terms: microcrystals, biliary sludge and microlithiasis. However, for a number of publications microcrystals can be determined as microscopically detected crystals of cholesterol monohydrate, calcium bilirubinate and calcium microsferolits [9], they do not cause any signs of clinical manifestations. Judging on the growth rate of gall stones in the average 1.5 mm per year, the size of the nucleus (embryo) of crystallization may be equal to 1-2 mm in diameter [21]. This position is confirmed by the fact that the study of the structure of small size cholesterol gallstones, referred as microlithiasis, scientists from Italy in the vast majority of cases have not detected the presence of the nucleus. So, out of 10 studied microstones only in two of them the nucleus was determined [16]. It should be noted that cholesterol microstones are unstable; they spontaneously dissolve and respond well to treatment.

It is known that most of the cholesterol stones have a nucleus of dark color. The study of chemical composition of cholesterol stones nuclei has shown that they are heterogeneous and contain cholesterol, bilirubin and high calcium compound [13]. Based on the fact that in the nucleus of cholesterol stones calcium is almost always detected, an American scholar E.W. Moor et al hypothesized the formation of cholesterol stones from calcium embryo. According to the authors of the hypothesis, perhaps, first the calcium nucleus forms, which then begins to grow thick with cholesterol crystals [38]. It should be noted that, according to modern concepts, the surfeit of bile by cholesterol is the main condition for the formation of cholesterol stones [52]. This formation can be accelerated or decelerated with the so-called protein-promoters and inhibitors of nucleation (stone nucleation). Nevertheless, a number of researchers have not confirmed the catalytic role of many proteins candidates for promoters [52]. Controversial is the inhibitory role of apolipoprotein A-I and A-II, as both lipoproteins were found in the bile not only

in patients with gallstone disease, but also in healthy individuals [30]. Mucin remains one of the few protein - candidates with potential role in the formation of gallstones in a human [52].

According to modern concepts, in the pathogenesis of formation of cholesterol stones there are several links:

- Cholesterol-supersaturated bile;

- Crystallization of cholesterol and the formation of the nucleus;

- Factors of the gallbladder, including its hypomotor dysfunction.

Genes - candidates of predisposition to cholelithiasis are identified on all of these links in the pathogenesis [18, 46, 52]. Genetic predisposition to cholelithiasis is oligogene and polygenic. Mutations in the genes: *CYP7A1, ABC1, ADCB4, CCK-1R, ATB7B, ATP8B1, ABCB11* and *ABCB4* cause oligogene cholelithiasis [17]. Polygenic is caused by multiple genes mutation responsible for synthesis, excretion and transport of cholesterol, bile acids and phospholipids, and mucin gene mutation, various receptors [17]. In experiments in mice over 80 the so-called *LITH* genes are identified. In humans, there are appearing more and more cholelithiasis genes - candidates.

Factors in the development of gallbladder gallstones. Gallbladder dysmotility, probably, is the "trigger" in the pathogenesis of cholesterol gallstones, providing the time, required for the precipitation of microcrystals of cholesterol from supersaturated bile. Polish scientists have revealed that in the patients with gallstones in the gallbladder the amount of interstitial telocytes (Cajal-like cells) significantly reduces [32]. Cajal interstitial cells are neural cells, playing a key role in regulating the motility of smooth muscle of the gastrointestinal tract, being a pacemaker for generating electrical pulses of the slow waves.

Besides a hypomotor dysfunction of gallbladder in the etiopathogenesis of stones' formation recently a number of new local factors of the gallbladder has been identified. Thus, not long ago American and Chinese scientists first identified the role of two single nucleotide gene polymorphisms of vascular endothelial growth factor A (VEGFA) in susceptibility to the development of gallstones. VEGFA gene encodes a protein that regulates vascular permeability and angiogenesis [26]. It is known that bile concentrates several times in the gallbladder (Table).

Table

The composition of the liver and gallbladder bile [48, 49]

Indicator	Hepatic bile	Gallbladder bile
pH	7.0 - 8.2	6.0 - 7.0
Specific gravity	1.010	1.040
Water,%	97.2	88.0
Dry residue	2.7	12.0
Bile acids, g / dl	1.1	6
Bilirubin, g / dl	0.04	0.3
Cholesterol, g / dL	0.1	0.3 - 0.9
Fatty acids, g / dl	0.12	0.3 - 1.2
Lecithin g / dl	0.04	0.3
Ca ++, mg-Eq / l	5	23

In the light of new data the gallbladder bile regulatory indicators can significantly be adjusted depending on the genetic characteristics of the vascular system and its permeability. Even in a healthy human gallbladder bile becomes potentially lithogenic due to the accumulation of lithogenesis activators: cholesterol, bilirubin, calcium and pH acidification. It should be noted that the optimum activity of bacterial ß-glucuronidase is observed at pH 5.2. Bilirubin goes to the gallbladder usually in a conjugated form; at bile acidification endogenous ß-glucuronidase can hydrolyze conjugated bilirubin into unconjugated one. The last is connected with Ca, forming insoluble calcium bilirubinate, and precipitates. With increasing bile alkalinity (pH ~ 7.8) and bile fullness with calcium carbonate precipitated [15]. British scientists led by R.P. Thompson found that the gallstones were more closely associated with the level of unconjugated bilirubin than the degree of saturation of bile with cholesterol. Based on these data, the authors concluded that bilirubin and its metabolites are likely to play an important role in formation of cholesterol gallstones [22]. The phenomenon of crystallization of bilirubin in bile unsaturated solution with pH and the presence of inflammatory changes observed in 1957 by V.A. Galkin and A.S. Chechulin

gets more evidence of the important role of this phenomenon in the pathogenesis of cholesterol stones.

The role of bacteria and inflammation.

After the discovery of the Galkin-Chechulin effect more than 50 years have passed, but recently there is increasing evidence to support the role of bacteria and inflammation in the development of gallstone disease, including the formation of cholesterol stones. According to surveys on this issue by A. Swidsinski, S.P. Lee [47] and T.V. Rukosueva [8], the bacteria are found in the bile, gallbladder mucosa and stones, including at their center. Often it is very difficult to set a time when bacterial infection joined CL: before stone formation or after. Perhaps in the development of cholelithiasis bacterial and non-bacterial mechanisms of disease pathogenesis are working closely, replacing each other for years and decades, creating unique personalized microstructure of gallstones. It should be marked that in the patients with cholesterol stones in 24% of cases in bile the presence of bacteria is detected, and at the use of quantitative PCR with primer, universal for bacteria, positive result is recorded in almost all cholesterol stones, even at a negative result of seeding. M. Kawaguchi et al in 1996 first discovered in the mucosa of the gallbladder in a patient with cholelithiasis Helicobacter Pylori [12]. Since there is increasing evidence of participation of the family of Helicobacter spp. bacteria in the pathogenesis of gallstone disease, including the formation of cholesterol stones.

Mechanism of bacterial lithogenesis is associated with activation of the bacterial enzyme systems: beta-glucuronidase, phospholipase, hydrolases and urease. It was established that bacterial phospholipase played an important role in brown gallstones lithogenesis. It frees palmitic and fatty acids from phosphatidylcholine which can form with ionized calcium insoluble compound of calcium palmitate, subsequently precipitating [47]. As for the urease Helicobacter spp., it hydrolyzes urea to ammonia and bicarbonate. The ammonia increases the pH in the bile; it promotes the formation of insoluble calcium salts and their subsequent precipitation [14]. Recently published studies, conducted with flawlessly chosen methods and extensive material, confirm that the bacteria may be one of the main factors that play an important role in the pathogenesis of gallstone disease [24, 23].

CONCLUSION

Thus, in the pathogenesis of gallstone disease, the Galkin-Chechulin effect plays a significant role in the formation of stable crystallization nuclei (embryos). Such bilirubin containing microlites do not spontaneously dissolve and there may be no symptoms for decades, and in the event of the conditions described by W.H. Admirand and D.M. Small [10] they become nuclei of crystallization of cholesterol stones of macroscopic dimensions.

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I.K. Sleptsov, D.K. Garmaeva

The Study of the Histogenesis of Female Fetus Reproductive System at the Mother's Urogenital Infections

ABSTRACT

The literature review is based on the analysis of sources, covering histogenesis and organogenesis of the reproductive system of the fetus in the mother's chronic urogenital infection. Topical issues were highlighted for further study of this problem.

Keywords: female reproductive system, fetus of human, urogenital infections.

INTRODUCTION

Currently, one of the pressing problems in medicine is the presence of female chronic urogenital infections and related pathological processes during pregnancy. The fetus develops in the difficult conditions of the relationship with the mother's organism, so the presence of niduses of infection during pregnancy is a risk factor for the development of pathological conditions of the fetus and newborn [5].

Intrauterine infection of the fetus is a significant cause of reproductive losses. Thus, the frequency of early neonatal morbidity and mortality in chronic urogenital infections mother ranges from 5.3 to 27.4% and stillbirths reaches 16.8%. In the structure of perinatal mortality, 10.1% is due to infections. Infectious and inflammatory diseases play even more significant role in the structure of perinatal morbidity, where they make up 20-38% [16].

