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LEADING ARTICLE

Burtseva T.E., Grigorieva A.N., Chychahov D.A., Evseeva S.A.

DYNAMICS OF THE BASIC INDICATORS OF THE CHILDREN'S POPULATION HEALTH IN THE REPUBLIC SAKHA (YAKUTIA)

Abstract

The article analyzes the main health indicators of children and adolescents of the Republic Sakha (Yakutia) in the period of implementation of major projects in the health field from 2000 to 2014. It is noted that according to official health statistics rate of primary and general morbidity of children and adolescents of the Republic Sakha (Yakutia) increased. Presented structure of the general and primary morbidity of children and adolescents can be an effective tool in improving the pediatric service of the Republic Sakha (Yakutia).

Keywords: children, health, disease, Yakutia.

INTRODUCTION

Child and Adolescent Health of the Republic Sakha (Yakutia) is an indicator of socio-economic development of the region. The healthy children and adolescents are the closest reproductive, social, economic, military and intellectual reserve of the society, are of paramount importance for the whole country. The health of children and adolescents is made up of the level of physical, mental, functional development, and directly depends on the development of a network of medical facilities in the region.

At the beginning of the XXI century in Russia there was an extremely worrying situation in the area of children's health, which is due to unfavorable levels of the most important indicators of the health of children and adolescents [1-3]. To a large extent this also applies to the region of the Far Eastern Federal District [4] and the Republic of Sakha (Yakutia) [5].

In recent years, Russia has implemented large-scale projects in the field of health as priority national project "Health", health care modernization program. All this, no doubt, played a role in changing indicators and indicators of population health.

MATERIALS AND METHODS

We analyzed the basic health status of children and adolescents of the Republic of Sakha (Yakutia) in the period of implementation of major projects in the health field from 2000 to 2014.

RESULTS AND DISCUSSION

Indicators of fertility, infant mortality, the incidence of child and adolescent population reflect the actual characteristics of the population living in the region and allow to develop the necessary measures to protect and improve public health.

The birth rate in the Republic of Sakha (Yakutia) is one of the positive indicators, so in the dynamics it increased from 13.7 in 2000 to 17.8 in 2014 (Table 1).

During the period there is a dynamic decrease in the infant mortality rate. So, if in 2000 infant mortality rate was 17,6 , in 2014 the figure was 8.0 per 1,000 live births (Table. 2).

Currently, primary morbidity of children population of RS (Y) remains high and continues to rise (Tab. 3). Index of general morbidity of children under 14 years in the Republic of Sakha (Yakutia) for the period 2000-2014 increased by 73.8 (Table 3). Today there are the obvious changes in the structure of morbidity of children. Over the past 10 years significantly the incidence of infections and parasitic diseases reduced. During the study period, the overall reduction in the incidence of children happened in the following categories "some infectious and parasitic diseases", "diseases of the endocrine system, nutritional metabolic and immunity disorders." A significant increase in the overall incidence occurred in the following categories: "neoplasm", "nervous system diseases", "diseases of the eye ", "diseases of the ear and mastoid process", "disease of the digestive system" and "diseases of the musculoskeletal system and connective tissue congenital anomaly".

Indicators of general morbidity in adolescents 15-17 years of Sakha (Yakutia) are presented in the Table. 4. The test indicator rose significantly (by 10 times) over the time period of interest. Such classes of diseases, as a "neoplasm", "diseases of the musculoskeletal system" has a 3-fold increase in morbidity, "respiratory diseases", "diseases of the ear and mastoid process", "injury and poisoning" increased by 2 times.

During the test the dynamic decade decline in the overall incidence of adolescents occurred in two classes of diseases: it is "infectious and parasitic diseases" and "diseases of the nervous system."

It is well known that the level of primary morbidity of children in the RS (Y) exceeds the average figures for the past few years. The growth of this indicator was mainly due to the incidence of neoplasm, diseases of the nervous system, digestive disorders and congenital anomalies. This circumstance can we explain the real increase in the incidence, increasing access to diagnosis and Disease Registry.

As shown in Table. 5 in the analyzed decade outstripping growth rates of

Table 1

The dynamics of the birth rate in the Republic of Sakha (Yakutia)

The birth rate	2000	2005	2010	2014
Sakha (Yakutia), 1000	13,7	14,3	16,8	17,8
RF 1000	–	10,2	12,5	13,3

Table 2

Trends in infant mortality in the Republic of Sakha (Yakutia) (per 1,000 live births)

The infant mortality rate	2000	2005	2010	2014
RS (Y)	17,6	10,6	7,2	8,0
RF	–	11,0	7,5	7,4

Table 3

Indicators of general morbidity of children from 0 to 14 years for 2000-2014 in the Sakha Republic (Yakutia) of the main classes of diseases, per 1,000 children

Designation of classes of diseases	2000	2005	2010	2014
All diseases of them:	1623,6	2195,2	2769,3	2823,2
infectious and parasitic diseases	105,8	75,9	83,2	86,7
neoplasm	4,4	11,6	14,2	15,3
diseases of the blood and blood-forming organs	19,3	27,6	29,1	23,7
endocrine, nutritional, metabolic and immunity	43,5	47,7	36,3	34,3
mental and behavioral disorders	18,6	17,7	16,0	19,7
diseases of the nervous system	88,7	132,6	155,8	163,8
Diseases of the eye	79,5	116,9	142,6	155,4
Diseases of the ear and mastoid process	29,0	52,8	55,9	59,6
diseases of the circulatory system	6,9	12,5	12,1	9,6
respiratory diseases	897,7	1156,0	1577,1	1634,1
diseases of the digestive organs	95,6	193,4	230,2	244,6
diseases of the skin and subcutaneous tissue	80,8	122,7	144,9	137,4
diseases of the musculoskeletal system and connective tissue	16,9	43,6	37,7	35,5
diseases of the genitourinary system	29,0	46,9	50,8	55,1
congenital anomalies (birth defects), deformations and chromosomal abnormalities	14,0	22,0	28,3	31,1
injury, poisoning and certain other consequences of external causes	59,3	79,1	95,8	97,9

Table 4

Indicators of general morbidity of adolescents aged 15-17 years for 2000-2014 in the Sakha Republic (Yakutia) of the main classes of diseases, by 1000 adolescents

Designation of classes of diseases	2000	2005	2010	2014
All diseases of them:	111,1	735,4	2001,6	2124,7
infectious and parasitic diseases	42,6	42,9	32,6	42,1
neoplasm	2,4	7,7	7,1	11,3
endocrine, nutritional, metabolic and immunity	66,7	120,4	83,5	68,2
mental and behavioral disorders	34,7	40,6	38,3	41,0
diseases of the nervous system	222,7	143,7	162,1	174,0
Diseases of the eye	–	167,7	215,4	221,3
Diseases of the ear and mastoid process	14,6	37,8	33,4	36,0
diseases of the circulatory system	21,8	36,3	31,8	37,3
respiratory diseases	346,1	520,1	708,7	775,4
diseases of the digestive organs	103,7	192,4	202,4	249,0
diseases of the skin and subcutaneous tissue	58,9	99,7	102,3	118,8
diseases of the musculoskeletal system and connective tissue	27,8	64,4	89,9	82,0
diseases of the genitourinary system	58,4	78,9	76,9	80,2
congenital anomalies (birth defects), deformations and chromosomal abnormalities	13,1	14,5	18,9	17,2
injury, poisoning and certain other consequences of external causes	76,3	114,5	158,5	134,6

Table 5

Indicators of primary morbidity of children from 0 to 14 years in 2000-2014 in the Republic of Sakha (Yakutia) for the main categories of diseases set out for the first time, 1,000 children

Designation of classes of diseases	2000	2005	2010	2014
All diseases of them:	1348,7	1591,7	2255,0	2412,5
infectious and parasitic diseases	86,7	67,3	76,0	80,6
neoplasm	2,4	5,9	8,1	8,8
diseases of the blood and blood-forming organs	10,3	13,8	13,3	11,7
endocrine, nutritional, metabolic and immunity	19,5	22,6	13,1	15,7
mental and behavioral disorders	4,8	4,0	2,6	3,7
diseases of the nervous system	24,8	47,4	63,1	82,6
Diseases of the eye	50,8	61,9	83,9	90,2
Diseases of the ear and mastoid process	31,5	39,5	49,0	49,7
diseases of the circulatory system	4,3	7,4	5,6	6,0
respiratory diseases	831,0	924,3	1464,3	1556,4
diseases of the digestive organs	77,9	133,0	171,3	199,2
diseases of the skin and subcutaneous tissue	71,3	84,6	118,1	222,5
diseases of the musculoskeletal system and connective tissue	16,2	33,8	25,9	27,0
diseases of the genitourinary system	17,4	28,8	34,9	40,0
congenital anomalies (birth defects), deformations and chromosomal abnormalities	2,5	6,9	7,6	11,5
injury, poisoning and certain other consequences of external causes	67,4	73,5	93,5	97,8

primary morbidity of children occurred in most major classes of diseases and totaled 78.8. The most substantial growth, an increase of 2 times or more, occurred in such classes of diseases, as a "neoplasm", "diseases of the digestive and urogenital system", "congenital malformations" and "diseases of the nervous system." In diseases such as "some infectious and parasitic diseases", "diseases of the endocrine, nutritional, metabolic and immunity" and "mental and behavioral disorders" has a dynamic frequency reduction of the initial registration.

The indicator of primary morbidity of adolescents in the Republic of Sakha (Yakutia) for the 2000-2014 increased by 93.9 reaching 1521.6. The greatest increase in incidence occurred in the primary category "neoplasm", "nervous system diseases", "diseases of the musculoskeletal system and connective tissue disorders," "diseases of the digestive system", "cardiovascular disease". The decrease of the index is observed in the incidence of such classes as "endocrine, nutritional, metabolic and immunity," "some infectious and parasitic diseases" and "mental and behavioral disorders" (Table. 6).

CONCLUSIONS

Incidence rates are based on the existing official health statistics underlie on the appealability of the population. It should be noted that our republic official data of medical statistics due to accurate work of pediatricians, specialists, medical statisticians are very reliable. There is a vast array to study health parameters and to support perspective areas of Healthcare service in the republic.

Today, in Yakutia, as well as in Russia, rate of primary morbidity of children and adolescents is increasing, as well as the number of chronic diseases. This does not only speaks about the deterioration of children's health, but also is an indicator of the effective operation of pediatric services in general to identify pathology in children and adolescents. Presented dynamics of health status of children and adolescents can be an effective tool in improving the pediatric service of the Republic Sakha (Yakutia). Taking into account the revealed pathology structure one can plan in the long term specialized pediatric health care services.

Table 6

Indicators of primary morbidity of adolescents 15-17 years of 2000-2014 in the Sakha Republic (Yakutia) of the main classes of diseases, by 1000 adolescents

Наименование классов болезней	2000	2005	2010	2014
All diseases of them:	784,5	1046,9	1339,9	1521,6
infectious and parasitic diseases	35,4	30,5	25,8	33,3
neoplasm	2,0	4,9	3,6	6,5
diseases of the blood and blood-forming organs	8,6	15,1	12,4	12,8
endocrine, nutritional, metabolic and immunity	32,8	30,6	21,9	26,1
mental and behavioral disorders	20,2	9,6	10,5	5,9
diseases of the nervous system	25,4	46,4	57,7	70,9
Diseases of the eye	49,6	57,5	78,9	97,5
Diseases of the ear and mastoid process	15,1	23,9	22,8	26,2
diseases of the circulatory system	7,7	16,9	13,8	19,6
respiratory diseases	343,8	416,5	622,3	691,0
diseases of the digestive organs	49,3	105,8	126,9	184,1
diseases of the skin and subcutaneous tissue	53,6	80,8	76,5	89,5
diseases of the musculoskeletal system	16,9	34,1	54,7	57,2
diseases of the genitourinary system	30,7	44,1	45,3	52,4
complications of pregnancy, childbirth and the postpartum period[1]	13,4	18,6	19,4	–
congenital anomalies (birth defects), deformations and chromosomal abnormalities	2,7	2,9	3,3	2,3
injury, poisoning and certain other consequences of external causes	78,7	114,8	152,5	134,6

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MODERN TENDENCIES OF LUNG CANCER MORBIDITY IN YAKUTIA

ABSTRACT

Analysis results of 6865 cases of lung cancer morbidity in the territory of the Republic Sakha (Yakutia) in the period of 1991-2010 are presented. Most of them are men-4789(69.8%), women-2076 (30.2%). Populational, territorial and temporal regularities are found out.

Keywords: lung cancer, morbidity, prevalence, dynamics, prognosis.

INTRODUCTION

Annually in the world about 1.5 mln new cases of lung cancer are expected, it's about 12%. According to the MAIR data in economically developed countries three kinds of diagnosed cancer are singled out: men have cancer of prostate gland, lung, bronchial tubes and colorectal cancer, women-cancer of mammary gland, cervix, lung, bronchial tubes, colorectal cancer.

In some developed countries the highest data of lung cancer morbidity of both sexes are observed (Population is 100000) in Germany-63.7 and 13.5, in England-51.2 and 22.0, in Canada-80.2 and 30.8, in the USA-85.9 – black people, 36.8- white people, in some provinces of China-44.4, Korea 49.0, Japan-41.9. The lowest data of men are in Uganda (Africa)-3.9. The highest data of lung cancer are found out in Canada-30.8-women,

the USA-36.8 – black people.

According to MAIR experts' opinion the main reason of lung cancer is smoking (80%-men, 50%-women and only1-2% -air pollution. [3,4]

In Russia in 2010 57000 cases of lung cancer are found out: men-84.9%, women-15.1%. In 2000-2010 data of new cases lowered (-12.9%), especially men by 12.3% but women data increased by 4.1%.

In general structure of oncological morbidity lung cancer is in the 3rd place (11.0%), but men are in the 1st place (19.5%) and women are in the 11th place (3.8%).

"Rough" morbidity data are 41.1, standardized-25.2 to 100000 population. Risk of malignant tumor of breathing organs of men is higher 10 times than of women. Morbidity is increasing with age, maximum age of men is 70-74–408.8 and of women 61.0 in the group of 80-85 years old. 64.3% of men and 72.4% of women are in the group of more than 60 years old. [1.2]

Research aim is finding out populous, territorial and temporal regularities of lung cancer morbidity of population in Yakutia.

MATERIALS AND METHODS

Initial documents of 6612 patients with the first diagnosis of lung cancer in the period of 1991-2010 were analyzed. It's 17.5% (in RF 11.0% in 2010) out of 37380 registered MT in the Republic of Sakha. (Fig.1)

Men make up 68.5%, the ratio of men and women is 2.2:1.0, Annual structure of MT morbidity of men and women is presented in Figure 2. Data calculation is done by applied program "Statistica".

RESULTS AND DISCUSSION

A portion of lung cancer in the structure of man MT morbidity is 24.1 (RF-19.5%), woman – 11.3%(RF-3.8%) in the analysed period of time. It's noticed that lung cancer of men is in the first place for many years, women's lung cancer is in the second place after mammary gland cancer (16.5%). According to the received data standardized data (SD) of lung cancer morbidity of men had a bright negative dynamics. By the end of observation the SD morbidity of the given population (2010-53.9±3.34) made up to 76.0% of the first level (1991-70.9±3.56% 000, p<0.05) Morbidity coefficient of women in 2010 made up to 64.4% (32.2±2.10 in 1991 till 18.5±1.86% 000 in 2010, p<0.05). Thus, average annual lowering of women was more significant and made up 1.85%, but men – 1.25%. Dynamics of rough data (population 100000) proves lung cancer morbidity character (13.0%), at the same times dynamics of SD had an opposite tendency (-24.6%). It stresses a high morbidity level among old and elderly people.

During the given period of time a number of population in the Republic Sakha lowered by 3.6% because of lowering men number (-5.9%), young people of 30 (-7.2%), old people of 60 and more years old (-1.7%). It's noticed a high level of men number lowering till 30 years old (-8.0%) and older than 60 years old (-4.7%). The given coefficient of women till 30 years old is 6.3% while those above 60 and more years old women (-0.32%)demonstrated positive dynamics. A change in the aged population structure, average annual lowering (-0.35%) can be explained

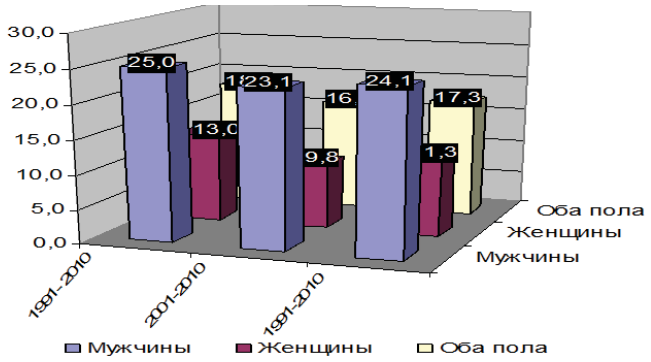

Figure 1. Dynamics of the incidence of lung cancer in the population of RS(Ya) in the period from 1991 to 2010 on 100 thousand population

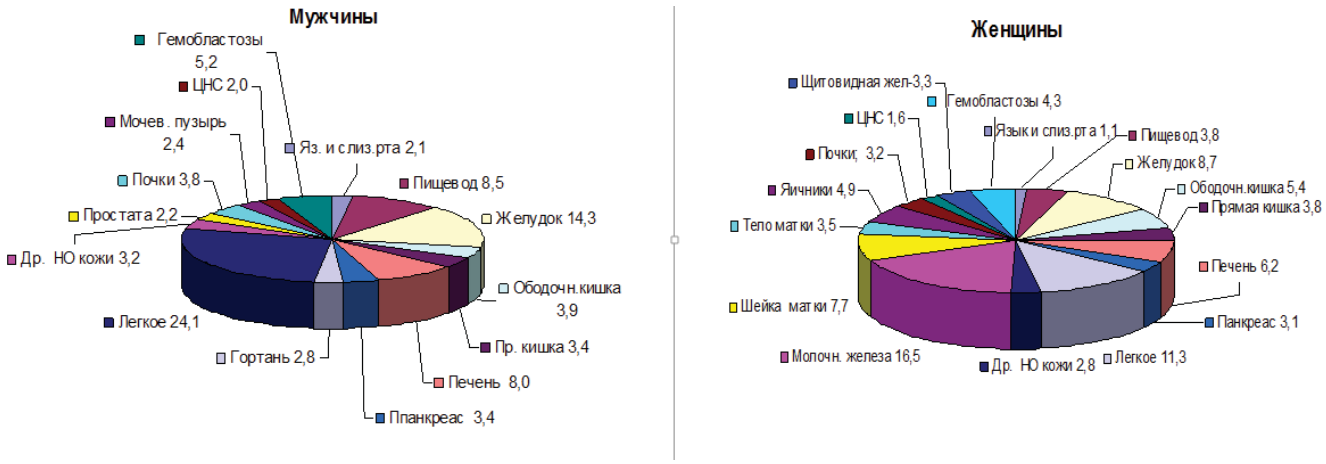

Figure 2. The structure of cancer incidence in the population of the RS (Y) for years 1991-2010. (%)

by unfavorable migratory movement in Yakutia. However, the migratory activity lowering is not compensated by increasing demographic data.

According to the analysis results man morbidity with lung cancer increased (from 40.9 in 1991 to 50.1% oooo in 2010) but SD lowered (from 70.9 to 53.9o/oooo accordingly),meanwhile woman morbidity data were stable (population 100000) (22.0 in 1991 and 22.4 in 2020), SD lowered, from 32.2 in 1991 to 18.5o\oooo in 2010 (Table 1).

Extrapolation of morbidity tendency (1991-2010) allowed defining a possible morbidity level of both populations in the nearest future. Thus, SD analysis in dynamics prognosticates by 2020 lowering men morbidity by 51.5%, average annual lowering is -3.0%. Lung cancer level of women will be 66.5% of the first data, average annual lowering is 2.15% (Fig.3).

Age lung cancer morbidity data of five-year-age groups are presented in Table 2. During the analyzed period lung cancer morbidity data of all age groups not depending on a sex have a tendency to lower except age group of 70 and more years old. In this group average annual increase made up 0.45% (from 196.4 in 1991 to 346.0 o/oooo in 2010). According to the prognosis by 2020 a possible level (402.1) lung cancer morbidity of 70 year-old will increase by 33.1% exceeding the first data (301.8 o/oooo in 1991). A possible level of aged women will be 228.5 o/oooo by 2010, it's higher by 50.0% of 1991 (152.4 0/oooo).

Average age of fallen ill patients in 2010 was 59.0 (RF-63.4) for men, for women – 59.7 (RF-63.2). Age median is 55.3 (RF-63.4) and 56.2 (RF-63.3) accordingly for men and women.