However, the true incidence of perinatal pathology caused by infectious agents remain unspecified, due to the absence of screening, cycle of the infection and the incidence of immediate, frequent latent course of the pathological process, the objective complexity of antenatal laboratory diagnostics. As a result, a significant portion of infections remains undiagnosed and statistical analysis is taken into account as a result of complications of childbirth and fetal asphyxia syndrome, respiratory disorders and other pathological conditions [16,17].

The leading criterion for evaluating normal and abnormal morphogenesis of organs and systems of the fetus is organ - and histometry [1].

Urogenital infections have a number of unique features. These include immune-morphological changes, tissue dysplasia, and delayed maturation of tissues and excessive proliferation of connective tissue as a manifestation of regenerative processes. However, these changes are not specific, since they may be due to other exogenous and endogenous agents, but

these symptoms are typical, along with such as local inflammation and vasculitis characterized by the presence of chronic urogenital infection [7].

The nature of damage to the embryo and fetus, the severity of inflammatory changes, as well as the peculiarities of the clinical symptoms in urogenital infections depend on several factors: the properties of the pathogen, the massiveness of infection, fetal maturity, the state of its protection systems, especially mother's and others immunity [6,13, 15, 17].

A feature of urogenital infections is a simultaneous destruction of several urinary organs by different agents, which may be asymptomatic, but often lead to infertility or cause severe fetal malformations, because even small nidus of infection lead to intrauterine infection of the fetus. Reproductive organs of female fetuses being the most vulnerable to disruption of morphogenesis [3].

Histometry criteria for pathological evaluation of the individual stages of morphogenesis during the intrauterine period development of the human fetus to the brain, lungs, heart and other internal organs are currently available [18, 21].

Precise quantitative criteria for the dynamics of growth of the female reproductive system disorders and their development during fetal development are not designed; only a few studies were made in this field [10-12].

Histogenesis of vagina is a complex process of interaction of embryonic tissue primordia from different backgrounds and even in normal pregnancy it is not sufficiently investigated [18]. Vagina is a target organ for being hit by a wide range of chronic urogenital infections pathogens, including specific organotropic ones [8].

In the presence of urogenital infections and mild forms of placental insufficiency during pregnancy, accelerated maturation of the fetal gonads (hyperplastic type of structure) is observed, that subsequently can lead either to primary infertility, or to early ovarian failure or occurrence of polycystic ovaries [25].

Genital infections are accompanied by diffuse infiltration of the mucous membranes of the genitals - mostly lymphocytes and plasma cells. Histology is characterized by neutrophilic exudation and infiltration of the mucous layer of the submucosa T and B lymphocytes, histiocytes, macrophages, dendritic cells. [9]

The question of the structure of the normal lymphoid structures in the organs of the female reproductive system causes a lot of controversy. Some authors deny the presence of

immune cells in them [19]; other researchers confirmed the presence of lymphoid nodules [21 - 23].

By immunomorphological structures of the reproductive system are known lymphoid accumulations beneath the epithelium of the mucous membranes of the genital tract (mucosa associated lymphoid tissue (MALT), which are presented in the form of scattered in the mucosa of the uterine body lymphoid cells, lymphoid nodules and inter epithelial lymphocytes in the glandular and surface epithelium [4].

This organ provides lymph epithelial local protective reaction and creates a protective barrier for the antigens passing through the mucosal epithelium. Lymphoid aggregates contain mostly T- and B-lymphocytes, which cooperate in the synthesis of the protein antibodies [13].

In ontogenesis, there is a continuous change in the cellular composition of the lymphoid tissue of the endometrium. With the newborn period to old age a number of blasts, large and medium-sized lymphocytesdecrease, a number of small lymphocytes, macrophages and degenerating cells increases.

The greatest development of lymphoid tissue in the endometrium reaches at 10-20 years of age and be maintained throughout childbearing years [2].

The available scientific domestic and foreign literature data on the effect of urogenital infections on the development of structures in lymphoid organs of the female reproductive system wasn't found.

CONCLUSION

Thus, despite the large number of publications dealing with chronic urogenital infections and associated intrauterine infection, the impact of chronic urogenital infections in the organogenesis of the fetus remains unadjusted and requires further research.

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Risk Factors of the Development and Rupture of Cerebral Aneurysms

ABSTRACT

Background and purpose. This review examines the evidence of epidemiological, pathophysiological and genetic studies on the search for risk factors of non-traumatic cerebral aneurysms and subarachnoid hemorrhage.

Summary of the review. The epidemiological studies indicate significant differences in the incidence of subarachnoid hemorrhage in different populations. No one of the established risk factors can explain this phenomenon, and thus, likely there are other risk factors affecting the development of the disease. Mechanisms of aneurysm's development and rupture are not sufficiently clear currently. It was established the influence of genetic factors on the development of the cerebral aneurysms in many studies.

Conclusions. The data of recent studies suggest that the development and rupture of cerebral aneurysms are due to a complex interaction of modifiable factors and genetic predisposition. The discovery of new risk factors of the disease, including genetic ones, contributes to the understanding of mechanisms of cerebral aneurysms, and could be the basis for the prevention of subarachnoid hemorrhage.

Keywords: cerebral aneurysm¸subarachnoid hemorrhage, genetics.

INTRODUCTION

Cerebral arterial aneurysm (CA) is a local protrusion of the brain blood vessel's wall and is the most common cause of non-traumatic subarachnoid hemorrhage (SAH). Despite impressive advances in the diagnosis and surgical treatment of ruptured CA occurred recently, SAH is a common disease with a high fatality rate. Mechanisms of development and rupture of the CA are largely unclear currently. The epidemiological, pathophysiological and genetic studies on the search for risk factors of cerebral aneurysms and subarachnoid hemorrhage are examined in the present review.

Epidemiology. The CA incidence is estimated at about 5-10% in a population [15]. Currently, a significant number of CA diagnosed incidentally as a result of surveys conducted in conditions not related to the SAH. This is due to the widespread introduction into clinical practice of such methods of examination as magnetic resonance angiography (MR angiography) and

computer tomography angiography (CT angiography, CTA) [56]. For example, the cerebral aneurysms were diagnosed in 1.8% of cases when the MRI examination of 2,000 people was performed (RotterdamStudy) [30].

The CA rupture leads to the development of subarachnoid hemorrhage. Approximately 85% of SAH are caused by rupture of saccular aneurysms in the brain base [2].The low rate of the SAH incidence in the population compared to the CA incidence is probably due to the majority of aneurysms is not broken [15].

SAH has the high mortality rate [2, 10, 11, 27]. It ranged from 8.3% to 66.7% according to the data of 33 population-based studies [10]. Recently, there has been a downward trend in SAH mortality, caused by the improvement of diagnosis and treatment [10]. After SAH the 12% of patients have significant limitations in daily activities (3 points on the modified Rankin scale), another 6.5% of patients are depending on outside assistance (4-5 points on the modified Rankin scale) [10]. Cognitive disorders associated with poor functional recovery and low life quality diagnosed in 20% of patients after SAH [40].

According to a meta-analysis of 51epidemiological studies [28] SAH incidence is approximately 9100000 person-years, but varies widely in different countries. Thus, the incidence in Japan and Finland has almost two-fold average, whereas in Central and South America, by contrast, the incidence is significantly lower (22.7; 19.7and 4.2, respectively)[28].

SAH incidence increases with age [28, 49]. For example, the incidence in age<25 years old was 2, 0100000 person-years; 25-35years –7.7; 35-45 years–0.52; 45-55years–19.5; 55-65years–24.8; 65-75years–25.4; 75-85years–26.2years; >85 years–31.3[28]. The SAH incidence in children is low and increases with age. According to the study [57], the incidence in the teens (15 to19 years) is 0.52per 100 000 person-years; while in the age from 0to 4years–0.06; from 5 to9 years–0.05; from 10 to14 years–0.09.

In addition, the gender-specific SAH prevalence is described: the incidence is higher in the female compared to the male (OR = 1.24 (95% CI: 1.09 -1.42)) [28]. The reasons for the high SAH incidence among the women are unclear, but a possible explanation are hormonal factors (including the use of hormone replacement therapy) [26, 53]. Gender distribution in different age groups are not identical: the incidence is higher in men in the young age (25-45 years), while in women – in age >55 years [28].

The differences in the SAH incidence depended on ethnicity and race are described. For example, the Blacks and Hispanics have a higher SAH incidence compared to the Caucasians [17,

51, 54, 58]. Ethnic features in the hospital hemorrhagic stroke structure, including the SAH, were established in the study [12]. Share of hemorrhagic stroke among the Asian indigenous is higher compared to the Caucasians in Yakutia (OR = 2.42; 95% CI: 1.72-3.41) [12]. The reasons for this phenomenon are currently unclear.

Significant differences in the SAH incidence, depending on the region of the world, are the subject of the many studies. This phenomenon is probably due to genetic causes and diagnostic features of the disease in different countries [21]. Several factors that can cause SAH high levels in Finland and Japan are described, but the extent of their contribution to the development of the disease remains unclear. For example, the high morbidity in Japan could be affected by such factors as the more elderly average age of the population (compared to the other ones) [61]; careful consideration of the sudden pre-hospital death, the cause of which could be SAH; as well as the widespread use of neuroimaging techniques for the diagnosis of hemorrhage [28]. The factors of the high level of SAH morbidity in Finland indicate greater prevalence of smoking, hypertension [50] and alcohol [34]. The low SAH incidence in the South and Central America are likely to be explained by the younger average age of the population [29]; lack of access to medical care in these regions [28], which could affect the quality of diagnosis. Another explanation for the differences in the SAH incidence may be due to the racial characteristics. However, none of the above factors can explain fully the difference in the SAH incidence between regions [28] and thus probably there are other factors affecting this phenomenon.

During the past decades, the SAH incidence decreased (approximately 0.6% per year) [28], while this decreasing is much moremodestthan the reducing dynamics of the stroke incidence in general. The reason for this phenomenon may be that the SAH development is more depending on genetic factors, than a stroke in whole [15].

Pathogenesis. Rare causes of the CA include Ehlers-Danlos syndrome type IV, a hereditary defect in collagen with saccular and fusiform aneurisms [55], and mycotic aneurysm [2]. Autosomal dominant polycystic kidney disease is a risk factor for CA, and it is the cause of less than 1% of non-traumatic SAH. The patients with this disorder have CA in 10-13%, most aneurysms are located in the middle cerebral artery [55]. Other rare risk factors for CA are sickle cell disease, coarctation of the aorta [55].

Most of the CA are not innate and develop over a lifetime. This is confirmed by the fact that aneurysms are very rare in children [28, 57]. The pathogenesis of the vast majority of the CA

includes several interacting mechanisms. The thinning of the structural elements of the vascular wall, such as the internal elastic membrane and the extracellular matrix, is considered as the main reasons for the development of CA [1]. The hemodynamic effects, which lead to changes in the internal elastic membrane, followed by thinning of the media and the outward protrusion of the vessel wall, play a key role inthis process [1, 35, 36, 47, 62]. Cerebral aneurysms are most common in places under the strong hemodynamic effects, such as in arterial bifurcations and angulations [22]. Various mathematical models have shown that the bifurcation and angulation areas are experienced the abnormally high hemodynamic stress, which leads to hemodynamic stress and remodeling of the vascular wall [22]. The formation of the aneurysm begins with the endothelial damage, with subsequent the development of inflammation, which leads, in turn, to the tear or defect of the vessel wall. The extension of this vessel defect produces a cerebral aneurysm [14]. Inflammation is a critical process that preceded the formation and rupture of CA [59]. Tumor necrosis factor alpha (TNF-α) is the key immune modulator, which is involved in the pathophysiology of CA [60].

The apoptosis of smooth muscle cells of a cerebral vessel is important in the mechanism of CA [2, 42]. Reducing the number of smooth muscle cells associated with apoptosis may lead to a violation of the elastic fibers synthesis [2]. Matrix metalloproteinase (MMPs) also take part in the extracellular matrix remodeling [25, 33, 45], resulting the loss of internal elastic membrane, medial thinning, and aneurysm formation. The structure of the vascular wall of the ruptured CA and the unruptured CA are different. Ruptured CA are characterized with the considerable infiltration of the aneurysm wall by macrophages, leading to the loss of smooth muscle cells, matrix proteins and rupture of CA [52].

Probably the atherosclerotic process plays an important role in the CA pathogenesis. This assumption is confirmed by the fact that arteriosclerosis is an important element in the development of aneurysms occurring in other vessels, such as aorta [37, 41, 63]. The presence of atherosclerotic vessel wall lesions is CA peculiarity, which occur even in the small size aneurysms, where in the progression of atherosclerotic lesions was positively correlated with the growth of the aneurysm [32]. According to some authors, the atherosclerotic process involved in the formation, growth and subsequent rupture of CA [5, 24, 32], while other ones do not support this hypothesis [19].

To date, there is no consensus about the CA growth dynamics. It is more likely that intracranial aneurysms generally not grow at a constant rate. According to study [20], the real

growth process is irregular and intermittent, with periods of stability or periods of growing with the low and high risk of CA rupture, respectively. The study [3] examined the chronology of the CA development by the method of determining the time of occurrence of a radioactive isotope of carbon (14C) in collagentype I, which is a dominant component of the molecular target audience. The samples of the ruptured CA and the unruptured CA of the Asian patients who underwent surgical treatment were studied. It was established that all samples with the age of the aneurysm's formation<5 years contained the collagen type I. This phenomenon was not depended on the patient's age, CA size, morphology, presence of aneurysm rupture. However, the collagen age was significantly lower in patients with a history of risk factors such as smoking or hypertension, compared to patients without risk factors (1.6 ± 1.2 vs. 3.9 ± 3.3years,respectively; $p = 0.012$). Thus, the presence of large amounts of newly formed collagen type I in aneurysm presupposes the existence of constant remodeling of collagen, which is much faster in patients with risk factors [3].

The most important factors affecting the risk of CA rupture are the size and location of the aneurysm [9, 15, 31, 43]. CA rupture risk increases when the aneurysm has a large size (>7 mm) [31]. The risk of rupture of the aneurysm increases when CA localization is front communicating artery [31], according to other authors – in the posterior part of the Willis'circle [43]. Additional risk factors are smoking hypertension, alcohol abuse, family history [31, 44, 46]. Use of skim milk and fruit, on the contrary, reduces the risk of SAH [48]. In addition, the same effect has been demonstrated for dietary antioxidants and soybean products [38, 39].

Genetic factors. The increased risk of aneurysms in relatives of patients with SAH confirmed the genetic component in the CA development [15, 43, 55]. The hereditary aneurysms more frequently localized in the middle cerebral artery, are larger and are often multiple compared to the sporadic aneurysms [15]. Most of the prevalence of CA in patients with polycystic kidney disease, Ehlers-Danlos syndrome type IV and fibromuscular dysplasia also supports the theory of the existence of the genetic mechanisms contribute to the formation and rupture of the aneurysm [55].

The recent large meta-analysis [4] included the research data of the possible associations of 41 single nucleotide polymorphism (SNPs) of 29 genes with the risk of CA, which have been published in electronic databases (PubMed, EMBASE, GoogleScholar) until December 2012. Total analysis summarized the data obtained in the study of 32,887 individuals with CA and 83,683 control subjects, who were unrelated individuals with confirmed (by CT / MRI - angiography and

digital subtraction angiography) of the populations of Europe, Japan and China. Cases of intracranial aneurysms with hereditary diseases, such as polycystic kidney disease in adults or Ehlers-Danlos syndrome are not included in the study. Total analysis included the 66 studies, as well as studies of 60 single nucleotide variants of candidate genes and 6 genome-wide studies. The analysis identified 19 SNPs, associated with the CA. The most robust associations were obtained for 11 of the 12 SNPs founded in the genome-wide studies: loci on chromosome 9 (rs1333040 and rs10757278), chromosome 8 (rs9298506 and rs10958409) and chromosome 4 (rs6841581), as well as variants 9p21.3 (rs2891168), 2q33 (rs1429412 and rs700651), 7q13 (rs4628172), 12q22 (rs6538595) and 20p20.1 (rs1132274). 8SNPs were identified in studies of association of candidate gene variants with the CAA risk. The genetic variant *SERPINA3* (rs4934) and 2 variants associated with collagen gene (*COL1A2* [rs42524 G> C] and *COL3A1* [rs1800255 G> A]), showed the most strong association with the disease. Another SNPs gene variants associated with CA included: geparansulfataproteoglikan 2 (rs3767137), versican (rs251124 and rs173686), and angiotensin-converting enzyme (*ACE) I / D* and interleukin 6 (*IL-6*) G572C. The diversity of genes identified in this meta-analysis indicates the existence of multiple pathophysiological mechanisms that contribute to the CA development and rupture. These mechanisms include regulation of the vascular endothelium and extracellular matrix integrity [4].

As a result of the search carried out in the database PubMed (2013 – February2015.), we found several new studies in the possible associations of genetic variants with the CA risk. The study [8] founded the association of *COL1A2* gene polymorphisms with CA risk in the German population. In the study of the possible relationship of three SNPs of *COL1A2* gene, namely rs42524in exon28, rs1800238 in exon32, andrs2621215in intron46, with CA, a positive association between SNP allele GC rs42524in exon28 with disease has shown (p = 0.02). Other polymorphisms showed no significant associations. The study [23] tested 9.4 million genetic variants to identify associations with the risk of saccular CA in the Finnish population. Four new loci associated with risk CA were identified (2q23.3; 5q31.3; 6q24.2; 7p22.1).

In the study [13] three polymorphisms of *EDNRA* gene (rs5335, rs6842241 and rs6841581) were genotyped to investigate the association with sporadic CA, as well as the size of the aneurysm. There was found no significant differences in the frequency distribution of genetic variants of the gene *EDNRA* between patients and the control group, but it was found that the GG rs6841581 genotype correlates with the size of aneurysms. Thus, it was established that the polymorphism rs6841581 of *EDNRA*gene has a significant association with the size of CA,

indicating a possible role for the gene *EDNRA*in genetic mechanisms of CA development and rupture [13].