Yakutia is considered to be a region of a high morbidity risk with lung MT (RS(Y) – 63.9±3.7 o/oooo, RF-54.0 in 2010) – men, women – (20.2±2.0, RF-7.1 o/oooo accordingly) among 87 administrative – territorial zones of RF (Table 3).

The first three places of men lung cancer morbidity (population 100000) are occupied by Allaikha (RD-95.0 o/oooo), Verkhnekolymsk (95.1), Olekminsk (75.9), women – Moma (41.7), Tatta (41.4), Allaikha (40.3 o/oooo)). The lowest level of men morbidity is in Gorny (19.7), Eveno-Butantaisk (28.9) and Churapcha (31.1 o/oooo), of women morbidity-Oimyakon (7.3), Mirny (9.1), Neryungri (10.5 o/oooo).

Relatively a high morbidity, higher than average Republican data (33.8 o/oooo) can be observed in South Yakutia (SD-46.7±5.0 o/oooo), Beyond the Polar circle zone (38.7±2.0) and in the Western Yakutia (39.2±9.7 o/oooo) (Table 4).

Component analysis of MT morbidity dynamics was used to settle a problem of morbidity increase depending on

Table 1

Dynamics of incidence of the population in RS (Ya) lung cancer for 1991-2010 and its probable characteristic for 2020 (0/000)

Year	Both sexes		men		women	
	DIRI	DISI	DIRI	DISI	DIRI	DISI
1991	27,7–30,9	37,7–41,4	38,2–43,6	56,9–63,4	15,7–19,3*	19,1–23,0*
1992	31,5–35,0	40,6–44,5	42,2–48,0	59,4–66,1	19,3–23,2*	22,7–27,0*
1993	30,1–33,5	39,8–43,8	41,5–47,2	59,1–65,9	17,2–21,0*	20,9–25,0*
1994	30,4–33,9	38,9–42,8	37,2–42,7	50,2–56,5	22,2–26,5*	25,7–30,3*
1995	31,7–35,3	24,0–27,2	43,9–49,9	58,8–65,7	18,2–22,1*	20,8–25,0*
1996	33,0–36,6	40,8–44,8	46,8–53,1	61,4–68,5	17,8–21,7*	20,5–24,7*
1997	33,6–37,4	40,6–44,7	43,7–49,8	56,9–63,8	22,2–26,5*	24,1–28,6*
1998	30,3–33,9	35,6–39,4	37,8–43,5	47,9–54,3	21,5–25,9*	23,0–27,4*
1999	28,2–31,7	32,1–35,8	38,8–44,6	47,9–54,3	16,5–20,3*	16,3–20,1*
2000	32,4–36,1	34,3–38,1	41,5–47,5	49,5–56,0	21,9–26,3*	19,3–23,5*
2001	31,8–35,5	33,8–37,6	39,3–45,1	45,6–51,9	22,9–27,4*	21,7–26,1*
2002	31,7–35,3	33,8–37,6	44,6–50,8	51,0–57,7	17,6–21,6*	16,4–20,3*
2003	28,8–32,4	31,9–35,7	40,9–47,1	49,7–56,5	15,8–19,6*	15,2–19,0*
2004	32,0–35,8	34,6–38,5	44,9–51,4	52,4–59,4	18,3–22,4*	17,7–21,7*
2005	30,8–34,5	33,2–37,1	45,4–51,9	53,9–61,0	15,5–19,3*	14,4–18,0*
2006	31,7–35,5	33,5–37,4	45,9–52,5	53,9–60,9	16,9–20,8*	14,9–18,6*
2007	32,4–36,2	32,7–36,5	43,9–50,2	49,8–56,6	20,1–24,4*	17,0–20,9*
2008	29,3–32,9	30,9–34,6	44,3–50,8	53,0–60,0	13,9–17,5*	12,8–16,3*
2009	36,9–41,0	36,0–40,0	53,1–60,1	62,7–70,3	20,3–24,6*	16,3–20,2*
2010	31,2–34,9	32,6–36,5	46,8–53,4	54,0–61,1	15,3–19,0*	13,6–17,2*
2020	35,2	30,0	54,1	52,7	18,1	10,7

Explanatory note: DIRI - dynamic interval of a rough index, DISI - dynamic interval of the standardized indicator;* – distinction statistically is significant in comparison with men ($p < 0.05$).

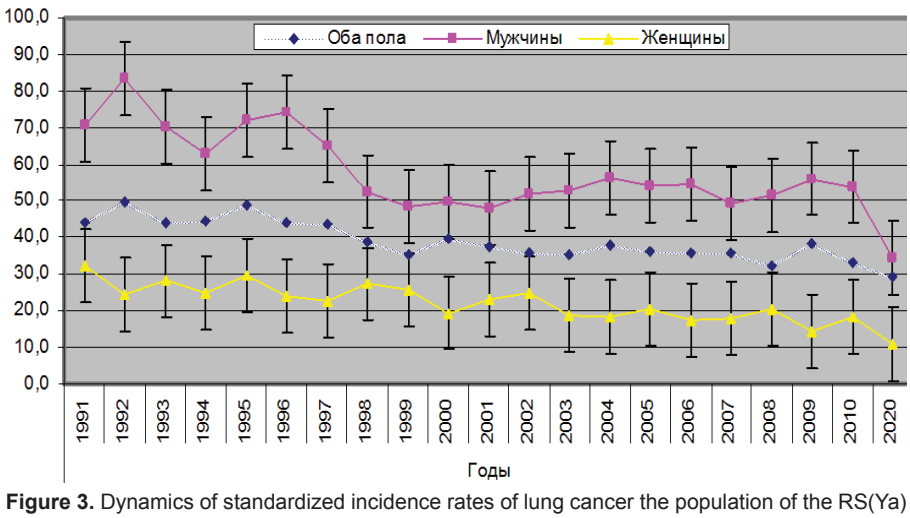

Figure 3. Dynamics of standardized incidence rates of lung cancer the population of the RS(Ya) for the 1991-2020 and its forecast in 2020

Table 2

Dynamics of incidence of the population in RS (Ya) lung cancer depending on gender and age for 1991 - 2010

Year	Number of patients with for the first time in life the established diagnosis, on 100000 population									
	до 29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	>70
Both sexes										
1991	0,0	1,6	6,3	25,6	35,1	85,3	205,5	245,1	334,7	196,4
1992	0,2	1,7	6,4	20,2	39,6	83,9	163,7	279,3	397,3	299,2
1993	0,2	2,7	3,7	9,8	44,7	92,3	183,4	313,1	289,9	181,9
1994	0,0	2,0	7,6	17,3	35,7	83,7	170,0	248,0	309,1	263,5
1995	0,2	0,0	1,9	3,3	10,6	19,4	42,1	67,7	134,2	134,1
1996	0,2	3,5	4,9	24,9	44,7	83,5	157,0	252,8	303,3	236,9
1997	0,0	0,0	5,0	20,5	49,1	74,8	173,7	211,9	332,8	249,2
1998	0,0	4,1	8,4	19,5	26,8	82,0	122,9	198,2	303,3	235,3
1999	0,4	1,5	2,2	14,2	34,9	78,8	129,4	186,7	212,5	222,1
2000	0,2	0,0	2,4	12,0	34,3	74,3	88,7	211,5	269,2	320,0
2001	0,0	0,0	5,1	7,6	38,7	69,6	100,4	198,6	266,1	279,6
2002	0,0	0,0	8,2	13,2	43,1	67,1	130,9	152,5	255,2	245,4
2003	0,6	1,4	2,9	8,2	31,9	63,8	109,5	183,8	272,0	232,3
2004	0,0	0,0	3,0	14,5	30,3	71,8	146,9	181,0	239,1	282,2
2005	0,2	0,0	0,0	7,6	26,1	68,3	102,4	168,8	299,4	272,9
2006	0,0	0,0	3,0	14,9	20,8	59,4	148,3	177,1	227,3	270,1
2007	0,2	0,0	1,5	10,1	28,1	62,4	110,6	181,1	205,8	314,5
2008	0,9	2,8	1,5	12,0	18,7	55,8	109,7	209,3	187,2	208,8
2009	0,0	1,4	0,0	9,3	32,1	64,9	118,9	191,5	209,9	346,0
2010	0,0	1,4	5,9	17,4	21,0	60,5	85,3	192,3	260,3	217,1
The forecast to 2020	0,3	-	-	6,2	17,4	48,6	64,2	131,0	160,1	313,8
Men										
1991	-	3,1	7,0	43,3	65,6	143,6	340,1	395,3	503,3	301,8
1992	0,3	3,3	8,9	24,2	52,9	143,6	262,6	443,3	636,0	587,6
1993	0,3	5,2	7,3	17,9	78,0	162,0	297,1	442,5	439,8	316,0
1994	-	1,9	13,0	25,6	61,5	150,5	249,1	262,2	384,0	431,8
1995	-	-	11,4	28,1	78,9	136,1	284,2	389,9	383,3	496,2
1996	0,4	6,7	3,8	43,1	81,3	136,7	268,4	375,0	443,4	497,4
1997	-	-	5,9	38,7	82,5	126,5	280,5	271,2	470,8	376,3
1998	-	5,3	14,3	28,0	41,0	115,4	185,5	308,1	402,0	335,8
1999	0,8	-	2,2	23,8	65,4	140,5	214,1	284,9	315,8	324,4
2000	-	-	4,7	17,3	54,9	129,8	151,3	370,2	371,1	406,4
2001	-	-	5,0	8,7	61,7	118,9	145,7	313,4	335,6	399,4
2002	-	-	16,2	26,3	70,9	121,8	236,8	261,5	319,7	402,6
2003	0,8	2,9	2,9	14,2	50,5	118,7	190,1	317,1	456,0	366,0
2004	-	-	6,0	24,5	52,5	121,0	255,2	284,7	378,6	471,9
2005	-	-	-	13,0	49,0	137,8	187,5	300,5	506,5	444,7
2006	-	-	6,1	24,9	38,2	100,4	278,4	320,3	404,9	395,1
2007	-	-	3,0	14,7	43,4	94,9	223,0	298,2	386,0	429,6
2008	1,7	5,6	3,0	21,5	26,0	99,2	219,7	389,9	313,0	339,8
2009	-	-	-	16,0	56,5	121,7	206,7	416,1	347,4	505,4
2010	-	-	9,0	26,0	41,2	115,0	164,3	329,0	478,5	360,0
The forecast to 2020	-	-	0,4	8,9	23,9	82,0	134,2	287,9	313,4	402,1
Women										
1991	-	-	5,5	7,1	4,7	26,4	85,2	135,1	239,8	152,4
1992	-	-	3,8	16,0	26,3	24,4	73,5	157,9	256,6	181,5
1993	-	-	-	2,3	11,6	23,9	76,5	216,3	197,9	127,7
1994	-	2,0	1,9	8,8	10,1	18,9	95,9	204,6	257,1	194,9
1995	-	-	2,0	4,4	12,1	21,6	73,0	119,8	211,4	190,6
1996	-	-	6,0	6,5	8,4	33,5	53,8	158,1	214,0	124,8
1997	-	-	4,1	2,2	15,9	26,0	75,6	165,4	243,5	193,5
1998	-	2,8	2,1	10,9	12,7	50,3	66,2	110,0	239,0	178,5
1999	-	3,0	2,3	4,4	4,9	19,8	53,8	107,3	144,3	169,4
2000	0,4	-	-	6,6	14,5	20,8	33,4	84,1	200,8	245,0
2001	-	-	5,2	6,6	16,6	22,2	60,7	106,1	219,1	222,7
2002	-	-	-	-	16,4	14,9	37,1	64,8	211,2	170,1
2003	0,4	-	2,8	2,3	14,7	15,0	40,6	82,6	147,3	167,5
2004	-	-	-	4,7	9,7	28,7	54,5	103,0	145,0	189,8
2005	0,4	-	-	2,5	4,8	8,3	30,1	69,6	161,6	188,8
2006	-	-	-	5,3	4,7	24,3	39,0	69,0	109,8	208,6
2007	0,4	-	-	5,6	14,1	34,4	18,0	92,9	87,1	257,4
2008	-	-	-	2,9	11,9	18,2	20,2	73,4	105,6	143,6
2009	-	2,8	-	3,0	9,8	15,5	48,1	22,7	121,2	258,9
2010	-	2,9	3,1	7,5	2,6	15,7	36,8	169,3	97,8	146,5
The forecast to 2020	-	-	-	1,0	5,8	14,2	-	8,9	17,6	228,5

"aging" of population and new or existing intensification of aetiology factors (Table5).

According to the analysis the first decade of analyzed period found out an increase of men number with the first diagnosis of MT (6.67%),because of a number change and age population structure (4.74%) and "risk to fall ill" (1.93). But at the same time men morbidity dynamics with lung cancer (2.36%) was positive under the influence of "risk to fall ill" increase.

A general number of women with MT (9.65%) is connected with a number change and age structure (9.71%). A low number of new patients with lung MT (-4.76%) can be explained by a low

Table 3

Annual incidence of the population of uluses of RS (Ya) of lung cancer for 2001-2010, (on 100 thousand population)

District	Both sexes	Men	Women
Abyjskij	42,1	51,7	32,9
Aldanskij	45,4	69,1	21,6
Allaihovskij	67,2	95,0	40,3
Amginskij	24,3	29,8	19,2
Anabarskij	29,8	44,6	15,0
Bulunskij	32,7	39,4	25,6
Verhnevilyujskij	39,3	41,8	36,8
Verhnekolymskij	65,9	95,1	35,5
Verhoyanskij	41,0	51,3	30,7
Vilyujskij	35,8	38,7	33,1
Gornyj	18,4	19,7	17,1
Zhiganskij	39,4	43,2	35,9
Kobyajskij	31,0	42,9	19,5
Lenskij	49,4	73,3	26,1
M-Kangalasskij	40,3	53,4	27,8
Mirninskij	23,3	37,2	9,1
Momskij	46,8	52,1	41,7
Namskij	27,5	36,8	18,9
Neryungrinskij	29,4	49,7	10,5
Nizhnekolymskij	35,4	54,3	16,7
Nyurbinskij	32,9	39,5	26,5
Ojmyakonskij	23,9	38,3	7,3
Olekminskij	50,1	75,9	24,5
Olenekskij	41,6	63,3	19,6
Srednekolymskij	32,3	44,0	21,1
Suntarskij	33,0	33,7	32,2
Tattinskij	37,9	34,4	41,4
Tomponskij	38,0	64,7	11,7
Ust'-Aldanskij	25,5	36,0	15,6
Ust'-Majskij	28,5	38,2	18,0
Ust'-YAnskij	27,0	38,5	14,5
Hangalasskij	27,0	37,2	16,0
Churapchinskij	28,8	31,1	26,4
Ehveno-Bytantajskij	32,6	28,9	36,3
Yakutskij	32,5	50,8	16,2
RS(Ya)	33,8	48,3	19,9

Table 4

Annual incidence of the population of territories of RS (Ya) of lung cancer for 2001-2010. (on 100 thousand population)

Zone RS(Ya)	All population		Men		Women	
	RI	SIw	RI	SIw	RI	SIw
Polar	38,7±2,0	45,2±7,4	50,5±3,3	66,4±3,8	26,8±2,4	28,5±2,4
East	30,4±1,8	30,8±5,6	47,6±3,2	54,2±3,4	12,0±1,6	11,7±1,6
Western	35,1±1,9	39,2±9,7	38,3±2,9	47,5±3,2	31,9±2,6	32,2±2,6
Central	29,8±1,8	36,9±7,5	37,6±2,8	52,6±3,4	22,2±2,1	24,2±2,2
Southern	49,7±2,3	46,7±5,0	74,4±4,0	84,1±4,3	25,4±2,3	20,3±2,0
Big cities	31,5±1,8	36,3±2,8	50,0±3,3	68,9±3,9	14,4±1,7	15,3±1,8
RS (Ya)	33,8±1,9	38,6±2,0	48,3±3,2	63,9±3,7	19,9±2,0	20,2±2,0

Explanatory note: RI - rough index, SIw - the standardized (world) indicator;* – distinction statistically is significant in comparison with men ($p < 0.05$).

Table 5

Components of an increase of number of again revealed patients with lung cancer in RS(Ya) from 2001 to 2010, (% of a datum level)

Localization of a tumor	General increase	Including in connection with change	
		of number and age structure of the population	of risk of disease
Men			
All new growths - (C00 – 97)	6,67	4,74	1,93
Lungs (C33, 34)	2,36	1,03	1,33
Women			
All new growths - (C00 – 97)	9,62	9,71	-0,09
Lungs (C33, 34)	-4,76	0,87	-5,62

influence of “risk to fall ill” factor (-5.62).

CONCLUSION

Thus, to achieve positive results aimed at perfection of “oncoepidemiological” situation in the Republic Sakha it’s necessary to pay a special attention to a negative demographic process and to intensity an effort to get rid of a risk factor to increase MT morbidity.

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ORIGINAL RESEARCHES

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VARIATIONS OF HOMEOSTASIS PARAMETERS IN HYPERTENSIVE PATIENTS

ABSTRACT

The aim of the study was analysis of the effectiveness of targeted antihypertensive treatment based and are not based on the correction of sympathicotonia in patients suffering from arterial hypertension, with choleric and sanguine temperament, and the activity of the renin-angiotensin-aldosterone system in phlegmatic and melancholic, for example, reduction of total cholesterol, total fraction of lipoproteins of low and very low density, the value of atherogenic index and increase in high density lipoprotein and magnesium in the blood serum. It is established that the content of magnesium and atherogenic lipid fractions, and the proportion of persons with complications in terms of antihypertensive therapy and, moreover, is not associated with the correction features of psychosomatic status, highanxiety phlegmatic and melancholic persons are at high risk of developing complications of hypertension.

Keywords: hypertension, magnesium, lipids, variants of antihypertensive therapy.

INTRODUCTION

In the structure of morbidity and mortality of the working age population cardiovascular diseases (CVD) occupy the first position. Currently, researchers identify a number of factors influencing the course and outcome of hypertensive (AH) and coronary heart disease (CHD) [6, 8, 9, 13]. It is known that some patients had a combination of hypertension with atherosclerotic defeat of vessels of heart and brain [4, 6]. On the other hand, a number of factors, including changes in the concentration of sodium, potassium, calcium, and magnesium (Mg) in the blood significantly affect the course of CVD. Deficiency of Mg can play a key role in the development of CVD [15]. But different people the severity and clinical features GB different that requires a customized approach in treatment and examination of patients [3].

The aim of the study was to examine concentration of magnesium and blood lipids in patients with AH-II men before and during treatment two variants of antihypertensive therapy (AHT) is empirical and focused on locking down some of the characteristics of patients with different temperament and level of anxiety.

MATERIAL AND METHODS

In the period from 1999 to 2012 in terms of the clinics surveyed 848 technical officers – men aged 44 to 62 years (average 54±1.8 years) who are diagnosed with hypertension, stage II (GB-II, grade 2, risk 3). Disease duration was on average 11.6±1.4 years. The presence of essential hypertension was established according to the criteria set forth in [8, 9]. Among the examined there were no manifestations of comorbidity. Controls were 422 healthy men, compatible on basic anthropo-social indicators. All analyses were performed 8.00 to 10.00 in the morning on an empty stomach. The prevailing temperament – choleric (Ch) sanguine (Sg), phlegmatic (Ph) and melancholic (M) is determined using a psychological test [10] by 3 times testing before treatment (0) and after 3, 6, 9, 12 and 18 months of AHT. Direct analogy with the personality of type "A", "B" or "D" not found [11]. The amount of reactive (RA) and personal (PA) anxiety was determined according to [14]. The differences between RA and PA were not reliable. To lowanxiety (LA) defined as those who scored 32,0±0,6 points, to high anxiety (HA) – between 42.8 ±0.4 points and above. The presence of depression was determined by the method of Je.R. Akhmetzhanov [2], where the condition without depression, I think from 20 to 50 points from 51 to 59 –

Table 1

The content of magnesium and HDL in the blood in patients with AH-II men after 12 and 18 months of treatment without edema (1; 2) and relief (1a; 2a) prevalence of SNS in the Ch and RAAS (aldosterone), Ph and M-patients during the study period f rom 1999 to 2012 (p<0.05)

Months AGT			Highanxiety					Lowanxiety			
			0	12	18	healthy		0	12	18	healthy
Magnesium, mmol/l	Ch	1 50	0,98±0,02	1,02±0,02	1,03±0,02	1,16±0,01 50	2 50	1,09±0,02	1,27±0,02	1,38±0,02	1,39±0,01 50
		1a 50		1,14±0,02	1,18±0,02		2a 52		1,38±0,01	1,49±0,02	
	Sg	1 52	0,89±0,02	0,96±0,02	0,98±0,01	1,04±0,03 51	2 54	1,00±0,02	1,18±0,02	1,27±0,02	1,24±0,01 51
		1a 54		1,03±0,02	1,05±0,02		2a 52		1,29±0,01	1,38±0,02	
	Ph	1 58	0,8±0,02	0,86±0,02	0,89±0,01	0,92±0,03 60	2 61	0,97±0,02	1,02±0,02	1,07±0,02	1,08±0,01 60
		1a 61		0,94±0,02	0,96±0,02		2a 56		1,12±0,01	1,18±0,02	
	M	1 50	0,68±0,02	0,72±0,02	0,74±0,01	0,80±0,03 50	2 50	0,82±0,02	0,91±0,02	0,96±0,02	0,98±0,01 50
		1a, 50		0,84±0,02	0,87±0,02		2a 50		1,03±0,01	1,07±0,02	
HDL, mmol/l	Ch	1	1,5±0,002	1,58±0,003	1,65±0,002	1,8±0,003	2	1,80±0,002	1,83±0,002	1,87±0,002	2,0±0,003
		1a		1,66±0,003	1,76±0,007		2a		1,88±0,003	1,98±0,007	
	Sg	1	1,3±0,003	1,40±0,005	1,46±0,004	1,5±0,005	2	1,59±0,002	1,64±0,005	1,68±0,004	1,8±0,005
		1a		1,46±0,003	1,54±0,003		2a		1,69±0,003	1,80±0,003	
	Ph	1	1,2±0,003	1,28±0,005	1,33±0,004	1,4±0,004	2	1,42±0,003	1,45±0,005	1,50±0,004	1,6±0,004
		1a		1,32±0,003	1,39±0,07		2a		1,52±0,003	1,57±0,07	
	M	1	1,1±0,002	1,17±0,005	1,21±0,004	1,3±0,004	2	1,24±0,002	1,27±0,005	1,31±0,004	1,45±0,004
		1a		1,20±0,003	1,25±0,07		2a		1,32±0,003	1,37±0,07	

Note: here and further in the denominator indicated the number of surveys.

Table 2

The OH content in the blood and of IA in patients with AH-II men after 12 and 18 months of treatment without edema (1; 2) and relief(1a; 2a) prevalence of SNS in the Ch and RAAS (aldosterone), Ph and M-patients during the study period from 1999 to 2012 ($p<0.05$)

Months AGT			Highanxiety					Lowanxiety			
			before treatment	12	18	healthy		before treatment	12	18	healthy
OH, mmol/l	Ch	1 50	5,4±0,02	5,30±0,02	5,10±0,02	4,9±0,01 50	2 50	5,09±0,02	4,89±0,02	4,78±0,02	4,5±0,01 50
		1a 50		5,06±0,02	4,87±0,02		2a 52		4,76±0,01	4,55±0,02	
	Sg	1 52	5,8±0,02	5,6±0,02	5,5±0,01	5,2±0,03 51	2 54	5,29±0,02	5,17±0,02	5,08±0,02	4,8±0,01 51
		1a 54		5,3±0,02	5,2±0,02		2a 52		4,94±0,01	4,69±0,02	
	Ph	1 58	6,2±0,02	6,08±0,02	5,86±0,01	5,5±0,03 60	2 61	5,65±0,02	5,48±0,02	5,30±0,02	5,0±0,01 60
		1a 61		5,76±0,02	5,49±0,02		2a 56		5,27±0,01	5,08±0,02	
	M	1 50	6,7±0,02	6,38±0,02	6,16±0,01	5,9±0,03 50	2 50	6,09±0,02	5,94±0,02	5,74±0,02	5,4±0,01 50
		1a 50		6,08±0,02	5,77±0,02		2a 50		5,60±0,01	5,38±0,02	
IA, c.u.	Ch	1	2,57±0,002	2,32 ± 0,02	2,09± 0,03	1,9± 0,002	2	1,83±0,002	1,67±0,02	1,56±0,03	1,2±0,03
		1a		2,05 ±0,03	1,78 ±0,02		2a		1,53±0,03	1,27±0,02	
	Sg	1	3,26±0,002	3,0 ± 0,02	2,75± 0,03	2,4± 0,002	2	2,33±0,002	2,15±0,02	2,05±0,03	1,6±0,02
		1a		2,68 ±0,03	2,37 ±0,02		2a		1,92±0,03	1,63±0,02	
	Ph	1	3,92±0,001	3,75 ± 0,02	3,41 ± 0,01	2,9± 0,001	2	3,00±0,001	2,79±0,02	2,53±0,01	2,2±0,01
		1a		3,36 ±0,03	2,95 ±0,02		2a		2,47±0,03	2,24±0,02	
	M	1	4,83±0,001	4,45 ± 0,02	4,09 ± 0,01	3,7± 0,001	2	3,91±0,001	3,68±0,02	3,39±0,01	2,9±0,01
		1a		4,06 ±0,03	3,62 ±0,02		2a		3,24±0,03	2,91±0,02	

Note: before treatment, the content of OH and IA have 1 and 1A (2 and 2a) are the same.

mild depression; the latter is marked only HA/Ph and HA/M. According to the conclusion of psycho HA-patients in-patient treatment is not needed. HA/Ch and HA/Sg were prescribed anxiolytic (Ax), and HA/Ph and HA/M is an antidepressant (Ad), except for drivers. From Ax at 96% was administered sibazon 2.5 mg in the morning and at night. From Hell is the experience of the use of antidepressants in the treatment of patients with arterial hypertension with disorders of the affective spectrum [1] 96% appointed coaxil 12.5 mg morning and night (in 4% of cases the zoloft at 25 mg/day). Appointment Ax and Ad of a driver and LA are not shown [12, 13]. The values of the initial vegetative tonus testified that Ch and Sg prevailed sympathetic (SNS) and Ph and M – parasympathetic (PSNS) is a division of the autonomic nervous system (ANS) [13].

The content of Mg in the blood serum was determined according to the method of Gindler, Heth, Khayam-Bashi through the use of biochemical reagents "BIOLABO" (France). Calmagite (metallochromic indicator) forms a colored complex compound with magnesium in the environment of the base [5]. The contents of serum total cholesterol (OH) were determined by enzymatic methods with the use of proprietary sets "CentrifiChem-600", and the content of cholesterol of high density lipoproteins (HDL) was determined after pre-deposition total fraction of lipoproteidov low (LDL) and very low (VLDL) density on the auto-analyzer "Technicon-AAII". The content of LDL was calculated by the formula: OH – HDL – VLDL where VLDL = triglycerides/2,181 [7]. We calculated the atherogenicity index (IA) [8, 9].

The effectiveness of the empirical variant of AHT (E-AHT) and targeted (T-AGT) for the relief of sympathicotonia have Ch and Sg, and the activity of the renin-angiotensin-aldosterone system (RAAS) was judged by the degree of alignment of the content of Mg and lipids with those in HA(LA)-healthy persons of corresponding temperament and proportion (%) of persons with acute cerebrovascular accident (CVA) and acute myocardial infarction (AMI) in patients.

Substantiation of variants of AGT. In the beginning of the study (1999 – 2004) the appointment of agents of AHT was empirical. From 2004 to 2012, the appointment of AHT was performed according to the order No. 254 of the Ministry of health and social development of the

Table 2

The content of total fraction of LDL+VLDL in blood serum in patients with AH-II men after 12 and 18 months of treatment without edema (1, 2) and with mild SNS Ch and Sg as well RAAS (aldosterone), Ph and M (1a, 2a) for the period from 1999 to 2012 (p<0.05)

Months AGT			Highanxiety					Lowanxiety				
			0	12	18	healthy		0	12	18	healthy
The total fraction of LDL+VLDL, mmol/l	X	1	3,91± 0,001	3,67±0,01	3,44±0,02	3,2±0,01	2	3,29± 0,001	3,07±0,02	2,92±0,03	2,5±0,01
		1a		3,40 ±0,01	3,19±0,01		2a		2,88±0,03	2,57±0,04	
	C	1	4,43± 0,001	4,18±0,01	4,04±0,01	3,7±0,01	2	3,70± 0,001	3,53±0,02	3,40±0,02	2,9±0,01
		1a		3,91±0,01	3,64±0,01		2a		3,25±0,03	2,92±0,07	
	Ф	1	4,90± 0,001	4,81±0,01	4,53±0,02	4,1±0,01	2	4,23± 0,001	4,03±0,02	3,82±0,01	3,5± 0,001
		1a		4,44±0,04	4,10±0,02		2a		3,75±0,02	3,55±0,06	
	M	1	5,52± 0,001	5,22±0,03	5,15±0,01	4,6±0,01	2	4,85± 0,001	4,67±0,03	4,45±0,03	3,9±0,01
		1a		4,88±0,05	4,63±0,02		2a		4,27±0,02	4,03±0,06	

Note: the number of examined table. 2.

Russian Federation dated 22.11.2004 (6 groups of drugs for the treatment of hypertension) [7]. However, analysis of the effectiveness of AHT showed that the incidence of complications in groups with the activity of the SNS-Department from HA/Ch and HA/Sg, treated with β-adrenoblockers (BAB) and a diuretic (D), and HA/Ph and HA/M(Sg) with the activity of the RAAS (aldosterone) and PSNS-section of VNS-treated angiotensinase enzyme inhibitors (aceis) + D were lower than in the groups treated with "empirical" AHT, in which drugs and doses are the same, but Ch and Ag took aceis+D, Ph and M – BAB+D. Thus, in the basic group, HA/Ch and HA/Sg-patients due to SNS-tonia received BAB, in 96% of cases – metoprolol (HA/Ch and HA/Sg at 200 mg/day (4% of its analogues) and LA/Ch, LA/Sg for 100 mg/day) and D (hydrochlorothiazide): HA/Ch and HA/Sg at 25 mg/day and LA – 12.5 mg/day. Have HA(LA)/Ph and HA(LA)/M as the main group the content of aldosterone was higher and cortisol lower than that of HA(LA)/Ch and HA(LA)/Sg, which was interpreted as the prevalence of RAAS (aldosterone), Ph and M in comparison with the hypothalamic-pituitary-adrenal system (cortisol), and Ch and Sg versa [12, 13]. It explains the purpose of the HA/Ph and HA/M-patients on the background of the PSNS-tonia and prevalence of activity in the RAAS (aldosterone) iace, 96% of the enalapril 20 mg/day (4% similar) + verospiron 100–200mg/day (75%), rarely (25%) and hydrochlorothiazide 25 mg/day, because the content of potassium in the blood have been lower than those of Ch and Sg. LA/Ph LA/M were administered enalapril 10 mg/day + hydrochlorothiazide (hydrochlorothiazide) - 12.5 mg/day. All patients were receiving panangin 2 tablets./day and cardiomagnyl on 1 tab./day. Exactly the same patients of the comparison groups received the same list of drugs in the same doses, but Ch and Sg an ACE-I, and Ph and M – BAB.

The results obtained were considered in 3, 6, 9, 12 and 18 months of AHT and processed by methods of variation statistics (M±M) using standard software package "Statistica 6.0" and the parametric student's t–test. Were considered as statistically significant values at p<0.05. This paper presents data before treatment (0) and after 12 and 18 months of AHT. The study was performed in compliance with the Helsinki Declaration, examination and treatment of the people and approved by the ethics Committee of the Novosibirsk state medical University 20.11.2009, protocol №18.

The results of the study and their discussion. We found that in patients before and during AHT, as well as in healthy persons the content of Mg in the blood significantly and consistently lower in the "temperamental" row: HA(LA)/Ch – Sg – Ph – M. The content of Mg was significantly lower than in La, and HA(LA)-patients is lower than in healthy HA(LA) persons of a corresponding temperament (table.1). It should be noted that the HA/Ph and HA/M the lowest content of Mg in the blood before treatment and only they have discovered depression mild neurogenic nature [12, 13].

The contents of the paps before and during treatment was significantly reduced in the same sequence as the magnesium content Ch > Sg > Ph > M. in contrast, the content of OH total fraction of LDL+VLDL in the blood and the amount of IA in the same row was significantly increased: M > Ph > Sg > Ch (table. 1-3). The obtained data suggest that the decrease in the content of insulin and aldosterone in row M > Ph > Sg > Ch combines the reduction of atherogenic lipid fractions and the magnitude of IA (table. 2).

The identified differences may indicate possible higher risk of atherosclerosis, "hypertension" HA/Ph and HA/M. Despite of AHT, the highest proportion of patients who have suffered complications of hypertension

in stroke and AMI happened to be in the group HA/Ph and HA/M. on the one hand, these differences indicate the specific manifestation of complications depending on the prevailing temperament, and on the other are likely to speak in favor of a combination of GB and atherosclerosis mainly in HA/Ph and HA/M. At the same locus minoris resistentio are often cerebral, and coronary vessels. From LA-patients given the lower lipid content of atherogenic fractions and less severe emotional reactions to environmental factors, the ratio of stroke/AMI patients was lower than in HA-patients the appropriate temperament that convinces you of the necessity of taking into account high and low anxiety and the relief of high anxiety in order to prevent possible complications.

Summing up, it should be noted that the lowest content of Mg and HDL in the blood in combination with the highest (of all the surveyed persons) content OH, LDL+VLDL in the same environment and ended up with HA/Ph and HA/M-patients. And this despite the fact that all patients received cardiomagnyl in the above mentioned dose. In turn, you might need to prescribe drugs of magnesium in higher therapeutic doses, using magnerot specified in [15] or its analogues.

The efficiency of AHT. As shown by our study, in contrast to the empirical version of AHT, treatment option T-AHT 18 months reliably brought the Mg content, OH, total fraction LDL+VLDL and HDL to that in healthy HA(LA)-persons of a corresponding temperament (table. 1 – 3). It would be less noticeable, if not significantly lower the proportion of persons with stroke and AMI in the groups HA(LA)-»temperaments», took option T-AHT. The ratio of the proportion of individuals with AMI, stroke groups showed the presence of three-fold prevalence of AMI on stroke in groups HA/Ph and HA/M. In addition, after a year of treatment under option T-AHT values of the studied parameters and the IA were what they were only after a further 6 months of treatment under option E-AHT in patients of comparison group (table. 1 – 3). That is, by a variant of the T-AHT for 6 months before they managed to reduce the risk of complications.

CONCLUSION

1. The content of Mg and atherogenic lipid fractions (OH, the total fraction of LDL+VLDL), as well as the proportion of persons with complications in terms of AHT associated and, moreover, is not associated with the correction features of psychosomatic status, HA/Ph and HA/M-patients are individuals at high risk of developing complications of hypertension. Compared to HA(LA)-patients of the values of the studied parameters is more preferable, suggesting the need for relief of high anxiety.

2. In contrast to Ch and Sg, the high lipid content of atherogenic fractions from HA/Ph and M combined not only with the highest level of complications, but three times the prevalence of AMI, stroke over (as a 3/1).

3. Compared to AHT without the relief features of the PSS, the effect of treatment based on the relief features of temperament (activity SNS division of the ANS for Ch and Sg and the RAAS aldosterone – Ph and M) appeared 6 months earlier, and the values of the studied parameters was significantly closer to typical for healthy persons of corresponding temperament and anxiety.

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INTRAPARTUM RISK AND NEWBORNS' HEALTH AFTER ABDOMINAL DELIVERY IN FULL CERVICAL DILATATION

ABSTRACT

Insufficient attention traditionally existing even in medical institutions that realize the principles of modern risk strategy impairs the perinatal outcomes. The birth outcomes in the newborns make up the main criterion for the implementation of accounting intrapartum risk factors. Since 2010 it is proved from a strong correlation between the growth of risk intrapartum and neonatal condition [EAGO, Lisbon, 2010; IN Kostin, 2012]. This study is undertaken in order to increase attention to the intrapartum risk factors, determining their contribution and force effects on birth outcomes.

Objective: to determine the main injuries in fetus and newborn delivered by cesarean section in full cervical dilatation.

We determined the threshold level of intranatal augmentation requiring changing labor management. The critical level of intranatal augmentation after abdominal delivery in full cervical dilatation is 82%. 41.7% of newborns with intranatal augmentation 82% and more need intensive care and resuscitation.

Keywords: pregnancy, perinatal risk factors, abdominal delivery.

The relevance of research

By the end of XX century in obstetric practice was the final formation of the perinatal risk strategy, aimed at preserving the life and health of the fetus and newborn. It was created

based on the study of factors affecting the level of perinatal morbidity and mortality, and the planning of measures to improve the outcomes of pregnancy and childbirth [1, 3].

As shown by numerous studies, the basis of many sorts, who had adverse outcomes for both mother and fetus, is underestimating or even ignoring the intrapartum risk factors (pathological preliminary period, meconium water anomalies of labor activity, etc.) [4, 5].

However, the new input in the scale factors and factors of intrapartum period led to an increase in the amount of risk points. The dynamic growth of the amount during pregnancy and during labor required to define any thresholds for clinical decision to change the tactics of pregnancy and childbirth. Convinced of the lack of effectiveness of modern electronic methods of fetal assessment, EAGO (2010) recommended the introduction of perinatal risk strategies to improve perinatal indicators. Underestimation of risk, and most importantly - it intrapartum component [2] can be one of the causes of the violation of the fetus and newborn.

Purpose of the study – to set the main health problems of fetuses and neonates recovered by caesarean section in full cervical dilatation.

MATERIALS AND METHODS

The objects of statistical research at various stages were 72 women who gave birth to the baby by cesarean section in full cervical dilatation.

The principle of the formation of the study group was typed score prenatal risk factors. To assess the

risk factors delivery table scoring intrapartum risk factors was used. It was developed at the Department of Obstetrics and Gynaecology with course of Perinatology of the Peoples' Friendship University of Russia. To determine the strength of the effect of intrapartum risk factors on birth outcomes was conducted correlation analysis [Spearman rank correlation (R)].

In the structure of perinatal morbidity were taken into account: congenital malformations, hypoxic CNS perinatal CNS lesion, aspiration syndrome, cephalohematoma, vertically transmitted infections, etc. Evaluate the activities carried out in the early neonatal period, length of stay, and transfer to the second stage of nursing.

Index of neonatal complications (INC) has been introduced for the assessment of birth outcomes for newborns by us. INC - it is an integral component of complications occurred in newborns and of interventions, be required in the early neonatal period. INC counting was carried out for every newborn to yield a range of values from 0 to 25. In order to analyze the impact of intrapartum factors on during the early neonatal period, all infants were divided into groups of INC.

The first group included the INC newborns who did not have complications, it was the largest (18-60% from the group of low and 24-57,1% from the group average perinatal risk). The second group included infants whose score was lower than the mean value of the INC in the total group of infants (8,8 ± 2,4), i.e. 1 - 9 points, there were 10 (33.3%) and 12 (28.6%), respectively. The third group included infants with INC, exceeding the mean value in the group - 10 points or more, there were 2 (6.7%), and 6 (14.3%), respectively.

RESULTS

The survey showed that the structure of the distribution of women according to risk during childbirth has changed radically. Due to revaluation of intrapartum risk factors in childbirth every third [28 (38.9%)] a woman came out of the low-risk group and included in the average, and 6 (8.3%) - a high perinatal risk.

The structure of the intrapartum risk factors in the first place - untimely rupture of membranes (8-11,4% in the low and 32-45,7% - average risk of perinatal), the second – abnormal labor (4-5,7% and 20-28,6%, respectively), in third place - and a lot of water scarcity (6-8,6% and 22-15,7%, respectively).

The main criterion for the implementation of intrapartum risk factors are birth outcomes for newborns, the reason it was a strong correlation between intrapartum factors and neonatal morbidity (R = 0,71, with p = 0,000 ...). Factors (complications in childbirth), is the most statistically significant impact on the incidence of complications in the newborn in the early neonatal period were: acute fetal hypoxia (the R = 0.6, p = 0.000 ...); cord entanglement (R = 0,5, p = 0.000 ...); meconium amniotic fluid (R = 0,4, p = 0.000 ...); abnormal labor (R = 0,3, p = 0.0004), with a stronger correlation with discoordination labor than with the weakness of labor activity.

After recalculation of the amount of intrapartum perinatal risk score, it was found that the average amount of intrapartum risk factors in the first group of the INC (healthy newborns) was 1.0; in the second group INC - 8.8; in the third (the most severe children) - 18.3 (!).

CONCLUSION

Thus, the parameter that determines the outcome of labor, is the degree of intrapartum growth. Most adverse birth outcomes obtained from women with high growth intrapartum corresponding 82% or more, so the tactics should be reviewed for them.