Association of endothelial nitric oxide synthase *eNOS* with the spontaneous CA risk and aneurysms sizewas investigated in the study [6]. It was studied two polymorphic loci (G-894T and T-786C) in *eNOS* gene. GG genotype G-894T polymorphism was associated with a higher risk of CA, compared to the GT and TT genotypes (OR = 1.897, 95% CI: 1.023 – 3.519, p = 0.04). Patients with CA had a higher frequency of allele C of polymorphism T-786C, compared to the control group. C allele was associated with a higher risk of CA, compared to T allele (OR = 2.116; 95% CI: 1.073 – 4.151, p = 0.030). It was found no significant relationship between *eNOS* gene polymorphisms with the size of the aneurysm. Thus, it was concluded that the *eNOS* gene may be involved in the occurrence and development of CA. The study [7] conducted in a population of India; it was shown that a gene *VCAN* is a candidate gene involved in the pathogenesis of CA. The study confirmed the previously detected rs251124 polymorphism association with the CA risk, as well as identify new association polymorphism rs2287926 (G428D) with the disease.

The study [16] found a new area associated with the CA risk, located on chromosome 7, which has been described as being associated with ischemic stroke and artery occlusion of large diameter, suggesting a possible genetic link between this subtype of stroke and intracranial aneurysms [16]. The study [18] conducted in Dutch and Finnish populations studied the relationship of individual alleles of SNP, associated with the CA, the localization of aneurysms in the middle cerebral artery (MCA) and rupture of the aneurysm at a young age. The authors concluded that genetic factors play a more significant role in the development of aneurysms, localized in the middle cerebral artery, compared to aneurysms in the other sites. This phenomenon, indicating the genetic aneurysms heterogeneity depending on location, must be taken into account in future genetic studies [18].

CONCLUSION

Thus, these studies suggest that the development and rupture of cerebral aneurysms are due to a complex interaction of modifiable factors and genetic predisposition. Search for risk factors conducted in different directions, including the epidemiology of stroke, clinical and experimental studies, and genetic studies. The discovery of new risk factors of the disease, including genetic, contributes to the understanding of mechanisms of cerebral aneurysms, and could be the basis for the future direction of individualized prevention of subarachnoid hemorrhage.

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The Correlation of the Subject's Quality of Life and Clarity of Self-Concept

ABSTRACT

The article presents the results of a pilot study of the correlation of quality of life (QOL) and clarity of self-concept among indigenous small in number people of the North. In pilot study 97 indigenous small in number people of the North were included (50 (51.5%) women and 47 (48.5%) men). The median age was – 39.9 ± 14 years. The study of psychological characteristics set average, close to the high clarity of self-concept (58.8%). Analysis of the correlation of QOL and perceptions of respondents about themselves showed the presence of correlation between self-esteem and quality of life of clarity of self-concept. Respondents who had a high self-concept clarity had higher rates of physical, social functioning, evaluation of physical and psychological components of quality of life. Thus, the findings suggest the importance of considering QoL along with the psychological characteristics of small peoples of the North.

Keywords: quality of life, SF-36, self-concept clarity (SSC).

INTRODUCTION

The last years scientific are set negative changes in a state of health of population, that is related to complication of public life, increase and change of character of loading on the organism of man, technogenic, ecological, psychological, political and soldiery рисками [15]. Thus by the special researches dependence of health of people was set on 50-55 % from the way of life, on 20 % from an environment, on 18-20 %% from genetic predisposition and only on 8-10 % from a health protection [7].

For the estimation of the state of health of man different methods are used, it is possible one of that to name research of quality of life, that a long ago is confessed in international practice as a высокоинформативного, sensible and economical method of estimation of the state of health of population on the whole. A method allows giving the quantitative estimation of descriptions of vital functions of man - his physical, psychological and social functioning [8].

By the important psychical phenomenon related there is consciousness to the individual health. It is accepted to consider that the origin of consciousness is possible at the certain level of development of consciousness that is the necessary condition of becoming of personality. Determination of Rubinstein is known in psychology of personality. Rubinstein in that

consciousness comes forward the psychical phenomenon, by consciousness by a man itself as a subject of activity, as a result of that the ideas of man about to itself are folded in mental "Image-Me" [10]. In turn, it is come forward basis of consciousness: estimation itself as personalities, realization itself, and selection by a man itself from the objective world [6].

Thus, consciousness supposes comparison itself with this certain, accepted man by an ideal "I", taking away of some self-appraisal and, as a result, origin of sense of satisfaction or dissatisfaction by itself [3]. Thus, personality with the high level of development of consciousness is able correctly understand reality and, taking into consideration it; it is adequate to estimate quality of life.

An **aim** put in our research was to study intercommunication of quality of life of subject and Me-conception, being expression formed of consciousness of personality.

MATERIAL AND METHODS

The Work was performed within the framework of the basic part of the state assignment of the Ministry of education and science of the Russian Federation on the topic «Adaptive capacity and health of the indigenous population of Yakutia in conditions of modernization of the socio-economic system».

A pilot study is undertaken among an adult population п.п. Оленек and Харыялах Оленекского улуса. 97 persons participated in all in a questionnaire, including 50 (51,5%%) women and 47 (48,5%%) men. Middle age made - 39,9±14. Middle age of men 40,5±16,7, for women - 39,5±11,1.

Criteria of including of respondents in research. In research persons were plugged of both sexes from 18 and older, from different task forces, without depending on a presence or absence for them of some somatopathy.

The capture of data came true by the questionnaire of respondents the direct questioning. After elucidation to the respondents of aims canvassed information was given about that, how it is planned to draw on research results and the rules of filling of questionnaires were explained, after a questionnaire was singly filled by a respondent independently.

Description of research instruments.

In research used the 36-item MOS Short-From Health Survey (SF-36), socio-demographic map and questionnaire self-concept clarity "SCC".

RESEARCH RESULTS AND DISCUSSION

The analysis of socio-demographic description of respondents testifies that most respondents made the group of domestic people, having the secondary special education, busy on a complete working day. The least number of polled was had unfinished secondary and unfinished higher education, busy on an incomplete workday.

Next block of questions, touched housing terms, where most (63,9%) respondents answered that is lived in the house of lacking amenities. Among polled 55 (56,7%) respondents live houses of municipal property (lease).

Satisfaction it is possible to define housing terms, how subzero, taking into account, what only 19,6% satisfied with the terms of accommodation and against to her fully dissatisfied - 21 (21,6%), had difficulty to answer/did not specify - 13 (13,4%), other chose answers "rather satisfied/rather dissatisfied".

In the moment of questionnaire 29 (29,9%) respondents specified in the presence of chronic disease.

The indexes of the quality of life of respondents, related to the health, are presented in a next table.

Table 1

Indicators of SF-36 questionnaire scales

SF-36 scales	Mode	percentile		
		25	50	75
FF	57,87	47,41	53,68	57,87
RFF	56,24	48,48	56,24	56,24
P	59,41	40,55	53,26	59,41
GHS	44,82	44,82	47,75	56,55
VA	45	45,01	50,67	57,76
SF	62,27	44,50	50,43	56,35
REF	57,05	47,55	57,05	57,05
MH	52,1	42,19	49,86	58,63

FF - physical functioning, RFF - role physical functioning, P - pain, GHS - general health state, VA - a vital activity, SF - social functioning, REF - role-emotional functioning, MH - mental health.

Results show that the subzero values of indexes of quality of life were marked on the scales of the general state of the general health (GH) and estimation of mental health (MH), i.e. respondents estimated the state of the health and psychological state low. Connection of indexes of QOL depending on sex is not educed. In the researches conducted in Russia, the decline of indexes of quality of life is marked with age [4, 5]. From our data the decline of the physical functioning (PF), and also strengthening of the pain feeling, was also marked with age (BP).

Respondents with the higher level of education marked more subzero expressed of the pain feeling (r=0,34; p=0,000), what persons by the low level of education.

Found out positive connection between the indexes of the physical, ролевого physical functioning and status of employment. So, among working respondents the indexes of the physical functioning were higher (r=0,22; p=0,025), their labor and domestic activity was not limited to the bodily condition (r=0,03; p=0,001).

From data of questionnaire the scale of pain (BP) testifies to absence of her influence on everyday activity of working (r=0,29; p=0,004). It is set that among working respondents the emotional experiencing related to the pain feeling did not prevent to conduct valuable life them, what at unworking, among that there were persons of able to work age (RE, r=0,24; p=0,016)

From data of questioning there are persons not consisting of official marriage felt pain (r=-0, 21; p=0,038) less than, than those that were bound by domestic bonds. This fact can be explained by more young age of not domestic respondents.

Among the polled respondents there were those that suffered chronic diseases. A cross-correlation matrix did not set connections with the scales of questionnaire of SF - 36, except the scale of vital activity (VT). Data specify in the presence of narrowing of range of displays of own potential at a respondent at presence of chronic disease (r=-0, 27; p=0,008).

The got results comport with present in literature data that especially at chronic diseases patients have forcedly to change the way of life, that negatively influences on quality of life [6, 7, 8, 9, 10, 11].

In turn, by psychological researches existence of connection was marked between the health of individual, his internal integrity, from one side, and by the degree of self-appraisal, with other [2]. With the purpose of exposure of adequacy of subjective estimation of QOL by respondents the degree of realized and idea was investigational about to itself, the results of that are presented in a table.