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COMPARISON OF CLINICAL AND LABORATORY PARAMETERS IN PATIENTS WITH END-STAGE RENAL FAILURE IN THE OUTCOME OF CHRONIC GLOMERULONEPHRITIS AND OTHER DISEASES

ABSTRACT

Frequent complications of hemodialysis treatments are coagulation disorders. First of all, this is due to activation of the coagulation of blood flow in the interaction with a dialysis membrane material vascular prostheses and extracorporeal circuit trunks. In addition, in hemodialysis patients receiving heparin for years, there is depletion of stocks in endothelial cells in tissue factor inhibitor, inhibits the activity of an external blood clotting mechanism. To evaluate the hemostatic system parameters in patients with end-stage renal failure, depending on the cause of renal failure and hemodialysis treatment duration conducted a study that included 100 patients observed in the department of chronic hemodialysis and nephrology hospital №1 Republican National Medical Center in the period of 2013-2016. It was revealed that the state of homeostasis in patients with end-stage renal failure in increasingly characterizes the level of fibrinogen and the activation of the hemostatic markers: soluble fibrin monomer complexes, D-dimers. In patients with end-stage renal failure in the outcome of chronic glomerulonephritis, a great expression of activation of blood coagulation confirm increased the mean concentration of fibrinogen, whereas in the group, which included patients with end-stage renal failure in the outcome of other diseases (type 1 diabetes, type 2 diabetes, systemic disease, polycystic kidney disease, hypertensive nephroangiosclerosis, anomalies of development of kidneys, chronic pyelonephritis, urate nephropathy), such is not different from the norm, and a higher rate of hyperfibrinogenemia, identified in 2/3 patients in this group. 18 patients (18%) were diagnosed with thrombosis of arteriovenous fistula, 5 patients (5%) was revealed thrombosis of vessels of other organs and systems. There was found in patients bleeding and anemia associated with all erythropoietin deficiency.

Keywords: hemostasis, terminal renal failure, renal replacement therapy.

INTRODUCTION

In Russia, according to the Register of the Russian Dialysis Society, in 2013, 35305 people received various types of renal replacement therapy, the annual increase in the number of patients with an average of 12.4%. The average age of the patients in our country, receiving renal replacement therapy, is 47 years, the young, able-bodied part of the population greatly affected [2, 10]. Frequent complications of hemodialysis treatments are coagulation disorders. First of all, this is due to activation of the coagulation of blood flow in the interaction with a dialysis membrane material vascular prostheses and extracorporeal circuit trunks [1, 5]. In addition, in hemodialysis patients receiving heparin for years, there is depletion of stocks in endothelial cells in tissue factor inhibitor, inhibits the activity of an external blood clotting mechanism [4, 11].

The **aim** of our study was to evaluate the hemostatic system parameters in patients with end-stage renal failure, depending on the cause of renal failure.

MATERIALS AND METHODS

The study included 100 patients: 59 women (59%) and 41 men (41%) aged 19 to 79 years (middle age 46.5 ± 14.6 years) observed in the department of chronic hemodialysis and nephrology of Republican Hospital National medical center №1 in the period from 2013 to 2016. All the patients at the time of inclusion in the study were diagnosed with end-stage renal disease (ESRD), which corresponded to the stage V chronic kidney disease (CKD), according to the criteria of clinical practice guidelines for CKD (KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease) by 2012 [10]. The cause of end-stage renal failure in most cases acts as chronic glomerulonephritis (CGN) - 43%, in second place (20%) - with diabetic nephropathy in type 2 diabetes [10].

The study was conducted in 2 phases: The purpose of Phase I was to find out what settings to change coagulation in patients with ESRD treated with hypertonia. In this part of the study included all patients who were treated in the department of chronic hemodialysis and nephrology hospital of Republican Hospital №1 - National Medical Center in the period from 2013 to 2016. The purpose of phase II study was to compare blood coagulation parameters in patients diagnosed with ESRD in the outcome of CGN, are on the program of the hemodialysis, and ESRD patients in the outcome of other diseases. 84 patients were included in this part of the study.

Inclusion criteria were: all patients diagnosed with a cause of ESRD treated with hypertonia. Exclusion criteria were: unknown cause of ESRD patient's refusal of the study.

The patients were divided into groups depending on the cause of ESRD: the outcome of the CGN or in the outcome of other diseases (type 1 diabetes, type 2 diabetes mellitus, systemic disease, polycystic kidney disease, hypertensive nephroangiosclerosis, anomalies of development of kidneys, chronic pyelonephritis, urate nephropathy). Group A consisted of 43 patients (20 men and 23 women) aged 19 to 61 years (38 ± 10.5 years), diagnosed with ESRD in the outcome of chronic glomerulonephritis. In group B included 41 patients (15m: 26w) aged 22 to 79 years (57 ± 15 years), diagnosed with ESRD in the outcome of other diseases.

To describe the data X calculated average value and standard deviation (σ) of the studied parameters. Determination was carried out by Spearman correlation method. Authentic differences at $p < 0.05$ shall be deemed. All calculations were performed on a PC using SPSS 10 for Windows software packages.

RESULTS AND DISCUSSION

The following results were obtained by processing the data: 18 patients (18%) were diagnosed with thrombosis of arteriovenous fistula (AVF), 5 patients (5%) was revealed thrombosis of vessels of other organs and systems. Bleeding in patients was found, anemia associated with all erythropoietin deficiency [8, 9].

In the study a total level of blood platelets, it was found that the platelet count in the total group averaged 263 ± 97,2 x 10^9 / L (55 to 502 x 10^9 / L). Thrombocytopenia rate was 10%, thrombocytosis - 13%.

The study revealed coagulation parameters: thrombin time (TT) in patients ranged from 14.5 to 32.9 seconds (average 22.5 ± 4.6 seconds) at a rate of 16-26 seconds. Prothrombin Time Indicators (PT) - from 8.1 to 17.9 seconds (average 10.65 ± 2.45 seconds) at a rate 9-12,6 seconds. Prothrombin index (PTI) - from 59.58 to 396.14% (mean 116 ± 40.2%) at normal rates 78-142%. The international normalized ratio (INR) of 0.75 to 1.34 (mean 0.9 ± 0.1), the norm: 0.81-1.13. Activated partial thromboplastin time (APTT) of 20 to 48.1 seconds (mean value of 30.2 ± 4.35 seconds) at a rate of 23,4-35 seconds. Fibrinogen level from 2.22 to 9.5 g / l (mean value of 5.0 ± 1.3 g / l) at a rate of 2-4 g / l.

A blood test for soluble fibrin monomer complex (SFMC) was taken in 26 patients, figures ranged from 4.5 to 26 mg% (mean 10 ± 6.3 mg%) at a rate of up to 4 mg%.

D-dimers were detected in 46% of patients ranged from indicators 0.34 to 1184 ng / mL (mean 230 ± 355,5 ng / ml) at a rate of less than 500 ng / ml [6, 7] (see the Table 1).

At the second stage of the study, we compared the patients with ESRD in the end of the CGN and the outcome of other diseases (of 84 people). Group A consisted of 43 patients (20m: 23w) aged 19 to 61 years (38 ± 10.5 years), diagnosed with ESRD in the outcome of chronic glomerulonephritis. In group B included 41 patients (15m: 26w) aged 22 to 79 years (57 ± 15 years), diagnosed with ESRD in the outcome of other diseases. From the study excluded 16 patients with unclear etiology of ESRD.

In both groups, the platelet count was almost the same. In group A platelet level averaged 276 ± 103 x 109 / L (range 61.2 to 502 x 10^9 / L). In group B - 265 ± 98 x 10^9 / L (55 to 495 x 10^9 / L). The frequency of thrombocytopenia and thrombocytosis was low and comparable in both groups (Table 2).

The average values of “routine” of hemostasis (TT, PT, INR, aPTT, PTI) did not deviate from the norm and were similar in both groups (Table 3).

In group A, the value of thrombin time in patients ranged from 14.5 to 32.9 sec, an average of 23.3 ± 4.8 sec. Shortening TT was observed in 3 patients, elongation - in 12. In group B thrombin time values in patients ranged from 16.3 to 31.8 sec, an average of 22 ± 4,8 sec. Shortening TT is not mentioned in any of the patient, TT elongation was 7 patients.

The values of the prothrombin time in group A patients ranged from 8.5 to 17 seconds, an average of 10 ± 2.45 seconds. Shortening PT was observed in 7 patients, elongation - in 15 patients. In group B prothrombin time values in patients ranged from 8.1 to 17.9 seconds on average 10.9 ± 2.6 seconds. Shortening PT was observed in 6 patients, elongation - in 16 patients.

The values of the international normalized ratio in group A patients ranged from 0.77 to 1.2 seconds, on average 0.91 ± 0,1 seconds. Reducing the INR was observed in 5 patients, an increase - in 1 patient. In Group B patients INR values ranged from 0.75 to 1.28 seconds, on average 0.9 ± 0.1 seconds. Reducing the INR was observed in 5 patients, an increase - in 6 patients.

Values of activated partial thromboplastin time in Group A patients ranged from 20 to 39.9 seconds on average 30.2 ± 4.5 seconds. The shortening of the aPTT was observed in 4 patients, elongation - in 8 patients. In Group B patients APTT values ranged from 24.5 to 48.1 seconds on average 30.5 ± 4.4 seconds. The shortening of the aPTT is not mentioned, the extension - in 4 patients.

Prothrombin index values in group A patients ranged from 73 to 181.8%, with an average 128,6 ± 27,2%. Reducing the PTI noted in 1 patient, increase - in 13 patients. In group B the values of prothrombin index in patients ranged from 68 to 396.14%, the average 109 ± 53,2%. Reducing the PTI noted in 3 patients, an increase - in 9 patients.

Average levels of antithrombin III (AT III) were normal [3, 4] and did not differ in both groups. In group A, the average level of AT III was 103.5 ± 21.7% (from 70 to 161.96%) in Group B - 104 ± 21,1% (from 82.92 to 134%). In this case more than 1/3 of the patients group B and up to 30% group A marked high values of AT III, exceeding the physiological rate.

In group A greater intensity of activation of blood clotting confirm increased the mean concentration of fibrinogen, whereas in group B such does not differ from the norm (cf. fibrinogen level in group B - 4.07 ± 1,6g / l, group A -. 5,09 ± 1,1 g / l (p = 0.004)), and a higher rate of hyperfibrinogenemia, identified in 2/3 patients in this group.

CONCLUSION

Thus, in group A (n = 43), which included those with ESRD in the outcome of CGN, lower figures of blood pressure were recorded than in group B (n = 41), which included patients with ESRD in the outcome of other diseases. In group A, patients with diagnosed hypertension accounted for 41.5%, in group B 61.4%.

Severity of anemia in patients with ESRD in the outcome of CGN was the same as that of untreated hemodialysis over a year. Patients in both groups did not differ (P> 0.05) in the levels of creatinine (865.2 ± 269 mmol / l in group A; 812,6 ± 226 mmol / l in group B.).

Thrombosis AVF in ESRD in the outcome CGN occurred in 7 patients in the outcome of other diseases of the kidneys - in 11 patients (in the outcome of

Table 1

Indicators of coagulation in the total group

Index	Norm values	The average		The middle value
		min	max	
TT	16-26	14,5	32,9	22,5±4,6
PT	9-12,6	8,1	17,9	10,65±2,45
IRN	0,81-1,13	0,75	1,34	0,9±0,1
APTT	23,4-35	20	48,1	30,2±4,35
Fibrinogen, g / l	2-4	2,22	9,5	5±1,3
PTI, %	78-142	59,58	396,14	116±40,2
SFMC	<4	4,5	26	10±6,3
D-dimer	<500	0,34	1184	230±355,5

Table 2

Frequency of thrombocytopenia in patients with ESRD in the outcome of CGN and patients with ESRD in the outcome of other diseases

Group	Уровень тромбоцитов, x10^9/л		
	thrombocytopenia <150 x10^9/л	Norma 150-400 x10^9/л	Thrombocytosis >400 x10^9/л
А (n=43)	5 (11,6 %)	31 (72,1 %)	7 (16,3 %)
Б (n=41)	4 (9,8 %)	32 (78 %)	5 (12,2 %)

Note: p > 0,004 (between t A and t B).

Table 3

Group	Group A	Group Б	Norma	p
ТВ, с	23,3±4,8	22±4,8	16-26	NS
ПВ, с	10±2,45	10,9±2,6	9-12,6	NS
МНО	0,91±0,1	0,9±0,1	0,81-1,13	NS
АЧТВ, с	30,2±4,5	30,3±4,4	23,4-35	NS
ПТИ, %	128,6±27,2	109,4±53,2	78-142	p=0,03

diabetic nephropathy in type 2 diabetes - 3, hypertensive nephroangiopathy - 3, systemic diseases - 1, polycystic kidney - 1, urate nephropathy 1).

Indicators of platelet hemostasis in both groups were similar (in grams. A 276 ± 103 x 109 / l, c. B 265 ± 98 x 109 / l. The frequency of thrombocytopenia and thrombocytosis was small and comparable in both groups.

The average values of "routine" of hemostasis (TT, PT, INR, aPTT, PTI) did not deviate from the norm and were similar in both groups.

In group A greater intensity of activation of blood coagulation confirm increased the mean concentration of fibrinogen, whereas in group B such does not differ from the norm (the average level of fibrinogen in g B -. 4.07 ± 1,6g / l, g A -. 5, 09 ± 1,1 g / l (p = 0.004)), and a higher rate of hyperfibrinogenemia, identified in 2/3 patients in this group.

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GENETIC RISKS OF DEVELOPMENT OF PELVIC ORGAN PROLAPSE RECURRENCE AFTER HYSTERECTOMIES

ABSTRACT

Objective: to establish immunohistochemical and genetic markers of POP on the basis of studying of features of connecting tissue of women with a disease recurrence.

Materials and methods. The study involved 168 women, 134 of them with POP relapses aged 35 to 65 (96 after hysterectomy by vaginal access because of a total and partial uterus and vaginal walls prolapse). The control group consisted of 44 women aged 35-52 with no POP signs, after abdominal hysterectomy for uterine fibroids, adenomyosis, endometrial pathology.

Used: immunohistochemical (to assess tissue biopsies of sacrum-uterine and round uterine ligaments), the expression of matrix metalloproteinases (MMPs) and tissue inhibitors of matrix metalloproteinases (TIMPs), genotyping by polymerase chain reaction of MMP/TIMP polymorphisms.

Results: Disturbances in the expression of the most important CT disorganization markers in POP shall comply with the expression of protein coding genes, in particular – MMPs and TIMP.

The results of studying the frequency of polymorphism genotypes in the groups of healthy women and those with POP are

presented in a chart.

Associations with GP development have been established among women with genetic polymorphisms: 5A5A (rs3025058) MMP3 gene. Statistical significance for the groups was preserved after the correction for multiple comparisons. The low frequency of CC allele of MMP2 gene (735 C>T) among patients with POP gave reason to consider it as a marker of biodegradation reduction in tissues connecting the core of pelvic organs.

The mutant CT allele of polymorphic variant rs 2277698 of TIMP-2 gene is more common among women with pelvic floor failure, but statistical significance was defined in relation to the protective CC genotype, revealed among half of healthy women.

Reducing of TIMP-1 accumulation on the background of metalloproteinases high expression indicates a substantial role of dynamic equilibrium violation in pathobiochemical disorders and pelvic dysfunction.

Conclusions. The determination of «risk» alleles predisposing to POP should be considered as a contribution to the understanding of the pathogenesis of the disease. They can be used as genetic markers of individual undifferentiated CT dysplasia manifestations.

Molecular and biological characteristics of tissue remodeling in POP allow us to consider immunohistochemical diagnosis as an improved capability of disease recurrence risk prediction after surgery and the choice of optimal treatment technology.

Keywords: pelvic organ prolapse, connective tissue dysplasia, collagen, extracellular matrix, matrix metalloproteinase (MMP), tissue inhibitors matrix metalloproteinase (TIMP), genetic polymorphisms.

INTRODUCTION

Pelvic organ prolapse (POP) is a serious medical and social problem among women of all ages, but mostly - in peri- and postmenopausal periods, with significant adverse consequences not only for health, but also for the quality of life, ability to work and social welfare. This problem is of high cost for the healthcare system as a whole [11]. POP incidence is believed to increase significantly in the coming decades due to the rapid growth of the elderly population in developed countries [19]. Delayed diagnosis of the disease is caused by the absence of any clinical manifestations of the pelvic floor insolvency among nearly two-thirds of patients with anatomical features of the pelvic descencia who happened to give birth [6]. According to the data acquired, only 40% of women aged 45-85 have objective POPevidence, but pelvic dysfunction symptoms, combined with incomplete emptying of the bladder and intestines, manifesting itself in the feeling of heaviness and the presence of a foreign body in the lower abdomen, urinary disorders and dyspareunia, were characteristic of only 12% of them [18].

Perennial discussion of etiological aspects and POPrisk factors contributed to the recognition of this disease being multifactorial. It was confirmed that the basis of pelvic failure is determined by anatomical and functional damage of phenotypically different tissues – supporting ligaments and striated muscles with prevailing changes in the connective tissue (CT) homeostasis [1,9]. The variety of CT functions, determining the active participation of its elements in a continuous renewal and restructuring in response to stress and damage, is regulated by hereditary, hormonal and metabolic factors [2]. CT morphogenesis dysregulation is initiated by genetic breakdowns that lead to the disruption of the formation of proteins' primary structure and extracellular matrix components [3,5]. Subsequently, it causes the destabilization of organ and tissue architectonics constituting the essence of dysplasia. Biological CT failure in cases of genital prolapse is reported to be formed as a result of qualitative changes arising because of collagen types I and III imbalance [11]. Protein metabolic disorder with enhanced lytic activity, decreased tensile strength, increased tissue extensibility, alongside with the reduction of another component of the extracellular matrix –elastin – were detected due to the study of the vaginal wall and supporting structures of the pelvic among patients with POP. All in all, this disease was indicated as a particular case of connective tissue dysplasia (CTD) [3,5]. Early detection of an imbalance in the CT structure, which plays an important role in maintaining the pelvic floor integrity, becomes possible due to identifying early signs of tissue degradation – violation of basic matrix protein correlation, altering protein properties and their morphogenetic functions. Remodeling of extracellular CT matrix by proteolysis or degradation of collagen fibers is performed by matrix metalloproteinases (MMPs) – extracellular family of zinc-dependent endopeptidases capable of destroying all kinds of extracellular matrix proteins [15]. Their involvement in tissue remodeling, angiogenesis, proliferation, migration and differentiation of cells, apoptosis, control over tumor growth proves to be regulated at several levels – nucleate, cell, tissue. It is known that MMPs include interstitial collagenase group (MMP-1, -2, -3) which cleave fibrillar collagen of corresponding types; gelatinases (MMP -2 and - 9) influencing amorphous collagen and fibronectin; stromelysins (MMP- 3, -10 and -11) affecting various components of the extracellular matrix including proteoglycans, laminin, fibronectin and amorphous collagen. The analysis of regulation of CT processes remodeling and the assessment of the role of matrix metalloproteinases (MMPs) involved in the degradation of extracellular matrix proteins remains the subject of scientific debates concerning POP pathophysiology.

The increase in MMP expression is connected with active remodeling of connective tissue structures – supporting ligaments of the uterus and vaginal walls, which promotes POPdevelopment. Specific MMP tissue inhibitors (TIMPs) perform the prevention of uncontrolled MMP excessive impact.

Considering the ideas about the genetic predisposition to the disease due to decreased activity of the enzymes involved in extracellular matrix formation and protein catabolism, the search for candidate genes as a missing link in biochemical conception of changes in the pelvic floor

structures becomes a significant trend in perineology [4]. Despite positive associative connections between individual genetic polymorphisms and the disease itself, general information about the genetic basis of POPappears to be haphazard and desultory.

Thus, the lack of comprehensive studies explaining the mechanisms of morphogenesis and pathological changes in the pelvic organs CT structures, with the detection of immunohistochemical and molecular genetic POPpredictors determines the prospects of suchlike analysis being aimed at reducing POPpostoperative recurrence.

OBJECTIVES OF THE STUDY

to establish immunohistochemical and genetic markers of POP on the basis of studying of features of connecting tissue of women with a disease recurrence.

MATERIALS AND METHODS

The study involved 168 women, 134 of them with POPrelapses aged 35 to 65 (96 after hysterectomy by vaginal access because of a total and partial uterus and vaginal walls prolapse).

The control group consisted of 44 women aged 35-52 with no POP signs, after abdominal hysterectomy for uterine fibroids, adenomyosis, endometrial pathology.

The study inclusion criteria: the presence of POP.

Exclusion criteria were malignant and autoimmune diseases.

The degree of genital prolapse was assessed by POP-Q classification (pelvic organ prolapse quantification), proposed by the International Continence Society (ICS) in 1996.

All women from the main and control groups had a comparable amount of parturition.