Table 2

Distribution of respondents' self-concept clarity

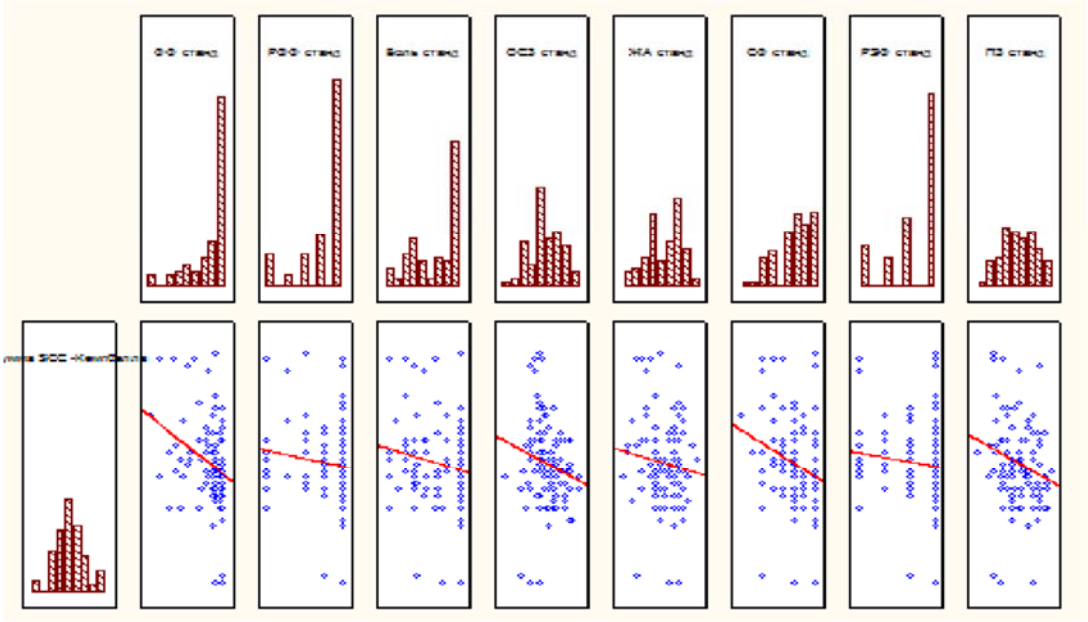
self-concept clarity, points	Abs. (n=97)	%	Mode
Very high (12-20)	3	3,1	12
middle, close to the high (21-32 ближе к высокой)	57	58,8	30
middle (33-39)	25	25,8	35
middle, close to the low (40-51)	12	12,4	40
Very low (52-60)	0	0	0

Distribution of clarity of respondents' self-concept

From these 2 tables evidently clear, that the more than half (58,8%%) of respondents had a middle clarity I am conceptions, nearer to high. At the fourth of respondents (25,8%%) the middle degree of clarity of self-concept is educed. Middle clarity of self-concept, near to subzero discovered at 12,4%%, and the extremely high values of this index are present only at 3,1%% respondents. In our selection of persons with the extremely subzero values of this index did not appear. At the analysis of modal values among respondents, showing middle, near to high (58,8%%), value self-concept most often met is a value 30 (Mo=30), that much nearer to the middle level of clarity of self-concept.

At statistical verification of modal values depending on sex, age, education and other social factors, it is not educed except the source of profit. For those respondents for whom the source of profit is a salary majority was had middle clarity of self-concept, nearer to high. Partly it can be explained by more adequate self-appraisal, plugged in society by means of labour relations.

It should be said, that the clarity of self-concept and self-appraisal of respondent is determined by personality lines, by individuality plugged in plugged in society by means of labour relations.



With the purpose of exposure of connections in the estimations of quality of life with self-concept a cross-correlation analysis was conducted. It is educed that, persons with high self-concept had the best indexes of subjective estimation of bodily, psychological, emotional condition (r=-0, 31, p=0,002), to satisfaction by the state of the health (GH) (r=-0, 25, p=0,011), social functioning (SF) (r=-0, 29, p=0,004).

Consequently the estimation of data of parameter of quality of life had intercommunication with the degree of clarity of self-concept.

CONCLUSION

In conclusion, we note that the potential physical health of people may be different, but the person to understand the value and the importance of taking care of your body, you need to have not an average or close to the high clarity of self-concept, but very high awareness and clarity.

Thus, summarizing the preliminary results of the study, it should be noted that in order to improve the quality of life there must be the formation of a positive self-concept, as clear formed self-concept, despite its dynamism, appears predictor of quality of life of the subject.

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Chronic Inflammatory Demyelinating Polyneuropathy in a Patient with Charcot-MARIE-Tooth (CMT) Disease Type 1A: Case Report

ABSTRACT

We report a patient with chronic inflammatory demyelinating polyneuropathy (CIDP) developed against hereditary motor-sensory polyneuropathy (Charcot-Marie-Tooth disease type 1A). It is shown that the presence of chronic persistent herpes infection, stratifying on the mutation in the gene PMP22 (peripheral myelin protein), may lead to the development of autoimmune process, manifested demyelinating lesions of the peripheral nerves of the limbs and cranial nerves. CIDP – an autoimmune disease characterized by lesions of the myelin sheath of peripheral nerves, it accounts for about 20-50% of undiagnosed polyneuropathy. The literature discusses the contribution of viruses of the family Herpes Viridae to the development of CIDP. Charcot-Marie-Tooth disease (CMT) – a large group of hereditary diseases of the nervous system characterized by chronic progressive weakness and atrophy of distal limb muscles, reduced tendon reflexes, foot deformities and hands, changes in gait and sensory impairments.

Keywords: Chronic inflammatory demyelinating polyneuropathy (CIDP), Charcot-Marie-Tooth (CMT) disease, comorbidity, case report.

INTRODUCTION

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired immune-mediated disease characterized by lesions of the myelin sheath of peripheral nerve fibers [5, 11]. CIDP difference from Guillain-Barre syndrome is a relatively slow progression of symptoms for more than 8 weeks [15], in children - up to 4 weeks [3, 6].

CIDP represents approximately 20-50% of initially undiagnosed neuropathies [10] and is the most common autoimmune demyelinating neuropathy. The prevalence of CIDP is 1,2-7,7 cases per 100,000 individuals [5].

Clinical features of CIDP are: 1) progressive symmetrical or asymmetrical polyradiculoneuropathy; 2) relapsing or progressive course (> 2 month); 3) proximal weakness usually prominent; 4) large filber sensory loss in the distal limb (vibration and join positive sense); 5) generalized hyporeflexia or areflexia [10, 11].

Clinical forms of CIDP include multifocal acquired demyelinating sensory and motor neuropathy (the Lewis-Sumner syndrome), sensory-predominant CIDP, distal acquired demyelinating symmetric neuropathy, and CIDP with a lesion of central nervous system [6, 11, 12]. Magnetic resonance imaging (MRI) of the brain has revealed demyelinating lesions in the central nervous system in some patients with CIDP, despite the rarity of cerebral or cerebellar symptoms [8, 11, 17, 18].

CIDP may be also associated with concurrent disease, such as infection with the human immunodeficiency virus or hepatitis C, Sjogran's syndrome, melanoma, lymphoma et al. Significant contribution to the development of CIDP make viruses of the family Herpes Viridae [2, 13]. Occasionally, CIDP may develop on a setting pf another polyneuropathy, even one with a hereditary basis, such as Charcot-Marie-Tooth [11].

Charcot-Marie-Tooth disease (CMT) is a large group of hereditary diseases of the nervous system characterized by progressive muscle weakness and atrophy of distal extremities, hyporeflexia, and deformation of foots and hands, changes in gait and sensory impairment [1]. Prevalence is approximate to 1:2500 [19].

A common classification uses as main criteria the inheritance patterns and molecular genetics: 1) CMT1, characterized by abnormal myelin, with an autosomal dominant mode of inheritance, is the most frequently (about 50% from all cases); 2) CMT2, having the main feature axonopathy, also an autosomal dominant form, is on the second place (approximately 20-40%); 3) Intermediate form, an autosomal dominant combination of myelinopathy and axonopathy in individual is rare; 4) CMT4 is a rare group of progressive motor and sensory axonal and demyelinating neuropathies; 5) X-linked CMT is characterized by a moderate to severe motor and sensory neuropathy in affected males and usually mild to no symptoms in carrier female and is responsible for approximately 10-20% from cases [1, 19].

CMT1 – as well as the others subtypes of CMT can be further subdivided primarily on molecular genetic findings. Each of these subtypes is identified based on detection of a mutation in the causative gene: PMP22 – Peripheral myelin protein 22 (subtypes 1A and 1E), MPZ – Myelin P0 protein (subtype 1B), EGR2 – Early growth response protein 2 (subtype 1D), and NEFL – Neurofilament light polypeptide (subtype 1F) [1, 19]. The CMT1 subtypes are often clinically indistinguishable. The most common form is CMT 1A type with an autosomal dominant mode of inheritance, the cause of which is a mutation in the gene PMP22 [21].

Currently, there is evidence according to which there may be cases of CIDP in patients with CMT [7, 9, 14]. M. Watanabe et al. (2002) described the development of inflammatory neuropathy in patients with type CMT 1B, which was positive dynamics in the neurological symptoms in response to corticosteroid therapy [22]. In the same year, Gabriel C. et al. based on clinical, immunological and histological studies in 12 patients with CMT type 1A found that at step progression of the disease is likely to have the inflammatory component, layered on the genetic background [20]

In this article, we report own clinical observation of 19-year-old female patient with Charcot-Marie-Tooth disease type 1A, which has developed a pattern of chronic inflammatory demyelinating polyneuropathy with remitting course.

CASE REPORT

The patient is a 19-year-old girl. She admitted to the neurological department of the Republican Hospital №2 – The Center emergency medical care (Yakutsk city) in January 2015 with complaints of unsteadiness of gait, lack of movement in the facial muscles on both sides, constant drooling, speech problem, choke when taking the liquid and solid foods, decreased vision in both eyes, expressed general weakness, daytime sleepiness, fatigue, intermittent dizziness turning the head, constipation.

Medical history: The first neurological symptoms appeared after acute viral infection in February and March 2010 in the form of repeated transient sensory disturbances on the face (feeling cold), numbness of the tongue and partial violation of articulation. In April, the patient vaccinated against influenza H1N1. In May, there were severe infectious symptoms: fever up to 39 ° C, general weakness, loss of appetite, nausea, diparesis of mimic muscles, left-sided facial hemianesthesia, dysarthria, dysphagia, vertigo. A patient was hospitalized in the pediatric center of the Republican Hospital №1 with stem encephalitis. Detected in cerebrospinal fluid protein-cell dissociation (protein level of 1.2 g / l in normal cell count). Linked immunosorbent assay was positive for cytomegalovirus, mycoplasma and chlamydia. Electroneuromyography (ENMG) significant impairment of axonal-demyelinating by type, more pronounced on the facial nerve. MRI of the brain was without pathology. Given the family history of CMT maternally (sick sister's son and brother of the mother) a patient was examined by a clinical geneticist, subsequent DNA diagnosis has identified gene duplications peripheral myelin protein (PMP22) on chromosome 17r11.2-12. A patient was diagnosed CMT type 1A. The department received a course of antiviral, immunomodulatory therapy. The girl was discharged with the positive dynamics: devolution of

infectious symptoms, decrease bulbar disorders, the emergence of movements in the facial muscles. A patient examined at the Children's Clinical Hospital in Moscow, where the diagnosis CMT type 1A was confirmed.

Since October 2014, a patient increased weakness, decreased appetite, dizziness, an expression of a systemic nature, increased weakness in the facial muscles, increased salivation, choking when receiving the liquid and solid food. In January 2015, she admitted to the neurological department.

Patient was born on the fourth child in the family; the mother pregnancy was uneventful, natural childbirth. Physical and mental development by age. Menstruation from 14 years, painless, regular. Currently studying for a 3-year university, with learning to cope.

State of medium severity. Skin is pale and clean. Visible mucous pale pink and clean. No peripheral edema. Palpable enlarged, not welded submandibular lymph nodes, painless. Nasal breathing freely, breathing in the lungs vesicular, taken over all the fields, no wheezing. Heart tones are muffled, rhythmic. Hypotension to 90/60 mm Hg, tachycardia up to 108 per minute. Language moist, clean. Abdominal palpation soft, painless. Liver and spleen were not palpable. Symptom effleurage negative on both sides. Urination free, painless enough. Tendency to constipation.

Patient oriented in space, time and self. Several not critical, intelligence corresponds to the age and education. Moderately elevated levels of situational anxiety. The general background mood somewhat depressed. On the part of the cranial nerves: convergent strabismus easy due to OU, diplegia of mimic muscles, horizontal nystagmus, bulbar syndrome (dysphagia, dysphonia, dysarthria, decreased gag reflex, drooping soft palate, tongue muscle atrophy with fasciculations). Tetraparesis with strength in distal muscle groups of the upper and lower limbs to 4 points, proximal muscle strength 5 points. Low muscle tone, severe diffuse muscle wasting, muscle wasting interdigital spaces. Reflexes from the hands are normal, uniform; knee reflexes uniformly reduced; Achilles reflexes are reduced, uniform. High arch, foot deformity by type Fridreykh. Sensitive no violations. Coordination tests performs with mild ataxia. Sensory ataxia. Pelvic function controls.

Patient went follow-up investigation.

ELISA HIV is negative.

ELISA virus family Herpes viridae: moderate increase in titers of immunoglobulin G and M to cytomegalovirus and herpes simplex virus type 2. In the immune status had elevated levels of immunoglobulin G and M (156 g / L and 13.5 g / l respectively).

According to the visual evoked potentials to reverse chess pattern revealed no pathology.

Stimulation ENMG facial nerve showed signs of axonal-demyelinating type conduction abnormalities on both sides.

MRI of the brain revealed symmetrical affected area (cytotoxic edema) legs of the cerebellum on both sides of the spread in both hemispheres of the cerebellum (the size of the right 4,3x1,6 cm., Left - 3,4x1,6 cm.) With a weak accumulation of contrast agent with intravenous contrast enhancement. Revealed the accumulation of contrast material in the course of the temporal part of the facial nerve on both sides and small areas of glial changes in the posterior portions of the bridge. Conclusion: reliably judge the nature of the observed changes is not possible, probably holds the active demyelinating process.

On the basis of complaints, history of the disease, the characteristic clinical manifestations, paraclinical data and immunological research, clinical diagnosis was established:

The main diseases: chronic inflammatory demyelinating polyneuropathy, mainly affecting cranial and bulbar group of nerves at the stage of exacerbation. Diplegia of mimic muscles. Bulbar syndrome. Easy distal tetraparesis. Sensory ataxia. Group risk of aspiration.

Background diseases: Charcot-Marie-Tooth disease type 1A of autosomal dominant inheritance, moderately progressive course.

Chronic mixed-herpes-virus infections: cytomegalovirus infection in the stage of replicative activity of HSV-1 infection. Secondary immunodeficiency in violation of the anti-viral infectious response.

The department patient received 3 sessions of plasmapheresis, pulse-hormone therapy, intravenous immunoglobulin course (IVIG), vitamin therapy. At discharge condition with some improvement in the form of reducing the overall weakness, improvement of appetite.

CONCLUSION

Stepwise progression of neurological deficits in patients with hereditary forms of neuropathy requires a more careful examination of their stratification to identify inflammatory demyelinating component. Chronic herpes infection starts a secondary dis- immune disorder of the peripheral nervous system by type of CIDP in the presence of predisposition to chronicity and recurrence of herpes virus infection, particularly in patients with a genetic defect of the protein

RMR22. CIDP, unlike CMT, refers to a group of potentially curable diseases and timely diagnosis; treatment significantly may affect the quality of life of patients. Layering on CIDP in CMT weights clinical course of two competing diseases.

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Health Schools as Preventive Technology

ABSTRACT

The paper deals with the problem of forming healthy lifestyle. Тыe aim of the development and introduction of organizational and educational programs in activity of children's medical organizations is a culture of healthy lifestyle. The purpose of the study is an analysis of the educational activity of consulting centre specialists of the polyclinic "Children's city hospital".

Keywords: schools of health, healthy lifestyle, children.

INTRODUCTION

The Priority of the preventive measures, directed to declining prevented reasons of children's diseases, disability and death-rate. Pediatrics is itself a preventive discipline; the object of its activity is not the sick, but also healthy child. However often means and efforts, first of all, are directed to the treatment, rather than to the preventive maintenance.

The leading factor in arising the deflections of health state and diseases of population is a lifestyle. Forming the view on healthy lifestyle of population is necessary to start at young age. Consequently, the main view on healthy lifestyle must be put at period of the school education [1]. The data of the literature are indicated to the low level of schoolchildren's motivation in healthy lifestyle [2].

Forming healthy lifestyle (FHL) is a complex of actions, directed on preservation of health; the propaganda of healthy lifestyle; motivation of children and teenagers to the personal responsibility for their health; the development of individual approach on forming healthy lifestyle; the prevention of the risk factors of the diseases; the enlightenment and informing the population about harm of tobacco and alcohol; the prevention of social-significant diseases; increasing active life expectancy [2].

The lifestyle of children is closely connected with the lifestyle of their parents. Atyoung age habits and values of the person are formed. Much a great deal in this plan depends on the personal example of adults, their behaviour, and relation with their child.

The Sanitary enlightenment, hygenic education and preventive maintenance of the diseases, vaccinated skills of healthy lifestyle, propaganda of the healthy lifestyle presents itself well forgotten old. On estimation of specialists, at present this is the most optimum way of the

real declining children’s diseases [2, 3]. The aim of the development and introduction of organizational and educational programs in activity of children’s medical organizations is a culture of healthy lifestyle. Medical activity of families is innovative technology of the preventive pediatrics.

Many forms of the pathological states are developed at child’s age under the influence of unfavorable factors of surrounding world. For instance, atherosclerosis, diabetes and particularly hypertensive disease causes at child’s age. Functional and morphological deviations of children often move over to chronic diseases. So, preventive maintenance of the chronic diseases must include increasing resistant strength of the organism and liquidation of the violation in health state [4].

The Program of health care of modern schoolchildren in condition of the complex informatization of the educational process can include the following components: rational nutrition, optimum motor activity, observance of daymode, warning bad habits and increasing psychoemotional stability. Education at school must not harm the maturation of the physiological child’ssystem. 80% of loads in school educational process accounts for visual analyzer of the children.

The **purpose** of the study is an analysis of the educational activityof consulting centrespecialists of the polyclinic "Children’s city hospital".

THE MATERIALS AND METHODS: analysis of sanitary and educational activity of the specialists on forming healthy lifestyle for 2011 - 2014 years on annual reports data.