4 samples of tissue were obtained from 54 patients: right and left sacro-uterine ligaments, right and left round uterine ligaments. Sections were made on glass slides Menzel Super Frost Ultra Plus, covered with an adhesive; immunohistochemical (immunoperoxidase) reactions were conducted by the standard method with thermal antigen unmasking (Dako Protocols) and using the first antibody to MMP-1 and MMP-2 (LabVision, ready to use) and TIMP-1 (LabVision, 1:50).The results of immunohistochemical reactions was assessed semiquantitatively scored on a 6-point scale based on the percentage of stained cells or colored extracellular matrix and color intensity: 2 points – less than 20% stained ECM / cells, 4 points – from 20 to 40%, 6 points – 40 %.

Used: genotyping by polymerase chain reaction of MMP/TIMP polymorphisms with separation of DNA samples from whole blood.

Genetic polymorphisms of MMPs and TIMP were analyzed: MMP 2 rs2285053 (rs2285052) (735 C> T); MMP2 rs243865 (1306 C> T); MMP3 rs3025058 (1171 del> T [5A> 6A]); MMP9 rs3918242 (1562 C> T); MMP9 rs17576 (836 (855) A> G (Gln279Arg)); TIMP2 rs2277698 (303 C> T (Ser101Ser)). Genotypes were determined by PCR, with the curves of melting analysis by modified «adjacent probes» method (adjacent probes, kissing probes) using commercial test kits «SPA DNA-Technology», Russia. DNA for genotyping was taken from peripheral blood samples taken from EDTA as an anticoagulant with a set of reactants «Probe-GS-genetics» («SPA DNA-Technology», Russia). Oligonucleotide probes melting temperature was determined with the help of the detecting thermocycler DT-96 («SPA DNA-Technology», Russia).

Statistical result processing was performed using the program SPSS 13 for Windows.

χ2 criterion was used to determine the statistical significance of differences in the frequencies of alleles and genotypes in groups of patients. The distribution of genotypes for the studied polymorphic loci was tested for compliance to Hardy-Weinberg equilibrium. Statistical analysis of the results was used to calculate the frequency of genes, genotypes and their combinations occurrence, the odds ratio (OR) and 95% confidence interval (OR 95% CI). In assessing the reliability of the identified differences between the samples' average values and the reliability of the identified correlations p error probability was calculated. Differences at $p \leq 0,05$ were considered to be significant.At assessment of reliability of the revealed distinctions between average values of selections the probability of a mistake p (the importance paid off at $p \leq 0,05$) with the accounting of corrective action of Bonferroni.

RESULTS OF THE STUDY AND DISCUSSION

In round and sacro-uterine ligament samples of patients with POPMMP-1 and MMP-2 expression was observed in the form of lumps of brown staining in the extracellular matrix, ligament apparatus fibroblasts and the vascular endothelium. A similar trend was noticed in marker TIMP-1 imaging. Quantitative estimation of the average MMP-1 expression levels showed a higher content of stained cells and ECM among patients with POP compared to healthy women: 4±1,2

Distribution of genetic polymorphisms of MMP and TIMP on groups of healthy women and with POP

Gene	Polymor-phismtype	Genotype	Frequency of genotypes				Criterion of distinctions Pearson's Chi-squared test	p	OR (CI 95%)
			Study group with POP		Control group				
MMP3	1171 del>T 5A>6A	5A5A	44	0,26	7	0,16	6,7	0,008*	2,6(1,3 -5,3)
		5A6A	91	0,54	20	0,45	6,3	0,01*	1,4 (0,7-2,8)
		6A6A	33	0,2	17	0,39	2,0	0,16	0,5 (0,2 –1,3)
MMP9	836/855 A>G	AA	80	0,48	23	0,52	4,3	0,6	1,2 (0,6-2,3)
		AG	68	0,4	14	0,32	1,3	0,96	1,5(0,7-2,9)
		GG	20	0,1	7	0,2	0,5	0,5	1,4 (0,5-3,6)
MMP9	1562 C>T	CC	73	0,43	25	0,57	2,5	0,11	1,7(0,9-3,3)
		CT	73	0,43	13	0,29	1,2	0,28	1,8(0,9-3,7)
		TT	22	0,13	6	0,14	0,01	0,92	1,0(0,4-2,8)
TIMP2	303 C>T 101 S	CC	59	0,35	23	0,52	4,3	0,04*	2,0 (1,0-3,9)
		CT	90	0,54	14	0,32	1,25	0,26	2,5 (1,2-4,9)
		TT	19	0,11	7	0,16	0,7	0,4	1,5 (0,6-3,8)
MMP2	735 C>T	CC	70	0,42	27	0,6	5,4	0,02*	2,2(1,1-4,4)
		CT	75	0,4	12	0,3	3,5	0,06	2,1(1,0-4,5)
		TT	23	0,1	5	0,1	0,16	0,7	1,2(0,4-3,5)

points to 2 ± 0,8 points (p <0,05).Index ofMMP-2 expression with POP(6±0,3 points) significantly exceeded the level of enzyme accumulation in the control group (4±0,5 points, p <0,05).

Other researches also show evidence of similarly increased MMP-1 and MMP-2 expression in the uterosacral ligaments and vaginal tissues among patients with POP. It corresponds to the predominance of extracellular matrix degradation in dysplastic morphogenesis. These results are consistent with ideas that MMPs and other proteases expression is not observed in healthy tissues and can be detected only in cases of remodeling, inflammation or high risk of postoperative disease recurrence.

The expression level of TIMP-1 (stained brown) appeared to be reduced in comparison with that in healthy women group: 1,5±0,5 points to 4±0,7 points, respectively (p <0.05).

The obtained data show MMP-1 expression increase among women with POP, alongside with reduced TIMP-1, compared with the control group, wherein the inhibitor deficiency remains unchanged regardless of age or menopausal status.

The results of numerous publications, despite some variability in the data due to the methodological aspects of various studies, indicate that abnormal metabolism of ECM proteins in the pelvic organs with the formation of an imbalance between the activity of MMPs and their inhibitors has a serious impact on various cell functions, including adhesion, migration, differentiation. Thus, MMP-1 and -2 can be considered as markers of collagen degradation. Disturbances in the expression of the most important CT disorganization markers in POPshall comply with the expression of protein coding genes, in particular – MMPs and TIMP.

The results of studying the frequency of polymorphism genotypes in the groups of healthy women and those with POP are presented in a chart.

It was stated that among MMP polymorphisms homozygote option 5A5A of MMP-3 gene (p=0,008; OR-1,5; CI 95% (0,7-2,9) was associated with increased POP risk, which proves its excessive effect on the destruction of collagen type I or biodegradable ability reduction.

The frequency of insertion-deletion polymorphism 1171 5A>6A, influencing the increased MMP3 gene expression, was much greater in groupwith POP(0.54 and 0.45).

6A6A homozygote frequency was much greater in the control group(0,4) (χ^2=2,0; p=0,16; OR-0,5; CI 95% (0,2-1,3), confirming its protective role in CT architectonics.

The low frequency of CC allele of MMP2 gene (735 C>T) among patients with POPgave reason to consider it as a marker of biodegradation reduction in tissues connecting the core of pelvic organs.

The heterozygous form CTof polymorphic variant rs 2285053 was found more frequently among women with pelvic floor failure, but showed no statistically important differences in the samples of patients with POPand healthy women (0,4 и 0,3).

The frequency of genetic MMP9 polymorphisms (1562 C>T) in the groups involved in our study did not differ significantly, despite the slight predominance of CT variant among patients with POP (0,43 and 0,3, p>0,05).

A polymorphic AG variant (locus rs 17576) of MMP9 gene (835/836) was bigger than its occurrence rate in the control group (0.4 vs. 0.32), but without any statistically significant differences.

The results obtained yielded to the data on the excessive biodegradable impact of MMP9 enzyme to collagen in the presence of the allele AG and GG in the study of Taiwanese scientists [16], but undoubtedly, the methodology of all scientific works presented on the subject should be taken into account.

The mutant CT allele of polymorphic variant rs 2277698 of TIMP-2 gene is more common among women with pelvic floor failure (0.54 and 0.32), but statistical significance was defined in relation to the protective CC genotype, revealed among half of healthy women (0.52) and only a third with POP(0,35) (χ2 = 4,3; p = 0,04; OR-2,0; CI 95% (1,0-3,9)).

The tendency to increase the activity of TIMP-2 enzyme in the presence of genetic determination causes the deficiency of molecular «protest» to the slowdown in progressive extracellular matrix degradation while considering CT protein synthesis retardation.

Reducing of TIMP-1 accumulation on the background of metalloproteinases high expression indicates a substantial role of dynamic equilibrium violation in synthesis processes, post-translational transformation and enzyme degradation in the tissues of the ligamentous apparatus – sacral and cross-uterine ligaments, indicating pathobiochemical disorders and pelvic dysfunction.

Conclusions. The determination of «risk» alleles predisposing to POP should be considered as a contribution to the understanding of the pathogenesis of the disease. They can be used as genetic markers of individual undifferentiated CT dysplasia manifestations.

Molecular and biological characteristics of tissue remodeling in POPallow us to consider immunohistochemical diagnosis as an improved capability of disease recurrence risk prediction after surgery and the choice of optimal treatment technology.

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A.A. Zakharov

CHANGES OF ORGANOMETRIC PARAMETERS OF EPIDIDYMIS OF EXPERIMENTAL ANIMALS AFTER ADMINISTRATION OF CYCLOPHOSPHAMIDE

ABSTRACT

The aim of this study was to establish the organometric features of epididymis of immature experimental animals after immunosuppression, simulating the negative impact of exogenous factors on the reproductive system.

Material and methods. The experiment was carried out on 60 immature white rats derived from vivarium of SE "LGMU" with an initial mass 40-50 g. For modeling immunosuppression rats received immunosuppressive drug cyclophosphamide in a dosage of 1.5 mg/kg body weight for 10 days. When working with experimental animals used recommendations ARRIVE manual prepared by National Centre for the Replacement, Refinement & Reduction of Animals In Research. Epididymides were weighed on a torsion balance, calculated relative to body mass, linear dimensions measured using calipers. The data were processed using the statistical program, the significance of differences between the indices of the experimental and control groups was determined by Student-Fisher's test ($p < 0.05$).

Results and discussion. The data may indicate that the epididymis of immature animals undergo some morphologic changes, after "soft" immunosuppression, which is accompanied by inhibition of morphogenesis, manifested by decrease of organometric parameters in comparison with controls. The development of these structural changes is also observed in a number of cases that have been observed by some researchers, under certain conditions of external and internal environment with the action on male sex organs systems of animals and humans. Conclusions. Epididymides of immature animals exhibit an active response to the "soft" immunosuppression. The most active change of organ morphometry indicators are set to 1, 7 and 15 days after administration of cyclophosphamide, which is probably due to the imperfection of the structure and functioning of the immature epididymis, as well as changes in the immune organs as a constituent of one of the regulatory systems of the body. Leveling morphometric changes in the later stages of observation (30 and 60 days) may be associated with the normalization of the immune system and the development of adaptation mechanisms in the male reproductive system organs.

Keywords: epididymis, cyclophosphamide, rats, immunosuppression, morphometry.

INTRODUCTION

The deterioration of the reproductive health of the male population is a recognized and widespread problem in the world in recent decades. Through the efforts of the World Health Organization has developed and implemented programs aimed at the formation of long-term policy of the WHO Regional Office, which is part of the European regional strategy in the field of sexual and reproductive health. The results of the latest clinical and laboratory studies support the concern of experts in this field regarding violations of the male reproductive function, increasing the number of which in different countries makes the research of various branches of medical science to draw attention to this problem very urgent [3]. The reasons for the changes in the structure and functioning of the male reproductive system is called a number of exogenous adverse factors, including those that cause systemic immunosuppression, including extensive use of drugs for the relief of immunopathological, cancer and autoimmune conditions [1]. The special position occupied by factors affecting the organism of children and adolescents due to the imperfection of the morphological and functional elements of the organs of the regulatory systems of the body, including the immune system. The existence of such health and socio-economic components of the problems of modern society stimulates the study of morphological changes in the foundations of the male reproductive function, especially before puberty. In this context, the aim of this study was to establish the organometric features of epididymis of immature experimental animals after immunosuppression, simulating the negative impact of exogenous factors on the reproductive system.

MATERIAL AND METHODS

The study was carried out within the framework of the research program of the Department of Histology, Cytology and Embryology SE "Lugansk State Medical University" "Structural features of organs of the immune and endocrine systems in immunostimulation and immunosuppression" (state registration number 0112U000096). The experiment was carried out on 60 immature white rats obtained from the vivarium SE "LGMU" with an initial body weight of 40-50 g. During the study the animals were kept under standard conditions with natural light and diet recommended for this type of animal. For the simulation of immunosuppression rats were administered an immunosuppressive drug cyclophosphamide in a dosage of 1.5 mg/kg body weight for 10 days. This scheme is widely used in clinical practice to achieve immunosuppression in various autoimmune diseases, transplantation. As a control, animals were administered with 0.9% sodium chloride in equivalent volumes by the same scheme. Rats were taken from the experiment under ether anesthesia at 1, 7, 15, 30 and 60 days of observation. When working with experimental animals used recommendations ARRIVE manual prepared by National Centre for the Replacement, Refinement & Reduction of Animals In Research [5]. Epididymides were weighed on torsion balance WT 1000, calculated relative organ mass, linear dimensions measured using calipers ShTs-I. The data were processed using the licensed program «StatSoft Statistica v6.0», the reliability of the difference between the indices of the experimental and control groups was determined by

Student-Fisher's test ($p<0.05$).

RESULTS AND DISCUSSION

Epididymis of immature animals of the control group adjacent to the dorsal edge of the testis, and has a head, body and tail. Absolute and relative organ weight increased during the observation period (Table 1). The linear dimensions of the body also underwent similar changes with increasing age of rats: so appendage length was 23.7±0.74 mm, 22.7±0.89 mm, 27.3±0.24 mm, 28.4±1.4 mm, and 43.8±1.3 mm, 1, 7, 15, 30 and 60 days of observation, respectively. Body width also increased in the same period, amounting to 2.67±0.07 mm, 2.79±0.12 mm, 3.94±0.15 mm, 3.9±0.12 mm and 6.94±0.25 mm, respectively. These changes of organometric parameters of epididymis related indicators of ontogenetic morphogenesis.

After administration of cyclophosphamide epididymis remain common morphological features of the structure. However, the immunosuppressive effect of causing significant changes in the morphometric parameters of the body. So, the early stages of observation (1, 7 and 15 days) a decrease of the absolute weight of epididymis indicators at 9.26%, 13.44% and 17.12%, respectively, was discovered (Fig. 1). After 30 and 60 days after treatment significant changes of organometric parameters have been not identified.

After immunosuppression the length indicator of epididymis undergone similar changes. At 1, 7 and 15 days of observation was significant reduction at 9.77%, 12.48% and 17.95% respectively, compared with those of control animals. Organ width index was significantly decreased in the specified time observations at 10.11%, 13.47% and 16.84% relative to the control data (Table 2). In the long-term period of the experiment (30 and 60 days), significant deviations of the experimental data from the control has not been established.

The data may indicate that the epididymis of immature animals undergo some morphologic changes, after "soft" immunosuppression, which is accompanied by inhibition of morphogenesis, manifested decrease of organometric parameters in comparison with controls. The development of these structural changes is also observed in a number of cases that have been observed by some researchers, under certain conditions of external and internal environment with the action on male sex organs systems of animals and humans. In particular, S.S. Ostrovsky et al. point to the oppression of morphological and functional parameters of the reproductive system of rats after exposure to heavy metals [4]. P.V. Loginov, P.A. Ivanov proved the reduction of the endocrine function of the male reproductive system in the background of nutritional stress [2].

Table 1

Changes in the absolute and relative mass of epididymis of immature animals in the control group (M±m, n=30)

Group	Days	Absolute mass of epididymis, mg	Relative mass of epididymis, mg
Control	1	27±0,55	0,19±0,001
	7	31±1,5	0,23±0,01
	15	37±1,8	0,23±0,008
	30	38±2,74	0,25±0,012
	60	58±3,1	0,36±0,014

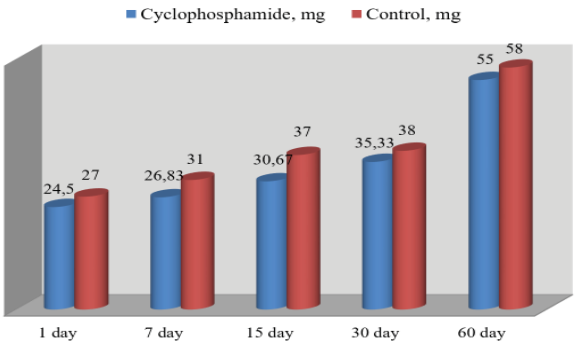

Fig. 1. Changes in the absolute weight of epididymis after use of cyclophosphamide and in control.

Table 2

Linear parameters of epididymis of immature animals after the administration of cyclophosphamide (M±m, n=30)

Group	Days	Epididymis length, mm	Epididymis width, mm
Cyclophos-phamide	1	21,38±0,42*	2,4±0,09*
	7	19,87±0,84*	2,42±0,03*
	15	22,4±0,38*	2,38±0,15*
	30	25,25±0,25	3,68±0,1
	60	42,65±1,19	6,72±0,21

* – significant difference from control, $p<0,05$.

CONCLUSIONS

1. Epididymis of immature animals exhibits an active response to the "soft" immunosuppression.

2. The most active change of organ morphometry are set to 1, 7 and 15 days after administration of cyclophosphamide, which is probably due to the imperfection of the structure and functioning of the immature epididymis, as well as changes in the immune organs as a constituent of one of the regulatory systems of the body.

3. Leveling the morphometric changes in the later stages of observation (30 and 60 days) may be associated with the normalization of the immune system and the development of adaptation mechanisms in the male reproductive system organs.

4. The obtained results are of interest for the study of the structural features of epididymis in an immunostimulation.

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METHODS OF DIAGNOSIS AND TREATMENT

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THE COMPLIANCE TO THE PREVENTION OF THROMBOEMBOLIC COMPLICATIONS AFTER REPLACEMENT OF LARGE JOINTS

ABSTRACT

The article presents an analysis of the level of compliance to the prevention of thromboembolic complications in patients after arthroplasty of large joints carried out in the Republican hospital №2 of Yakutsk from January 2012 to December 2013. Studies have shown low levels of compliance in patients treated with parenteral and indirect anticoagulants.

Keywords: compliance, prevention of thromboembolic complications.

The reluctance of patients to follow treatment protocol is one of the most serious and compelling problems of modern medicine [1,2]. Compliance is a term that belongs to the everyday life of practitioners, both abroad and in our country. The word means the right, and moreover, conscious and consistent implementation of all advice received from the doctor by patients [3]. Lack of compliance (noncompliance) is an actual problem for all areas of clinical medicine [2]. According to modern studies, doctors in their practice address relatively rarely to the methods that can effectively influence the compliance of drug therapy, which may partly be explained by their lack of awareness on this issue. This review deals with the problem of compliance with anticoagulation therapy. The analysis of existing methods of compliance assessment, basic errors connected to the noncompliance with the regime of anticoagulation by patients is carried out.

Refusal of anticoagulant therapy or taking them in notoriously inadequate doses can lead to a number of serious adverse consequences, both for the patient and for the health system. Despite the awareness of the importance of regular intake of drugs, many patients do not take medications as prescribed.

The aim of this study is to assess the level of commitment to the prevention of thromboembolic complications after replacement of large joints, identifying the causes of noncompliance, as well as factors that reduce the compliance in this cohort of patients.

MATERIALS AND METHODS

During the period from January 2012 to December 2013 in the trauma and orthopedic department of Republican hospital №2, Center of Urgent Medical Aid, 665 operations of degenerative diseases of the hip and knee joints were performed.

In order to prevent thromboembolic complications we used three treatment regimens:

1. Parenteral low molecular weight heparins (LMWH) as monotherapy (nadroparin calcium salt (fraxiparine)), enoxaparin sodium (clexane) and dalteparin sodium (fragmin).

2. Parenteral LMWH with the transition to indirect anticoagulants (warfarin).

3. Oral anticoagulants: Rivaroxaban (Ksarelto) and Dabigatranetexilate(Pradaksa).

Anticoagulant therapy is prescribed to all patients after surgical treatment. Treatment regimen is fully explained to patients by the attending physician before the operation, the patient then chooses which method is considered more convenient (the best) for him. The patient continues the selected thromboembolic complications prevention scheme during outpatient treatment.

Parenteral anticoagulants (enoxaparin sodium, nadroparin sodium, deltoparin sodium salt) were injected subcutaneously 1 time per day at the recommended doses (the first injection was pierced 12 hours before operation, the second - 12 hours after surgery) for 20-35 days. Oral anticoagulants (rivaroxaban, dabigatranetexilate) were given 6 hours after surgery for 25-35 days. The patients of the third group were injected with parenteral anticoagulants the day before surgery and for 10 days after surgery. From the sixth day of LMWH injection an indirect anticoagulant (warfarin) was added. Upon reaching the figure of INR 2 LMWH was cancelled and indirect anticoagulants as preventive measures were continued up to 20-30 days, depending on the operation. All patients underwent coagulation control in the day of admission, one day after the operation, then on the fifth and tenth days after surgery and before release. Also indicators of CBC were monitored.

At release from hospital, all patients were given recommendations for further prevention of thromboembolic complications, the objectives of these medications and possible complications having been explained. Also the control of INR indicators were recommended for the patients having taken anticoagulants of indirect action.

RESULTS

According to the study the average age was 59,55 ± 11,49 years (from 17 years to 86 years). By gender: women 403 (60.6%), 262 men (39.4%). By referring arthroplasty: a knee joint 350 (52.63%), a hip joint 315 (47.37%). During the observation period patients received a monotherapy of parenteral LMWH (19 patients), which corresponds to 2.85%, 246 patients (37%) obtained parenteral LMWH with a transition to indirect anticoagulants and 400 patients (60.15%) – oral anticoagulants.

There are many methods, but none of them is considered ideal for the assessment of compliance. The most reliable of them is a count of used packaging. But it does not apply in practice, because many patients live in remote from the clinic locations. In connection with this, we carried out a telephone survey.

In this study, patients' compliance was assessed on the basis of the data

provided by them and the similar kind of compliance, obviously, can be called "declared compliance." The survey was conducted by questionnaire observation program HA2011-01RU, Soprano.

The survey of 469 patients was carried out as a result. 258 patients (55.01%) implemented fully the medical recommendations, from which the patients having taken anticoagulants according to Scheme 1 were 10 people, 28 people followed Scheme 2, 220 followed Scheme 3. 22 (4.69%) patients breached a drug receiving as a single pass, 12 (2.55%) patients replaced a product to other anticoagulants. However, these violations, in our opinion, could not significantly influence the development of thromboembolic complications, so this group of patients was assigned to the category of "conditional compliance." 58 (12.36%) patients completely ignored the medical advice that manifested in refusal to accept not only the anticoagulant, but other drugs. 13 (2.77%) patients randomly replaced it with a drug with different mechanism of action (antiplatelet agents), as well as taking medication not in the recommended doses. 72 (15.35%) patients did not undergo or underwent coagulation control only once. Exceeding of a recommended dose is not ascertained. Also social factors have made their contribution to the structure of noncompliance. So 25 surveyed did not take recommended oral anticoagulants due to the absence of the drug in pharmacies, and 7 patients for the same reasons were forced, instead of an oral anticoagulant, to take its cheaper analogue because of the high cost of the drug.

According to the study, compliant are those patients who were assigned a parenteral and oral LMWH anticoagulant as monotherapy. Noncompliant are those patients who were recommended to take indirect anticoagulants. To these patients the recommendations to control coagulation were given, but this procedure was performed with 21 patients (once), the remaining patients either did not attend the clinic (13 patients) or in MPIs this procedure is not performed or they were not sent to specialists to whom they had addressed (8 patients).

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THE EFFECTIVENESS OF SELF-LOCKING SUTURES IN LAPAROSCOPIC MYOMECTOMY

ABSTRACT

The authors present a comparative analysis of the efficiency of laparoscopic myomectomy (LM) with bed unit closure with individual sutures and a monofilament self-locking barbed suture.

It was found that the use of knotless suture at LM helps to reduce the duration of closure of the myometrium defect, intraoperative blood loss, general surgical risks and the complexity of the intervention, the formation of a wealthy uterine scar due to full recovery of its anatomy. Statistically significant differences in the duration of operations, hospitalization periods, hemoglobin levels and postoperative complications were not observed.

Keywords: laparoscopic myomectomy, barbed suture V- lock, duration of suturing the myometrium defect.

The priority of organ-saving technology in uterine fibroids treatment (UF) is connected with the rejuvenation of women who are interested in their reproductive function in the presence of this disease. The need to improve aspects of choosing various technologies of reconstructive plastic surgeries is determined by symptoms, size and location of the tumour and the number of fibroids [2,7].

Despite obvious advantages of laparoscopic myomectomy (LSM), widespread use of this method has contributed not only to the fibroids removal, but also triggered a debate about the viability of scars on the uterus. The cases of uterine rupture at the scar during parturition favoured the study of risks related to the adequacy of the technical restoration of uterine walls integrity during laparoscopy, as well as suture healing conditions.

Optimum regeneration of dissected tissues is determined by the conditions of blood supply, that means by the way of uterine wall defect restoration and the type of suture material. Taking into account the necessity to achieve complementary hemostasis, especially

for large-sized fibroids, which in its turn affects the duration of the intervention, the possibility of endo-suture imposing is discussed, being a method of suturing the defect myometrium, contributing to the formation of solid scar on the uterus and the reduction of the risk of histopathic uterine rupture during pregnancy.

Discussions about the benefits of suture material and creating optimal conditions for full-fledged suture scarring in the uterus are still continued. It is believed that the braided thread of polyglycolic acid or polydioxanone, traditionally used in myomectomy, is associated with the risk of local ischemia and necrosis, the violation of suture remodeling processes because of uneven distribution of a tension gradient. The negative effects can be avoided by using alternative options – the V-lock system, which is an absorbable monofilament polydioxanone thread with a loop at the free end and unidirectional laser incisions along its entire length.

The strength of different types of threads differs very slightly, but pulling the braided thread through the tissues is more traumatic and can cause significant inflammatory reaction, compared to monofilament one. The knotless suture with a firmly fixed first stitch and the possibility to pull the thread freely through the tissue exclude excessive pulling of the units that can negatively affect the healing of the tissue when using individual and continuous sutures. The problem of effectiveness of using absorbable monofilament sutures due to the paucity of data encourages the analysis and comparison of high-tech and traditional techniques of intraoperative defect myometrium suturing.

The **objective** of the study is to compare the efficacy of suturing the bed of the node unit using V-lock system (self-locking monofilament thread) and individual sutures in laparoscopic myomectomy.

MATERIALS AND METHODS

To achieve the goal a prospective study was carried out, including 40 women with hysteromyoma who were examined at clinical bases of Obstetrics, Gynecology and Perinatology Department of the Kuban State Medical University in 2014 – 2015. The study was conducted on the basis of high-tech medical care and clinical testing of prevention, diagnosis, treatment and rehabilitation methods.

Depending on the way of the uterine wall closure during laparoscopic myomectomy 2 groups were formed among 40 women: in group I (n = 20) a monofilament synthetic thread of poliglecaprone (Monocryl Plus 0) was used by individual Z-shaped sutures; in group II (n = 20) a node-free uninterrupted suture was used with the thread with a serrated design and a fixing loop (V-lock 180 “0”).

Laparoscopic myomectomy (LSM) was performed traditionally, including the following steps: cutting serosa and myometrium above the node in its outermost part and possibly most distant from appendages and vascular bundles, husking myoma node without pseudocapsule by rigid fixation and tractions of the unit by 10mm bullet forceps with a following gradual “withdrawal” from the site of the myometrium. Further on, spot coagulation of bleeding vessels was carried out using bipolar coagulation, then postoperative defect suturing by sero-muscular sutures, gripping the bottom of the wound for the prevention of hematomas in the myometrium and the formation of a high-grade scar, with extracorporeal knot tying. The myoma node was removed from the abdomen by morcellation in an airtight container.

All women were examined in connection with infertility of various duration in accordance with generally accepted standards, significant deviations from the standard indicators haven’t been identified. The main criterion for inclusion in the study was the presence of individual subserous-interstitial myoma nodes ranging in size from 5 to 7 cm.

Exclusion criteria were chronic extragenital diseases in decompensation and acute stages, acute inflammatory diseases and cancer.

The duration of patients’ observation after the surgery was 12 months.

Statistical processing of the results was performed using the statistical software package Statistica v.6.0. and Microsoft Office Excel 2003. The program calculated the arithmetic mean M and standard error of the mean m. Student’s parametric test was used to assess statistically significant differences between the groups under consideration. Differences were accepted as statistically significant when $p < 0,05$.

RESULTS AND DISCUSSION

The operative time (the time spent directly on LSM) and the volume of intraoperative blood loss were assessed in the sample of patients with hysteromyoma (UF). The criteria for the effectiveness of organ-saving surgical treatment included the removal of the clinical symptoms of the disease (poly- and dysmenorrhea), the reduction in the amount (volume) of the uterus on the basis of gynecological research data and transvaginal ultrasound scan.

Comparability of the groups was emphasized by almost identical age of the patients (35,6 ± 1,8 and 33,8 ± 1,4 years old, respectively), as well as the duration of the fibroids presence (4,8 ± 1,5 and 4,3 ± 1,7 years). The comparative analysis of the effectiveness of various uterus integrity and recovery techniques in cases of LSM showed no statistically significant differences in the duration of the surgery in the following groups: in I – from 30 to 85 minutes, on average 68,5 ± 22,5, in II – from 30 to 65 minutes, on average 51,7 ± 14,4. Some of the differences in the time intervals can be explained by the need for additional coagulation and imposing additional sutures, especially at major nodes. The advantages of continuous knotless suture and surgical difficulties reduction are presented in the study by T. Song et al. (2015) [3]. However, the reduction of overall contact length during myomectomy was not observed in our case. It should be noted that in general, the number of women with node size up to 5 cm (32% and 40%) and larger (7.5 cm) (78.0% and 60.0%)

in the groups was not significantly different.

Average hemoglobin levels in the groups under study with some variants of suture material usage did not differ much (122,7 ± 5,6 g / L and 136.4 ± 8.3 g / L respectively, p> 0,05).

Reducing the time, required for closing the uterine wall defect using a continuous knotless monofilament suture during LSM (10,9 ± 4,3 min. vs. 17,4 ± 3,8 min., p <0.05), being compared to individual joints using, proved the research of foreign colleagues. In the studies by A.R. Gargiulo et al. (2012) the advantages of V-lock suture were observed both in traditional and robotic myomectomy [6].

The reduction of intraoperative blood loss (56,4 ± 34,5 vs. 86,8 ± 56,3, p <0.05) was a distinctive feature of V-lock system in LSM.

Other kinds of research also report on the optimization of LSM technology when using knotless monofilament thread by reducing perioperative blood loss and the duration of the myometrium closure process [5]. It is believed that the closure of the surgical wound in the uterus using self-locking filaments with laser notches simplifies the surgeon's work in conditions of limited endo-manipulative activity, reduces stress and eliminates the need for a third assistant [1]. V-lock system notches being focused in one direction helps to put together the wound edges anatomically, facilitates reliable hemostasis in the wound by a light pull of the thread through the myometrium. Monofilament thread reduces the chance of developing an inflammatory process in the wound, promotes optimal vascularization and healing while minimizing complications which are often observed when using individual sutures – poor or excessive thread pulling and loosening, negatively affecting the quality of the scar formation on the uterus.

The absence of the need in laparotomy, blood transfusions or sonographic signs of postoperative scar inviability indicates efficacy and safety in all cases of V-lock system using during LSM. A similar opinion is shared by other authors [4]. However, they deny the connection between the type of suture material and the frequency of complications.

CONCLUSION

Our research allows denying the significant impact of different types of suture material in the early and late postoperative periods, terms of rehabilitation and recovery after laparoscopic myomectomy. The advantages of V-lock system should also be noted. It has physical and biological properties required for a full restoration of the anatomy of the uterus compared to conventional sutures: simple overlay, putting the edges of the wound matched without the need of constant pull, absence of necessity for knotting and the so-called "third hand". LSM with continuous knotless monofilament suture helped to reduce the chance of intra - and postoperative complications, medicamental burden (including the duration of anesthesia) and shortened hospital stay and rehabilitation period.

The formation of a solid uterine scar with preservation of tissue architectonics, which is extremely significant for patients who are interested in their reproductive function, proves the effectiveness of high-tech innovations when mastering the appropriate skills to use them.

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ASSESSMENT OF EFFICACY OF TYROSINE KINASE INHIBITORS IN TREATMENT OF CHRONIC MYELOID LEUKEMIA

ABSTRACT

This research demonstrated treatment results of 45 patients with chronic myeloid leukemia who were monitored from 2006 to 2015 year. The article is aimed to evaluate a frequency of achievement of hematologic, cytogenetic, molecular responses in patients administered with tyrosine kinase inhibitors, prevalence of resistance to imatinib and its toxicity. It is shown that the treatment of choice for CML is tyrosine kinase inhibitor – imatinib. The use of tyrosine kinase inhibitors allows to reach deep cytogenetic and molecular remission in patients with chronic myeloid leukemia which leads to increased survival. Authors have noted a high prevalence of primary and secondary resistance to first generation tyrosine kinase inhibitor – imatinib. Investigation of results demonstrated that regular hematological, cytogenetic and molecular monitoring is required for effective disease control.

Keywords: chronic myeloid leukemia, tyrosine kinase inhibitors, imatinib.

INTRODUCTION

Chronic myeloid leukemia (CML) is a rare disease new cases of which are approximately 1:100,000 per year. According to data presented in register there are 6466 patients with CML in Russia, 93% of which is alive by 2015 year [5].

Discovery of BCR-ABL tyrosine-kinase inhibitors (TKI) has become one of the most significant achievements in modern oncology. The use of tyrosine kinase inhibitors has led to improvement of patient's outcome and reduction in disease progression to an accelerated stage or blast crisis. The survival rate of CML patients has increased from 3-4 years to 15 years or more, reduction in the frequency of progression to advanced phase [1]. The majority of patients are able to lead a normal daily lifestyle and work.

Imatinib is a generally accepted standard first-line therapy for patients with chronic phase of CML. Numerous studies have found that imatinib blocks binding of BCR-ABL tyrosine kinase with ATP. This leads to suppression of BCR-ABL-dependent signaling pathways and excessive proliferation of myeloid cells. The results of International randomized study IRIS has demonstrated that imatinib has a significant advantage over IFN combination with low-dose cytarabine. Patients with chronic stage CML has shown good tolerability and a high level of complete cytogenetic response (87%) and major molecular response (39%). The subsequent 7-year follow-up and analysis of the results of the study showed a high survival rate among patients receiving imatinib therapy: event-free survival rate was 81%, disease-free survival - 93% and the overall survival – 86% [7].

The article is aimed to evaluate a frequency of achievement of hematologic, cytogenetic, molecular responses in patients administered with tyrosine kinase inhibitors, prevalence of resistance to imatinib and its toxicity.

MATERIALS AND METHODS

The research included 45 patients with verified chronic myeloid leukemia who were monitored from 2006 to 2015 year. A retrospective analysis of medical records was carried out. During investigated period we have found 22 women (49%) and 23 men (51%) with CML. CML most commonly is seen in people aged between 50 and 69 (average age - 44,7 ±15,2). In 42 patients (93,3%) the diagnosis was confirmed with cytogenetic and/or molecular studies. 3 patients (6,7%) doesn't have a results of studies.

At the moment of diagnostic 25 patients (55%) had chronic stage of disease, 20 (45%) – accelerated stage. For risk stratification J.E. Sokal score was used and according to it majority of patient had low risk – 54,2%. Intermediate risk group was established in 37,5%, high risk in 8,3%.

All patients were administered a tyrosine-kinase inhibitor imatinib as first-line therapy. Therapy started with the dose 400 mg/day. In case of no response to treatment or in case of previous complete hematological and/or cytogenetic response loss the dose was increased up to 600-800 mg/day. In case of evidence of disease progression or serious adverse drug effects patients were transferred to other TKI (nilotinib, dazatitnib). Previous therapy with hydroxyurea was found in 12 persons (26.7%), busulfan in 2 (4.4%) and interferon in 1 (2.2%). One patient receives "5 + 2" chemotherapy prior to treatment with imatinib. The median time from the diagnosis of the disease prior to therapy was 4.4 months (range 0 to 48 months). The median duration of imatinib therapy was 49 months (ranging from 6 to 149 months).

Dynamic control of treatment

response was estimated based on complete blood count, morphological and cytogenetic analysis of bone marrow and level of *BCR-ABL* gene expression according to polymerase chain reaction (PCR). Laboratory studies were performed according to federal clinical recommendations on diagnostic and treatment chronic myeloid leukemia [1]. Efficacy of therapy was estimated according to frequency of achieving of hematological, cytogenetic and molecular response, its stability and survival rate. Depending on the depth of clonal neoplastic cells reduction there are different types of response to therapy (table). Rates of overall (OS) survival and progression-free survival (PFS) were calculated with Caplan-Meier method using «Statistica 13.0» software package. In analysis of OS event is implied a death from any cause and loss of patient from monitoring; point of counting is beginning of therapy with first-line TKI. In analysis of PFS event is implied disease progression to accelerated phase or blast crisis.

RESULTS AND DISCUSSION

Complete hematologic response (CHR) is the first reference point of treatment response prognosis. In our study 36 patients (80%) achieved CHR by 3 months of treatment. During the whole therapy time CHR was registered in 43 patients (95,2%), 2 patients (4,8%) has showed primary hematologic resistance.

Cytogenetic study should be performed every 6 months until maintaining complete cytogenetic response (CCyR) then once a year or if loss of CCyR is suspected [1, 6]. Dynamic cytogenetic control of treatment in this study was carried out in 32 patients (71.1%). In 12 patients (26.7%) cytogenetic analysis was aimed only to confirm the diagnosis. Due to the inability to evaluate the cytogenetic response, these patients were excluded from this analysis.

By 6 months of therapy, only 3 (9.3%) patients achieved a CCyR. During the same period 3 patients (9.3%) achieved a partial cytogenetic response (PCyR), 1 (3.1%) - a major cytogenetic response (MCyR) and 1 (3.1%) – minimal cytogenetic response (MinCyR).

By 12 months of therapy 6 patients (18,8%) achieved a CCyR, 3 patients (9.4%) PCyR, 1 patient (3.1%) MCyR, and 1 (3.1 %) - MinCyR. During 18 months of therapy new cases of achieving CCyR observed additionally in 2 patients (6.2%). In any period of therapy CCyR was achieved in 7 people (21.9%).

The total amount of patients who achieved CCyR in imatinib therapy equaled 56,25% cases with median time of achieving CCyR 19,4 month (ranging from 6 to 36 month)

Molecular monitoring the quantitative level of BCR-ABL-transcripts with real-time PCR is commonly used to evaluate response to treatment in patients with CML. This method is particularly important in the era of TKI therapy of CML, when the level of residual leukemia cells are usually below the sensitivity of cytogenetic studies [6]. The level of molecular response is a predictor of disease-free survival, thus molecular analysis is very important.

Regular molecular monitoring is performed in 27 patients (60%). In 15 persons (33.3%) study was conducted in amount that insufficient for response assessment, or not performed at all, and in 3 patients (6.7%), identified in 2014-2015, was excluded from molecular response analysis because of the short duration of treatment. By 12 months of therapy 3 patients (7,4%) achieved major molecular response (MMR), by 18 months additional 5 patients (11,1%). During any time of therapy period MMR was achieved in 17 patients (37,03%). During the whole time of therapy MMR was achieved in 22 patients (48.14%).

Frequency CCyR and MMR according to different authors varies widely depending on the disease stage at the moment of diagnostic, imatinib dose, pretreating and the presence of risk factors [1,3,4,6]. So, with a starting dose of imatinib 400 mg of CCyR rate ranges from 49% to 77%, and the MMR from 18% to 58%. With increasing doses up to 600 or 800 mg improves response to therapy - CCyR up to 49-77% of cases, and the MMR - up to 43-47% [6].

It should be noted that regular hematologic, cytogenetic and molecular control are needed to evaluate treatment response. Unfortunately nowadays the lack of

Types of response to therapy in CML

Type of response	Definition
Hematologic	
Complete hematologic	WBC less than $10x10^9$; basophils less than 5%; no myelocytes, promyelocytes and myeloblasts in the differential, platelets less than $450x10^9/l$
Cytogenetic	
Complete cytogenetic (CCyR)	No Ph+ metaphases
Partial cytogenetic (PCyR)	1-35% Ph+ metaphases
Minor cytogenetic (MCyR)	36-65% Ph+ metaphases
Minimal cytogenetic (MinCyR)	66-95% Ph+ metaphases
None (no CyR)	>95% Ph+ metaphases
Molecular	
Major molecular	Ratio *BCR-ABL/ABL*<0,1% or >0,01 on international scale (IS)

regular cytogenetic and molecular control is a problem as in our region, as in Russian Federation. According to the Russian Register of CML treatment, in 2013, only 41% of patients had regular cytogenetic/molecular (two or more analyzes per year) follow-up, and in 2014 only 20% [5].