Activity of the Health schools of consulting centre of the chidren policlinic is specified following federal normative documents: Resolution of the Government of RF № 413 from 18 May 2009 "About financial provision in 2009 to account of the funding the federal budget action, directed on forming healthy lifestyle by citizen of the Russian Federation, including reduction of the consumption of the alcohol and tobacco", Order of the Ministry of Health and Social Development of Russia № 302 from 10 une 2009 "About measures on realization of the resolution Government of Russian Federation from 18 May 2009", Order of the Ministry of Health and Social Development of Russia № 597 from 19August 2009 "About organizing Health centres activities on forming healthy lifestyle citizens of the Russian Federation, including declining of the alcohol and tobacco consumption". On their foundation were prepared following normative documents by Ministry of Health of the Sakha Republic: order of the Ministry of Health of the Sakha Republic №01-8/4-745 from 02.07.2009 and Territory Fund of Obligatory Medical

Insurance of the Sakha Republic №270 from 02.07.2009 "About position of "Health schools for children", about statement methodical recommendations".

According to the orders of the Chidren’s city hospital № 313 from 14.10.2010 "About organizing activities of the Health Schools for children" and № 097 from 25.03.2013 "In addition to order № 313 from 14.10.2010 "About organizing activities of the Health Schools for children" are approved educational programs of health schools and are nominated responsible physicians-specialists on conducting the health schools, and is approved the Order of the conducting medical documentation. In consulting centre 7 health schools work: for sick children - 3 schools (the individual occupations), for conditionally – health children - 4 (the occupation in small groups). For sanitary-education of the sick children Gastro-school, Allergo-school work. There is aschool for children with the epilepsies in the individual occupation. For the conditionally –health children of the school age work the schools of health on preventive maintenance cardiovascular diseases, caries, myopias, girls’ reproduction systemdiseasesin small group occupations.

Function of these schools is the conducting of the preventive lectures in educational institutions. Each school consists of 4 occupations, the first half of the occupation is the theoretical part, and the second is the practical. Each specialist of the health school conducts a journal of the certain form with children’s signature trained at school.

The educational purpose of the sick children in the health schools is an improvement of lifes quality. The tasks of the health school for the sick children are: 1. Giving to patient and his parents the notion about nature and reasons of the diseases, teaching the skills to warn and get over the symptoms of the diseases; 2. Forming the partners’ relations between physician and patient, his parents and forming rational active relations to disease, motivations to recovery, adherences to treatment and execution the recommendations of the physician.

Allergo-school is conducted by two educational programs: "Preventive maintenance of the allergic diseases and children’s dermatitis" and "Preventive maintenance of the allergic diseases and bronchial asthma of children". Gastro - school has several programs: "Medical actions and preventive maintenance at constipation", "Dyskinesia of bile ducts", "Lyamblioz and helminth invasion ", "Dietotherapy under tseliakia".

The Educational program "Preventive maintenancesof the diseases of the girls’ reproduction system" comprises the following themes: "Healthy lifestyle - a base of girls’health care", "Preventive maintenance of the diseases feminine sexual spheres of girls-teenagers", "Preventive maintenance of unplaned pregnancy of girls- teenagers", "Preventive maintenance

of the sexual diseases of girls - teenagers". The educational program "Preventive maintenance of cardiovascular diseases" consists of the following themes: "Notion about diseases of the cardiovascular system, factors of the risk", "Healthy lifestyle is a preventive maintenance of the cardiovascular diseases", "Principles of the healthy nutrition. The Motor activity", "Preventive maintenance of bad habits: tobacco consumption and beer alcoholism".

Ophthalmo - school is conducted as an educational institution for small groups of chidren. The teaching is organized by two programs: for preschool children and schoolchildren. From the multiple methods of the preventive maintenance in the program are enclosed three methods. They are distinguished by high efficiency, reality of the introduction and not requiring significant financial expenseses: enlightenment the population about the risk factors of the declining visual abilities, hygiene of the vision and carrying out medical-training occupations with contingent "risk group".

The Purpose of the education: warning the declining of the children's vision in educational institutions. Ophtalmologist estimates the visual abilities of children for discovery vision violations and the contingent of "risk group"; carries out the occupations: "Preventive maintenance of the declining of the visual abilities" for the preschool children and "Myopia is the main reason of the declining of the vision of children from the age of 7 till 11; the risk factors, the hygiene of the vision, preventive advices" for schoolchildren; carrying out medical-training occupations for the contingent "risk group" , video training for the children with the violations of the vision, computer program "Relax", magnet – stimulation of biologically active points; the conversations and medical-training occupations with the tutors, parents.

Efficiency of the education of preschool children was valued by the following criterions: the reduction of complaints; increasing the reserves of the relative accommodation; the active participation of the parents in the preservation of the child'svision. Efficiency of the education of schoolchildren was valued by the following criterions: increasing of the the reserves of the relative accommodation; improvingthe sharpnesses of the vision on 10-40%; the weakening refraction of the myopia on 0.5-1.OD; the active participation of the parents in the preservation of the child's vision.

Statistical processing of results was conducted bythe computer program Microsoft "Excel".

RESULTS AND DISCUSSION

24156 persons are trained in health schools, 62328 visits are organized in education institutions in 2011-2014. Number of schools is increasing each year: there were 3 schools in 2011: Allergo-school, school of the preventive maintenance of the diseases girls' reproduction system, school of the preventive maintenance of cardiovascular diseases. In 2012 was introduced the school of the preventive maintenance of the caries. In 2013 were introduced Gastro-school, Epilepsy- school, Myopia – school (Tabl.1). In 2014 the most amount of the children were trained in educational institutions by the physician-gynecologist (37,3%), ophthalmologist (20,9%), pediatrician (19,1%).

Table 1

Assignment the healthschools in 2011 - 2014 (abs. number)

Name of the schools	**2011**	**2012**	**2013**	**2014**
Gastro-school	-	-	524	826
Allergo-school	40	50	339	219
Protection of the reproduction health	2124	2360	2372	2776
Ophthalmo-school	-	-	819	1556
Preventive maintenance of the caries	-	87	387	437
Epilepsy school	-	-	40	196
School of the preventive maintenance	2905	4456	681	1419
	5069	6903	4755	7429

Before and after the carrying out the healthschool the questionnaire is conducted for estimation of efficiency of the educational program. For instance, the questionnaire for the preventive maintenance of the tobacco consumption has shown the following results. Before the visiting the health school each fifth teenager (20%) has considered that advertisment of the tobacco in mass media is directed to adults, after the listening lectures with showing the film about harm of the tobacco the share of the teenagers who revised their look at advertisment of the tobacco has increased in 4 times and has formed 77,1%. In most cases the teenagers (65,5%)would like to have the non-smoker family in future, after the visiting the health school their share has increased on 7% and has formed 72,5%. The full prohibition of the tobacco advertisment was supported by 57,6% of teenagers before the visiting the health schools and 70,9% after the visiting the school (+13,3%).

For this period in health schools were trained 1556 children, 76 of them were of the preschool age (4,9%), schoolchildren - 1480 (95,1%). Ophthalmo – schools were organized inkindergartens№77 "Fairy tale", №45 "Strawberry", in schools №6, №7, in physics - technical liceum.

Table 2

Factors of the Opthtalmo - school functioning in 2014

Revealled pathology		6 age		7-10 age		10 -17 age		total	
		Abs number	%	Abs number	%	Abs number	%	Abs number	%
trained		76		1127		353		1556	
Revealled		10	13,2	423	37,5	126	35,7	559	35,9
Spasm of the accommodation		6	7,9	236	20,9	0		242	15,5
Myopias		0		119	10,5	126	35,7	245	15,7
Astigmatisms		2	2,6	55	4,9	0		57	3,7
Hypermetropiya		2	2,6	11	1,0	0		13	0,8
Innate anomalies of the development		0		2	0,2	0		2	0,1
Efficiency	Improvement	8	80,0	324	76,6	69	54,7	401	71,7
	Without change	2	20,0	99	23,4	57	45,3	158	28,3

35,9% of them had pathology of the vision organs. In most cases on nosology are diagnosed: spasm of the accommodation - 15,5%, myopia - 15,7%. Efficiency of the education in Ophthalmo -school has formed 71,7%.

Educational functioning of the centre includes: presentation of the lectures on the different subjects; the demonstration of the video materials: films "Truth about tobacco", "Prodigy of the lifes", "Chizhik-pyzhik, where were you …", "Taking careof yourself", "Carbohydrates"; the development, publishing and spreading the information brochures, booklets devoted to varied themes; work with mass media; the forming thematic stands for the preventive actions, dedicated to memorable date: ”Non-smoking day”, "International non - smokingday", "Day of the fight with AIDS", "International girls day " and others. Besides are conducted the parental conferences on forming the motivation to healthy lifestyle ("The role of the familyon the formingthe healthy lifestyle", "The happiness to be a father! » thematic meetings and lectures for the parents ("Healthy nutrition", "Sexual education", "Bad habits", «Save the child’svision").

On the whole for 2011-2014 are organized 2141 actions on propaganda the healthy lifestyle, the participants - 22726 Tabl.3). For 4 years the number of the participantshas been increased in 1,6 times, work with mass mediawas actuated.