Despite the high effectiveness of imatinib some patients develop primary or secondary resistance. Primary resistance is defined as the absence of hematologic response in 3 months, MinorCyR - after 6 months, Major - 12 months, CCyR - after 18 months of therapy. Secondary, or acquired, resistance is the loss of hematologic, cytogenetic or molecular response or progression to the advanced stages. In our study, 20% of patients has demonstrated primary resistance and 17.8% - secondary resistance to imatinib.

Progression to advanced stages is extremely negative outcome of disease. During the whole time of treatment disease progression was noted in 13 patients (28,9%), of which 4,4% (2 cases) - to blast crisis, and 24.5% (11 cases) – to the accelerated stage. During imatinib therapy progression was observed in 10 patient (71,4%), another 4 (28,6%) gets progression during 2 generation of TKI administration. Investigation of treatment results demonstrated that 5-year PFS of patients with CML in chronic stage is 77.64%, 10-year – 58,48% (fig. 1).

In general 12 (26,7%) of the patients died during the follow-up period. Progression of disease occurred in 13,3% of cases, death from comorbid disease was noted in 6.7%. In 4.4% patients the cause of death has not been registered. The 5-year OS rate in patients with chronic stage of CML treated with TKI is 91.57% and 10-year-survival - 80.12% (fig. 2). Review of literature showed demonstrated that our results correspond with survival data from other regions of RF, where 5-year OS is 92,9 and 90,6% [3,4].

Clinical studies have shown that imatinib is well tolerated drug with acceptable ratio of the expected benefits and potential side effects for patients in all stages and lower risk of serious side effects. The frequency and severity of adverse drug effects depend on the drug dose and CML stage.

Common side effects include fluid retention, myelosuppression, nausea, vomiting, fatigue, cramps, headaches, joint pain, rash, and increased activity of the enzymes alanine and aspartate transaminase [4]. Myelosuppression of 3-4-th degree is noted more frequently in CML patients with advanced stages.

Adverse side effects of wide spectrum were observed in 30 patients (66.7%). Periorbital edema, headache, arthralgia, dyspepsia were observed in 18 patients (60%). Side effects associated with imatinib, were mostly mild or moderate (1st and 2nd degree). Serious adverse events that required drug withdrawal were found in 33.3% of patients (10 of 30). Imatinib withdrawal mainly was caused by cardiotoxicity manifested by arrhythmias and toxic cardiomiopathy, severe toxic dermatitis and long-lasting dyspeptic syndrome with nausea and vomiting. In 66.7% of patients (20 of 30) adverse drug effects managed with dose reduction, temporary cancellation of the drug and supportive care. Hematologic toxicity of grade 3-4 was noted in 15,5% of patients (7 of 45). It required drug withdrawal for not more than 14 days, followed by resumption of the previous dose. One patient demonstrated persisting anemia, leukopenia and thrombocytopenia, so she was started therapy with 2 generation TKI.

CONCLUSION

Currently, imatinib is still the drug of choice in the treatment of patients with chronic myeloid leukemia. Analysis of the treatment of chronic myeloid leukemia in the Republic of Sakha (Yakutia) during last 10 years has shown that imatinib allows to achieve clinical remission in 95.2% of cases, complete cytogenetic response in 56.25%, and major molecular response in 48.14%. 10-year progression-free survival rate was 58,48%, and the overall 10-year survival rate of 80,12%.

Despite the effectiveness of imatinib, we found high prevalence of primary and secondary resistance, which requires administration of 2 generation TKI.

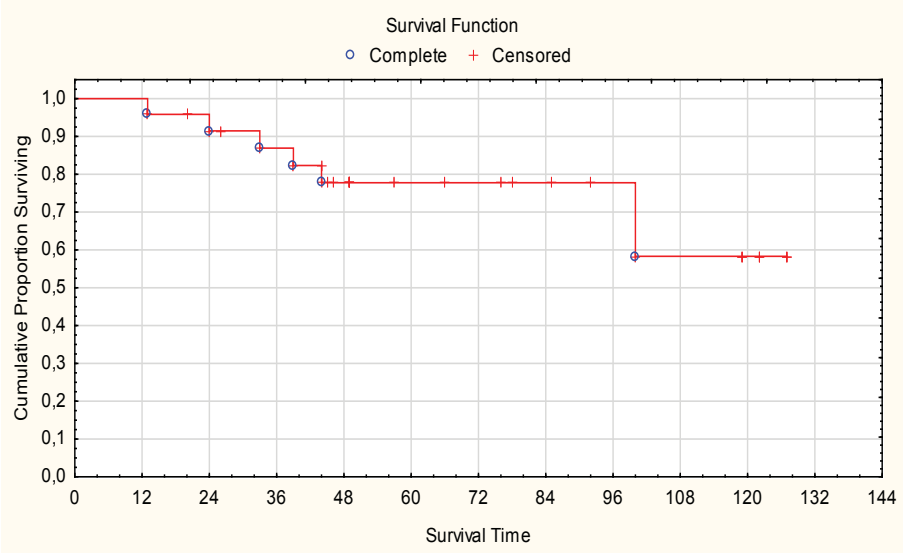

Fig.1. Progression-free survival of patients with CML treated with TKI

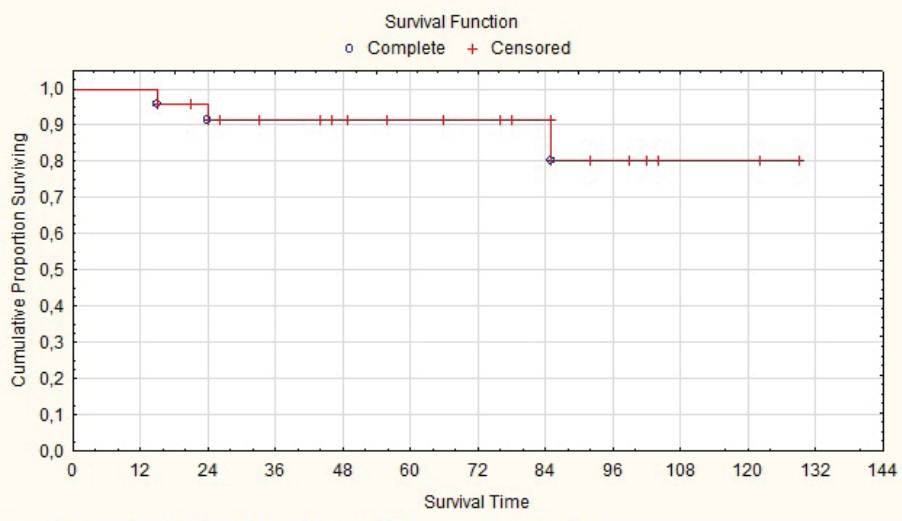

Fig.2. Overall survival of patients with CML treated with TKI

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HEALTHY LIFESTYLE. PREVENTION

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COMPARATIVE EVALUATION OF THE ADAPTATION CHARACTERISTICS

ABSTRACT

The given article presents the investigation of the adaptation characteristics and the comparative analysis of the adaptive opportunities of the first year students as well as the young men who are recruited in the armed forces. The authors present the conclusion concerning the multidirectional dynamics of the adaptation indicators of the first year students and the young men who do military service during the first year- negative dynamics for the University students and positive one for military servants. Successful adaptation to the conditions of military professional activity is due to more comfort environment for the young men organism.

Keywords: adaptation to environmental factors, students, soldiers.

INTRODUCTION

The health of the young men during their professional formation is one of the actual problems of the modern public health. The adaptation to some new environmental factors is currently considered to be a permanent process of the individual's developmental adaptation to the social and activity conditions. This process affects all levels of human functioning. The adaptation of young men to the military service is of the particular interest as it originates from the specificity and high social importance of human activities to protect the state interests and national security. According to A. S. Kislitsina's data psychological hardships during military service can be represented by a hierarchical scale of the 12 stress factors (the main of them are the restriction of freedom, helplessness, hard and dangerous work, uncomfortable living conditions). These factors allow considering the military service conditions as difficult living conditions [9]. At the same time, the students' adaptation to some new factors specific to high schools, is accompanied by a large flow of information, acceleration of the pace of life, bad habits, frequent violation of the work – rest schedule and nutrition regime, regular mental and psycho-emotional stress, especially during training sessions [1,3,8].

The **purpose** of the given study is the investigation of the young men's adaptation capabilities, depending on the conditions and requirements of the human environment.

MATERIALS AND METHODS

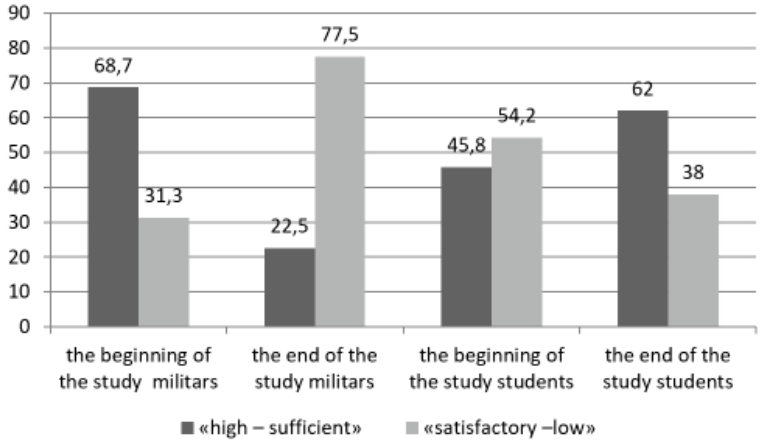

Fig. 1 Personal adaptation potential at young men of the studied groups at initial and final investigation phases

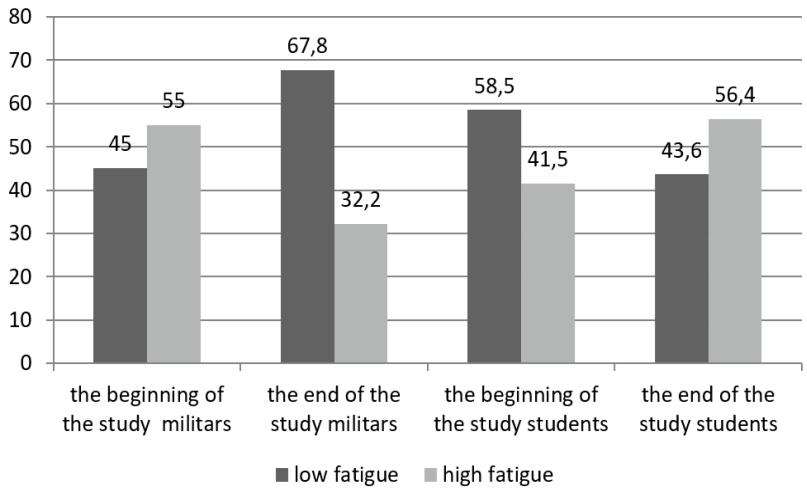

Figure.2. Fatigue of boys in the study groups at initial and final stages of the study

The objects

Table 1

Indicators of urgent alarm and personal uneasiness at young men of the researched groups at initial and final investigation phases, (point/%)

Urgent alarm, and personal uneasiness, regulation (point)	military personnel			students		
	0-30	31-45	more than 46	0-30	31-45	more than 46
Urgent alarm, point/%, beginning of a research	26,6/10,1	39,3/49,4	52,6/40,5	25,5/20	36,1/75,6	55,4/4,4
Urgent alarm, point/%, end of a research	27,3/22,5	34,4/75,0	47/2,5	23,8/24,1	37,4/66,7	51,4/9,3
Personal uneasiness, point/%, beginning of a research	29,3/4,5	38,8/67,4	51,8/28,1	26,4/15,5	36,8/84,5	–
Personal uneasiness, point/%, end of a research	27,4/32,5	35,1/67,5	–	27,8/31,5	39,246,3	52,08/22,2

Table 2

Physical training of boys studied groups at the beginning and the end of the study, M±m

Name	Students		military	
	test	Students	military	конец исследования
	Beginning	12±0,54	6±0,5	10±0,5*
researches	End	4,17±3,2	4,39±4,2	3,49±2,3*
researches	Beginning	32,8±0,29	30,91±0,24	26,9±0,1*
researches	End			
researches				
Pulling up	11±0,6	12±0,54	6±0,5	10±0,5*
Run on 1000 meters	4,05±2,7	4,17±3,2	4,39±4,2	3,49±2,3*
Shuttle run (10x10 m)	32,5±0,29	32,8±0,29	30,91±0,24	26,9±0,1*

* $p<0,001$.

of the study were the young men enrolled in the first course of the Irkutsk Technical University (n =60) and the young men who were called up for National Service (n =40). The study was conducted as at the beginning of the academic year and the recruitment to the RF Armed forces, as at the end of the academic year and at the end of the military service period.

A multi-level personality questionnaire (MLQ "Adaptability-200") was used to explore the adaptive capacity of an individual. The values of the 4-th level (the integral scale of personal adaptation capacity (PAC) and the values of the 3-level (scale of behavioral regulation, communicative potential and moral normativeness) have been determined.

The self-assessment scale by Ch. Spielberger - Hanina (actual alarm and personal anxiety) was used to define subjective estimation of experiencing and the levels of alarm and anxiety. The results of the study were estimated by the values (points), characterizing the low, middle and high degrees of actual and personality anxiety [11].

The identification of persons with the symptoms of chronic fatigue and exhaustion was conducted by the means of the questionnaire "«Accompaniment», allowing to define the violations in a communicative, active and psychosomatic areas. The area of health disorders (stress and overstrain) has been marked out in 4 separate groups: the absolute norm area; the area of the norm options; the area of extreme variants of norm and premorbid states; the area of premorbid and pathological conditions according to the standard methods by the B. V. Ovchinnikov, M. M. Reshetnikov et al. [12]. We have combined the absolute norm area and the area of the norm options into one group – "normal", the others have been united in " premorbid and pathological states" group.

Physical indicators of speed, power and endurance were determined by standard methods on the base of such physical activity results, as shuttle running 10 x 10 meters, pulling up on a crossbeam and running 1000 meters.

The obtained results were processed with the application of the mathematical-statistical methods used in medico biological researches. Data processing was carried out in the computer programs « Microsoft Excel-2007», «Statistica 6.0».

Results and discussion

The data of the conducted researches made among students and the military personnel during the process of training and military career, are submitted in figures 1, 2 and Tables 1, 2.

According to S. L. Solovieva, the anxiety can be considered, on the one hand, as a normative phenomenon, providing adaptation, and, on the other hand, as one of the main factors of mental disadaptation. The probability of passing or permanent adaptation violations increases in the process of anxiety intensity [13]. Actually the trouble in this case is regarded either as the main component of psychopathology, or as a basis for the mental disadaptation [4].It is evident that in the beginning of the research, the indicators of "high – sufficient «and "satisfactory –low" levels of PAC were distributed approximately equally among the University students. In the group of military men, almost 70% of young people had a "satisfactory - low "PAC levels (Fig.1). The analysis of the LAP structure and its components has shown that from 37% to 66,2% of the soldiers are in the area of low and satisfactory physical characteristics , in comparison with a group of students (from 29 to 41.2%). In addition, the military men significantly differed from University students on the levels of the actual and personal anxiety. So, the majority of students were within the zone of moderate current and personal anxiety at the beginning of the academic year, at the same time from 28 to 40% of the military men had high levels of anxiety in the beginning of the military service.

It is known that the mental aspect of fatigue is reflected in the form of

negative or positive feelings (fatigue, apathy, aversion to activity, joy of success achievement, etc.) as well as its physiological aspect is reflected in the change of some features ensuring the activity in performing labor tasks. As experiences so functional activities are interrelated, they always accompany each other [5]. The research of fatigue in the studied groups at the initial stage allowed to reveal a slight predominance among the students who had absolute norm and norm option indicators (58.9 per cent) compared to military men (45%). It should be noted that 55% of military men in the group were in the area of the extreme variants of the norm, premorbid and pathological states of fatigue (Fig.2).

The indexes of young men's physical development in the groups are presented at the beginning and the end of the study (table 2). In our opinion, the chosen physical tests sufficiently prove the strength, speed and endurance of young people. As it turned out, the students dominated in terms of physical strength and endurance (pull-ups and running 1000 m.), but conceded n speed (shuttle running) to the military men.

At the second investigation phase – at the end of the academic year and the termination of military service, it was evaluated that the military men who had high and sufficient PAC levels made up to 77,5% of the examined. Thus, the proportion of the military men with high and the sufficient PAC level has increased by 2,5 times in comparison with a similar indicator when the young men were called up for National Service . The opposite pattern we observed among University students . So, by the end of the first academic year we revealed the lowering of students having high and sufficient PAC levels for 16,2% and consequently the increase of young men having the low and satisfactory level of adaptation (Fig. 1).

The PAC components of students and the military personnel also have undergone changes at by the end of the observation term. We have found the considerable increase in the structure of the military men's PAC including all its components to the area of high and sufficient level, but most of all − the component of behavioral regulation (to 41,2%). The similar changes in the PAC structure, but of the regressive character, were revealed among the University students: partial indicators of behavioral control, and moral normativity of the sufficient and high level area were decreased by 22.2 and 4.2%, respectively.

The studying of the indicators of actual and personal anxiety in the researched groups allowed us to establish the divergence of dynamics of these indicators between students and military men (table.1) by the end of the observation period. So, despite the significant increase in the number of young people having a low level of relevant and personal anxiety (4.1 and 16%, respectively), the number of University students, having high anxiety level made 22% , taking into account that we did not identify any students with a high level of anxiety at the beginning of the academic year, At the same time, we noted the opposite trend of the studied parameters in the group of military men. The majority of the young men were in the area of moderate current and personal anxiety by the end of the military service period anxiety, in contrast to the similar indicators they had when they were called up for National Service. Meanwhile there weren't identified any military men having high levels of personal anxiety, and the number of young men with a high level of current anxiety was minimal (2.5 percent).

We noted the similar dynamics of fatigability indicator at the final stage among the boys of the studied groups. So, by the end of the academic year, the number of students in the area of the extreme variants of the norm, premorbid and pathological states increased by 14.9%, in comparison with the beginning of the academic year. While in the military personnel group , this indicator decreased by 22.8% by the end of the service.

We have made the conclusion concerning the positive dynamics of the physical development in the group of military men as the rates of physical strength, speed and endurance have authentically increased by the end of the observation period.

At the same time, we haven't noted any significant changes in physical fitness of the University students within the academic year.

The optimization of relations in the individual-environment system can hardly be overemphasized, as it is the essence of the adaptation process. C. B. Bondarenko believes that the majority of students don't achieve satisfactory level of adaptation to the effects of negative environmental factors. The working efficiency under such conditions is determined by the level of mental and physiological reserves of organism, but not at the expense of adaptation and it leads to health problems of an individual [6].

The group of objective criteria for success evaluation of students' adaptation to training process in higher education institution was identified by T. P. Brown on the basis of the criteria [2] proposed by V. G. Aseev in 1986. They are success in the academic activity, the stability of the functional state of students' organisms in the process of studying (the lack of sharp changes in psycho physiological functions), the lack of the fatigue evident signs [1, 7].

CONCLUSION

Taking into account the facts considered above and the results of our own research, we believe that more than 60% of first-year students do not reach a satisfactory level of adaptation to the University educational environment and to new conditions of activity by the end of the first year. It is manifested by low values of PAC, due to the regression of its components -behavioral regulation and moral standard, increase in levels of actual and personal anxiety as well as a high degree of exhaustion.

At the same time, the majority of young men (as it is shown in our research), have shown the effectiveness of military-professional adaptation despite the well-known difficulties of military service. It results in the LAP increasing, primarily due to the index of behavioral regulation, anxiety and fatigue reduction, and

finally, to the effective increase of their physical development to the end of military service. In our opinion successful socio-psychological adaptation of young men to military service is associated with rational modes of military training and labor, proper nutrition, regulated daily routine and the psychological atmosphere that accompanies the process of military service.

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ARCTIC MEDICINE

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REGIONAL CHARACTERISTICS OF POPULATION MORTALITY FROM EXTERNAL CAUSES IN THE REPUBLIC SAKHA (YAKUTIA)

Abstract. Mortality from external causes of death (accidents, poisonings, traumas, murders, suicides, etc.) is in second place in the structure of causes of death of population in the Russian Federation and in the Republic Sakha (Yakutia). Positive trends in the reduction of the absolute number of deaths, the proportion of these causes in the overall mortality were observed in the dynamics of mortality from external causes. However, mortality rates are not much changed in comparison with 90-s years of the last century.