Table 3

Sanitary-educational functioning of the "Children's city hospital" for 2011-2014

Actions	**2011**		**2012**		**2013**		**2014**	
	total	number	total	number	total	number	total	number
Total	390	14071	497	12643	560	11908	405	22726
Work with mass media	6		20		42		46	
Lectures, group conversations	69	5212	54	3571	161	4916	70	3501
Round tables	7	2117	10	295	14	597	14	508
Healthlanding	0		9	1032	21	1427	18	4439
Sport health actions	4	101	3	51	6	70	4	79
Publishing activity	1	500	23	1800	18	500	10	1500
Sociological investigation	20	680	12	246	6	278	5	210
Health schools	266	5318	345	6903	259	5177	382	7429
Health fairs	6	601	5	251	8	329	14	382
Parental conferences	1	42	11	295	8	556	12	845
Radio broadcasts	2		2		6		8	
Publications in the press	8		3		11		19	

In 2013"Children's city hospital" has won the Grant of the Head of Jakutsk (250000,00 rubles) for conducting healthy lifestyle among children and teenagers and has won the nomination "The best work with population" in contest hold by Republican organization of the trade union workmen of the Health on preventive maintenance for the tobacco consumption. On these facilities the book "Advices to the parents", brochures, booklets were designed and published; the models of organs and systems of the person for demonstration in the occupations of the health schools were bought. In 2014 "Children's city hospital" has won the nomination "Lodestar" of the International Fund Children of Asia " Bargaryy" for the active work with the chidren on propaganda for the healthy lifestyle.

CONCLUSION

Educational and social environment forms the lion's share of the contribution in the forming the health of the children and teenagers. It can be modified and corrected. It is necessary to change the existing lifestyle, education conditions, nature of the nutrition, and the mode of

the labour and rest not only for children and teenagers, but also for the parents. The Success in educational functioning is possible to reach only on condition of the partner's interaction, having united efforts of medical workers, teachers, psychologists, social workers, parents and children themselves.

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Surgical Correction of the Chest Wall in the Treatment of Chronic Nonspecific Pleural Empyema with Bronchopleural Fistulas

ABSTRACT

Empyema with bronchopleural fistula is one of the most severe complications of pulmonary pathology. In the case of chronic course the disease becomes long-term for reducing the quality of life of the patient. The authors have shown a clinical case of empyema with bronchopleural fistula. The successful implementation of collapse surgical intervention on the thorax to eliminate empyema cavity and further improvement of the patient at the ineffectiveness of classic minimally invasive surgical treatments is demonstrated.

Keywords: bronchopleural fistula, empyema, thoracoplasty.

INTRODUCTION

The most severe complications in thoracic surgery reflected in the outcomes of treatment and quality of life of the patient, are bronchopleural fistula and, as a consequence, the development of pleural empyema. The presence of bronchopleural fistula complicates the treatment of pleural empyema, preventing the creation of a negative pressure in pleural cavity, necessary unfolding of the lung, contributes to the formation of residual cavities. In the acute phase of the disease the method of endoscopic treatment of bronchopleural fistulas - the valve bronchoblocation - should be used [2,3]. In the case of chronic process, damaged lung is becoming covered with visceral mooring which does not allow the lung to spread. Gradually, the thickness of the moor increases, while lung tissue is being replaced by connective tissue, it develops pneumatic cirrhosis. At this point conservative therapy is ineffective. Empyempleurectomy with a decortication of the lung is used as a method of surgical treatment. This type of operation is accompanied by the visceral pleura traumatization, and as a result it stimulates the formation of fistulas, which also prevents the smoothing of the lung. The thoracomyoplasty is used with an aim to eliminate the residual cavity with no tendency for a lung smoothing and bronchopleural fistulas closing [1].

Clinical surveillance. Patient K., 32 years old, entered the hospital with the clinic of parapneumonic empyema with a bronchopleural fistula on the right side 3.11.09. From

anamnesis: the patient had recurrent right-sided pleural effusion for 10 years before and which in 2002 was defined as a specific process. The patient received treatment with anti-TB drugs for 8 months with a positive effect. In the summer of 2009 another relapse of pleurisy happened, reactivation of a specific process was rejected. Fever, weakness, shortness of breath on exertion made the patient enter the RCH, drainage of the right pleural cavity was done and purulent exudate was allocated up to 1000 ml by drainage, then the patient was sent to a specialized department of RCH №1. The pattern works as a docker in the seaport, work involves heavy physical labor. The department conducted antibiotic therapy, rehabilitation empyema cavity, physiotherapy. After 16 days the drainage was removed. With a positive result of treatment in the form of a resolution of empyema, with an outcome into pleural pneumatic cirrhosis with a dry residual cavity, on the 17th day the patient was discharged from the department.

The patient was rehospitalized on the 26th of January, 2010 and entered the OHT department in RCH №1. He was diagnosed with a chronic empyema on the right in the acute stage. The right pleural cavity was drainaged. Within 50 days of receiving the treatment, there were signs of bronchopleural fistula, though in spite of this a positive result was achieved, in a stage of remission of a chronic empyema. The patient was discharged to dispensary and scheduled for surgery a month later. One month after the discharge the patient entered the OHT on the 23rd of March, 2010 in the stage of remission of a chronic empyema with a bronchopleural fistula on the right. The surgery was performed on the 5th of June, 2015 which included the thoracotomy on the right side, subperiosteal resection of the ribs 6,7,8, pleurectomy and decortication of the lung. During the thoracotomy, due to bone deformation of the rib hull, the need for resection of the side portions of the ribs appeared. Decortication of the lung was performed with technical difficulties, the thickness of the moore was up to 0.7 cm, pleurectomy was perfomed over the back-side surface, large defects of the lung were sutured. The postoperational period was marked by slow smoothing of the lung due to bronchopleural fistulas. Despite of the repeated draining fistula occlusions of the bronchi on various levels (segmental, lengthwise, medium), the lung was not cracked down, and a cavity in basal sides of the right hemithorax remained. Further treatment was conservative, in a state of a chronic empyema on the right with bronchial fistulas and a dry residual cavity. After 119 days of treatment, the patient was discharged (20.08.10.) to the dispensary stage for further correction of the chest wall by surgery in 2 months.

On the 21st of October, 2010, the patient was hospitalized. On the 9th of November, 2010, the imposition of torakostomy was performed along with a resection of the lateral sections of the 5, 6, 7 ribs for the purpose of conducting an open cavity empyema. On the 7th of December, 2010 the patient had a massive bleeding from the empyema cavity, which was stopped conservatively. After 55 days (15.12.10) of the hospitalization and after cupping the next exacerbation, the patient was discharged from the department.

Against the backdrop of a chronic empyema of the right pleural cavity the patient was admitted to the RCH №1 for the second stage of surgery on the 31 of January, 2011. As a result of the microflora of empyema cavity, Ps. Aeruginosa was detected. On the 24 of February, 2011 thoracorhinoplasty was performed with a resection of the chest wall on the right side, pleurostoma was closed. Side access was provided to 6 intercostal space with an excision of the pleurostoma, thoracotomy was continued to 6 intercostal space to the shoulder line. The lung was in atelectasis, covered with a moor up to 0.5 cm. The residual cavity extended up to the rear section of the rib 4, down to rib 9. Subtotal resection was performed from the 3rd to the 10th rib from the shoulder to the midclavicular line, including the previously resected 6-9 ribs. Together with ribs intercostal muscles were removed from the pleural moorings, with thickness up to 3 cm. Partial resection of 2 ribs was perfomed also. Mobilization of the body of the blade was followed by a resection of 1/3 of her body. Then excision of pulmonary moorings was done. Muscle flaps were fixed on the edge of the moor. Intermuscular spaces in the area of mobilization anterior of pectoral muscles (the major and minor pectoral muscles) were drained through counterpunctures. A pressing bandage was placed on the right side of the chest. Early postoperational period was complicated by a pneumothorax on the contralateral side, there was performed a puncture, a drainage of pleural cavity, and the complication was cropped conservatively. As a result of healing of the postoperational wound, seroma cavity formed in the deeper layers of muscles, the cavity was closed with the passage of time, the fistula of the postoperational scar healed. After 59 days of hospitalization the patient was discharged (31.03.11).

Last admission was on the 31 of January 2012, the patient entered the department because of the discovery of a new postoperational fistula ligature. On the 2nd of august, 2015 the excision of fistula ligature was performed, and a dacronic ligature was removed. Wound healing was carried out by primary pulling. On the 24th day of hospitalization (13.03.12) the patient was discharged with a complete healing of the fistula and recovery.

The last survey was conducted in April 2015. The chest was deformed due to thoracoplasty, there also was postoperational scarring with no signs of inflammation, the right lung was reduced, there wasn not neither free fluid in the right pleural cavity nor infiltrative changes in the lungs. The patient was brought through with a help of a healing process.

CONCLUSION

Chronic empyema with bronchopleural fistulas accompanied by long-term treatment, in this case more than 3 years, and as a consequence, disability and massive antibiotic therapy with an expanding range of resistant pathogens in foci of chronic infection, and the addition of hospital flora. A clinical example is given to demonstrate the successful implementation of collapse surgical intervention on the chest wall to eliminate empyema cavity and further improvement of the patient with the ineffectiveness of classic minimally invasive surgical treatments.

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