The contribution of specific causes of external mortality in the overall mortality rate for this class of causes of death varies considerably. While reducing the share of road traffic deaths there increased contribution to such causes as suicide occurs, which raises serious concerns in terms of preservation of social well-being of the population.

Significant disparities persist across the gender. Index of high mortality of men for external causes of death is much more substantial than in general for all causes of death; and he does not disappear, but worse. The contribution of causes of death in the general mortality rate in men is more than 39%, whereas in women, only 26.9.

Excessive mortality from external causes remains a major feature of mortality of the working population. And at the end of 2015, the mortality rate from external causes exceeded death rate from diseases of the circulatory system. In territorial terms, the mortality from external causes in Northern and Arctic regions of the Republic is especially high.

The high mortality rate from accidental drowning is the specific feature of mortality by external causes in Yakutia; the largest gap with indicators for RF and DFO notes on the cause of death. In 2014, the mortality rate from accidental drowning was 3.24 times higher than in Russia.

A significant influence of external causes of death for the loss of the demographic potential should identify priority measures to reduce mortality from external causes in the hierarchy the goals and objectives of regional demographic policy. In measures aimed at reducing external mortality of paramount importance must be given not so much medical prevention, as in most measures of social prevention, which will be more effective in the decline of mortality from external causes.

Keywords: processes of mortality, external causes of death, high mortality of men, the Republic Sakha (Yakutia).

INTRODUCTION

The processes of population mortality are of key importance in ensuring the reproduction of demographic potential. As in other Northern subjects of the Russian Federation in the Republic Sakha (Yakutia), the situation with mortality of the population has a number of rather negative effects [4]. In the structure of the mortality causes mortality from external causes is on the second place after circulatory system diseases, identifying more than 17% of all population losses. This class covers quite a wide range of causes of death, including accidental poisoning, road traffic accidents, injuries, fires, accidents on manufacture, alcohol poisoning and other external influence.

Analysis of mortality from external causes is of particular interest because they can determine a significant reserve to reduce overall mortality. The specificity of mortality from injury and poisoning is their almost complete dependence on social factors. In addition, another characteristic feature – the high mortality of males and the high mortality rate of the working-age population.

The purpose of the study: analysis of regional features of the mortality from external causes in the Republic Sakha (Yakutia).

MATERIALS AND METHOD

In the analysis we used statistical data for 1990-2015 years in the number of the dead in total and from external causes of death, the coefficients of mortality in working age from different causes of death, the coefficients of mortality from external causes, the coefficients of mortality from individual causes of external death - murders, suicides, accidental drowning, injuries, poisoning, on high mortality index of men i.e. excess of men death rate over women mortality rate. We used the comparative data for the Far Eastern Federal District of the Russian Federation. The contribution of individual causes in the overall mortality rate from external causes was calculated.

THE RESULTS AND DISCUSSION

In 1965 external causes among the other mortality causes were at the first

Table 1

Dynamics of mortality from external causes in the Republic Sakha (Yakutia), per 100 thousand people

Gender	1990	2000	2005	2010	2011	2012	2013	2014	2015	2015/1990
Men	269,2	403,6	384,9	319,2	303,4	286	266,5	259,3	242,9	0,902
Women	58,5	89,5	80,7	78,2	66,9	62,9	60,4	56,7	53,1	0,908

Table 2

Dynamics of the number of deaths from external causes in the years 1990-2015, people

Indicator	1990	2000	2005	2010	2011	2012	2013	2014	2015	2015/1990
The number of deaths, in total	7470	9325	9696	9402	8992	8918	8351	8239	8165	1,09
Deaths from external causes	1836	2341	2186	1872	1740	1637	1533	1482	1392	0,76
Percentage in total number of deaths, %	24,58	25,10	22,55	19,91	19,35	18,36	18,36	17,99	17,05	0,69

place; this proportion remained until 1980, when these causes are moved to the 2nd place.

The positive dynamics continued in 1990-2015. The total number of deaths from external causes decreased almost at 24.2%, however mortality rates were not much changed compared to 1990 (Table 1).

The mortality rate from external causes of death for both men and women in general for 1990-2015 decreased from 164.4 to 145.3. Together with a decrease in the absolute number of deaths from external causes in 1990-2015 there is reduction in the share of them in the total number of the dead. After a peak in 2000 this indicator reduced by 2015 to 17.05% (Table 2). Though there are positive trends in mortality from external causes, it should be noted that, unfortunately, one can only speak about the return to the level of 1990-ies of the last century.

The same situation is characteristic and for Russia as a whole. At the same time these positive trends are not comparable with the situation in developed countries. "In the United States, a country with a population 2.2 times more than in Russia, and in 2012 external causes took away less lives (190 thousand vs 194 thousand in Russia)" [2].

Mortality from suicide and murder deserves more attention in the structure of external causes of death. These causes of death are predominant in the structure of the circumstances of violent deaths. Together in 2015 they gave 47% of the total number of deaths from external causes. Suicide

Table 3

The contribution of different causes to the overall mortality rate from external causes of death, %

	1990	1995	2000	2005	2010	2015
Murder	16,1	10,1	21,6	22,9	17,6	14,2
Suicide	14,7	13,6	19,8	21,0	20,9	23,9
Death by road accidents	20,7	8,9	7,5	9,6	7,4	8,9
Accidental alcohol poisoning	4,4	6,4	4,6	5,3	4,1	3,3

Table 4

Contribution of mortality from external causes in the overall rate of mortality for men and women, %

	2002	2005	2010	2011	2012	2013	2014	2014/2002
Men								
Russian Federation	38,7	34,1	30,2	29,4	29,9	29,9	29,9	0,771
Far Eastern Federal district	40,5	35,6	32,3	33,3	33,1	33,4	32,9	0,813
The Republic Sakha (Yakutia)	44,7	40,5	36,5	37,6	36,6	38,4	39,2	0,877
Women								
Russian Federation	29,5	26,3	22,9	22,0	22,5	21,8	21,5	0,729
Far Eastern Federal district	31,8	27,9	25,1	24,4	24,9	24,0	23,9	0,751
The Republic Sakha (Yakutia)	32,2	27,0	28,4	27,1	26,9	29,3	26,9	0,837

Table 5

Index of supermortality of men (mortality rate of males over mortality rate of women, the number of times)

	2002	2005	2010	2011	2012	2013	2014
On the overall mortality rate	3,49	3,75	3,66	3,47	3,77	3,76	3,62
On mortality rate from external causes	4,85	5,63	4,71	4,82	5,13	4,93	5,27
Exceeding the overall supermortality of men over supermortality men from external causes of death	1,39	1,50	1,29	1,39	1,36	1,31	1,45

began to make a major contribution to the mortality rate from external causes of death (nearly 24% of the total mortality from external causes) (Table 3). Over the years 1990-2015 growth of mortality rate from suicide in 1.4 times was observed. The number of deaths from murder tends to decline by 1.2 times. The decrease in 1.5 times the number of deaths from accidental alcohol poisoning it should also be noted. The dynamics of deaths due to road accidents is most favorable. Between 1990 and 2015, the number fell by more than 2.5 times.

The distribution of mortality from external causes by sex and age in the RS (Ya) shows as the total for all countries and for Russian traits and regional differences.

A comparative analysis of the gender structure of causes of mortality in the Republic Sakha (Yakutia) showed a marked change in the contribution of major causes of death by sex. So, external causes predominated in 1990 in the structure of mortality of the male population of the Republic, accounting for 33.5%, but by 2015, this class of causes of death retreated to the second position after diseases of the circulatory system, which accounted for 45.4% of all deaths.

The contribution of external causes

Table 6

Mortality rates of the working age population for different causes of death in the Republic Sakha (Yakutia), per 100 000 people of working age

The cause of death	2000	2005	2010	2015
Certain infectious and parasitic diseases	18,6	17,5	12,5	14,1
Cancer	78,4	79,0	64,2	63,3
Diseases of the circulatory system	193,2	264,2	260,3	188,6
Diseases of the respiratory system				
Accidents, poisoning and injuries (external causes)	324,2	291,7	252,9	192,2
Among them:				
Suicide	68,9	67,0	56,1	49,6
Violence (murder)	74,8	70,5	47,7	30,5
In total	732,9	773,6	725,5	542,9

Table 7

The excess of mortality from external causes in the RS (Yakutia) in comparison with the RF and the FEFD (number of times)

	2002	2005	2010	2011	2012	2013	2014
Men							
RS(Ya) / FEFD	1,03	0,91	1,05	1,01	1,03	1,03	1,04
RS(Ya) / RF	1,16	1,10	1,37	1,42	1,38	1,36	1,32
Women							
RS(Ya) / FEFD	0,89	0,70	0,96	0,96	0,88	0,94	0,87
RS(Ya) / RF	1,16	0,98	1,44	1,44	1,31	1,38	1,27

Table 8

The excess of mortality from various causes of external mortality for 100 thousand people in the RS(Ya) on mortality rates in the RF and the FEFD

	1990	1995	2000	2005	2010	2011	2012	2013	2014
Mortality from traffic injury									
RS(Ya) / RF	1,17	0,88	0,67	0,78	0,72	0,91	0,79	0,99	0,76
RS(Ya) / FEFD		0,80	0,67	0,73	0,64	0,80	0,70	0,92	0,77
Mortality from accidental alcohol poisoning									
RS(Ya) / RF	0,67	0,57	0,44	0,42	0,60	0,58	0,49	0,54	0,61
RS(Ya) / FEFD		0,63	0,60	0,41	0,61	0,63	0,54	0,59	0,73
Mortality from accidental drowning									
RS(Ya) / RF		2,09	2,25	2,02	2,46	3,02	3,02	2,90	3,24
RS(Ya) / FEFD		1,73	1,63	1,46	1,74	1,65	1,76	1,72	1,94
Suicide mortality									
RS(Ya) / RF		0,85	1,25	1,50	1,74	1,82	1,93	1,78	1,86
RS(Ya) / FEFD		0,70	0,97	1,11	1,20	1,25	1,30	1,23	1,24
Mortality from murders									
RS(Ya) / RF		0,86	1,89	2,12	2,58	2,38	2,59	2,59	2,33
RS(Ya) / FEFD		0,59	1,17	1,18	1,34	1,18	1,29	1,25	1,24

of death for men of Yakutia was much more in comparison with Russia and Far Eastern Federal district in 2002 and in 2014 (Table 4). The dynamics of this indicator were unidirectional both in Russia, in the Far East and Yakutia. However, the reduction of the contribution of external causes in the total mortality rate in the Republic was, unfortunately, minimal.

For women the general vector of changes of the contribution of external causes in total mortality was the same, but at lower levels compared to men. However, as both in men and women of the Republic Sakha (Yakutia) reduction of the contribution of external mortality to the overall mortality rate was markedly lower in comparison with the RF and Far Eastern Federal district women.

Supermortality of men, which is typical in general for the processes of mortality, in external causes of death is even more pronounced (table 5).

In 2015 the mortality from the external causes in men was in 4.5 times higher than for women. Moreover, excess is not decreasing, but, on the contrary, becomes more and more aggravated.

Not only gender but also age differences are characteristic of mortality from external causes. External causes rank first place among causes of death of able-bodied population for a long period, surpassing diseases of the circulatory system and neoplasms (Table 6). Between 1990 and 2015, a slight decrease of the coefficient of death from these causes occurred – 324.2 up to 192.2, or almost in 1.7 times.

Among the dead men the share of working-age is 60%. The excess mortality in men compared with similar indicators in women, especially in the group of working age continues to persist [5]. About a quarter of all deaths of women are in working age. In the context of individual causes of death the highest rates in the General population occur among deaths due to external causes.

High mortality from external causes has also territorial features. The Northern regions have a higher mortality from external causes, even in the Far Eastern Federal district Northern group of subjects also has a more high characteristics [1].

In the Republic Sakha (Yakutia) population mortality from external causes in Northern and Arctic areas is almost 2 times higher than the death rate average in the Republic [3].

The analysis of external causes of death of population in comparison with the Far Eastern Federal district and the Russian Federation finds higher mortality of men in the Republic of Sakha (Yakutia) in comparison

with Far East and especially Russian Federation (Table 7).

In women we observe another situation; the excess is only in comparison with Russia as a whole, moreover, what is more against the background of growth of the excess. In comparison with the Far Eastern federal district the mortality rates of women from external causes in the Republic are lower.

Significant regional specificity is noted on some causes of external mortality. The smallest gap with the mortality rates in Russia and the Far East can be traced in mortality from accidental alcohol poisoning and transport injuries (Table 8).

Mortality rates from alcohol poisoning in 2007, for example, were in 4 times lower compared to Russia and in 3.5 times in comparison with Far East. Mortality rates from transport injuries in the same 2007 year were in 1.9 times lower than in Russia and the Far Eastern federal district.

A different situation can be traced in other causes of external mortality. The high mortality rate from accidental drowning is the specific feature in Yakutia; for this reason, the greatest gap exists with indicators for the RF and FEFD. The gap in the mortality rates from murders and suicides is slightly less. However, during 1990-2014 vector dynamics changed its direction in contrast to mortality from accidental drowning, where excess rates were observed throughout the period under review. In the case of mortality from suicide and murder, the situation is reversed: if in early 90-ies of the last century, the situation of mortality from these causes in the Yakutiya was more favorable compared with RF and DFO, since 2000 the ratio has changed. The excess of mortality from murder and suicides became steady and fairly high, especially in deaths from murder in comparison with the Russian Federation.

CONCLUSIONS

Thus, in the Republic of Sakha (Yakutia) external causes of mortality have the same importance as disease of the circulatory system in terms of reduction of losses of demographic potential. Analysis of regional features of population mortality from external causes of death shows that in the Republic formed a significant loss of the demographic potential, which in turn should define priority measures to reduce mortality from external causes in the hierarchy the goals and objectives of regional demographic policy. Analysis of mortality from external causes proves once again that not all aspects of health and mortality depend on the health and preventive work within its framework. A deeper interagency approach is required for the purpose of strengthening of measures of social prevention, which will be more effective in the decline of mortality from external causes.

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THE INFORMATIVENESS ACTIVITY OF TRANSAMINASES IN DETECTING SIGNS DISTURBANCES OF LIPID METABOLISM

ABSTRACT

The authors report their study on estimation of informativeness of biochemical tests in men living at high latitudes, for revealing signs of disorders of lipid metabolism. We examined the indigenous and non-indigenous residents of Yakutia in age from 22 to 67 years. It was revealed that significant differences of enzyme activity depended on the degree of adaptation to the conditions of high latitudes. Signs of lipid metabolism have been linked to an indicator of the metabolic state of the body (coefficient de Rytis). Thus, it was found that the ratio of activity of transaminases (coefficient de Rytis) can be used for the formation of a group of persons with signs of lipid exchange and timely preventive measures.

Keywords: enzyme activity, coefficient de Rytis, lipid profile, adaptation, high latitudes.

INTRODUCTION

The main reason for the development of various pathologies is the failure of the adaptive mechanisms under organism of inhabitant of Yakutia both in alien and indigenous [9]. Despite the fact that at the indigenous people of Yakutia in the process of centuries of selection has formed a particular, optimal for the harsh conditions of the far North, the genotype of the circulatory system, not predisposing to the development of atherosclerosis and its associated diseases [2,3,8] currently, the pathology of the cardiovascular system occupies one of leading places in structure of mortality of the working age population as among the newcomers and the indigenous people of Yakutia [1,4,5,6,].

One of the most important tasks of clinical and biochemical research is to identify the most informative tests in various pathologies, but, unfortunately, there are currently no organ-specific markers, as the biochemical spectrum of blood serum reflects not only pathological processes, but in General metabolic processes in the body.

On this basis, to assess the functional state of the organism and for the formation of groups of risk associated with the development of cardiovascular pathology among population of Yakutia it is necessary to identify the most informative changes in the spectrum of biochemical parameters of blood serum.

The purpose of the study. Assess the informative value of biochemical tests at men living at high latitudes, for identify signs of disorders of lipid metabolism.

MATERIAL AND METHODS

The sample of 300 inhabitants of Yakutia aged 22 to 67 years (average age was 45,13±0,58). The number of indigenous men, adapted to the conditions of the North, was 126 people, newcomers men, unadapted to the conditions of the North, – 174. Exclusion criteria from the study was exacerbation of chronic diseases, the presence of cancer, infectious and viral diseases, persons with coronary artery disease, heart attack and stroke in anamnesis.

To assess the objective status a survey was conducted on the questionnaire developed in FBGO “Yakut scientific center of complex medical problems”; obtained the informed consent of the respondents to research, at surrender blood. Blood for biochemical studies was taken from the cubital vein in the morning on an empty stomach, 12 hours later after a meal.

The determination of the enzymes activity, total cholesterol (TC), HDL cholesterol (cholesterol high density lipoproteins), triglycerides (TG) was performed by enzymatic method on the automatic biochemical analyzer “Labio” using reagents “Analyticon” (Germany). LDL cholesterol and VLDL cholesterol was calculated by the formula of Friedewald et al. [13].

Statistical data processing was performed using the package of applied statistical programs SPSS Statistics 17.0. Applied standard methods of variation statistics: calculate averages, standard errors, 95% confidence interval. Data in tables are presented as M±m, where M – average, m – error of the average. The significance of differences between means was assessed using the student’s t test and Kolmogorov-Smirnov. The probability of a justice of the null hypothesis was accepted at $p<0.05$. Correlation analysis was performed according to the method of Pearson and Spearman.

THE RESULTS AND DISCUSSION

Adaptation to extreme conditions of high latitudes is associated with stress and complex restructuring of the homeostatic systems of the organism [10,11] and causes structural damage and functional disorders associated with the development of chronic diseases [7]. In men blood biochemical parameters did not differ from normal values, but includes to statistically significant of differences among ethnic groups have (table. 1).

In men, the activity of enzymes involved in oxidative phosphorylation, had a dependence on the degree of adaptation to high latitudes conditions and point to different energy requirements for the adequate functioning of the organism (table.1). So in alien inhabitants of Yakutia in comparison with the natives were statistically significantly high activity of creatine kinase, coupled with the relatively high activity of AST, indicates more intensive receipt of metabolites in the tricarboxylic acid cycle (TCA) and on the functioning of the malate-aspartate mechanism.

Among newcomers men than indigenous significantly higher levels

of creatinine (100,14±79,32 1.48±1,18 mmol/l, respectively, p=0.000), combined with the activity of creatine kinase (CK), possibly associated with the adaptation of the organism to far North conditions (tab. 1). CK is stress dependent enzyme, that is an indicator of utilization of the energy potential of the and adaptability of the organism to new conditions [10].

In alien inhabitants significantly high levels of glucose associated with significantly high levels of triglycerides, total cholesterol, cholesterol of lipoproteins of low and very low densities indicates the activation of lipid metabolism while reducing use of carbohydrates, metabolic sources of energy (table. 1).

In for fittest the residents of Yakutia, a significantly high activity of gamma-glutamyl transferase (γ-GT), lactate dehydrogenase (LDH) and alkaline phosphatase (ALP) was associated with significantly low levels of glucose compared to non-adapted residents. So, γ-GT is involved in the transport of amino acids, and increased blood alkaline phosphatase, ensures not only the dephosphorylation and release of glucose from cells, but also produces considerable amounts of inorganic phosphate that affect bioenergetics in the cell and in the organism as a whole. High activity of LDH ensures an easier dissociation of oxygen and hemoglobin, leading to increased exchanges in all organs and systems. As a result of more rapid and intense the passage of the substrates of metabolic pathways is provided by the high activity of all enzymes. Significantly high activity of lactate dehydrogenase indigenous men compared to newcomers reflects not only the rate of anaerobic glycolysis, but also points to the adaptability of the organism to hypoxia of the indigenous population. The increase in activity of these enzymes in the indigenous population indicates a mobilize switching protein and carbohydrate metabolism.

Under extreme conditions of high latitudes quantitative and qualitative conversion of the enzyme systems due to the mobilization of energy resources and increased energy metabolism as a whole [12] and physiological (not pathological) condition is provided and maintained by many thousands of reactions occurring within cells and in the extracellular environment, i.e. in the metabolic equilibrium of the body.

Normal course of metabolic reactions at the molecular level due to harmonious combination of processes of catabolism and anabolism, and the activity is transaminases indicator of the metabolic is state of the organism is the. The ratio of AST and ALT (de Ritis coefficient) reflects not only the functional state of the liver or the heart, but also an figure of adaptive reactions of the organism [10]. Based on the fact that metabolic balance is achieved in the range of 1.3–1.5, we have formed 3 groups: the first group of de Ritis coefficient corresponded to the norm, in the second group exceeded the norm, and the third was below the norm (table. 2).

As can be seen from table 2 in the groups inhabitants of Yakutia of enzymes activity not had significant differences depending on the de Ritis coefficient. The enzyme activity had significant differences depending on ethnicity. In group with normal value of de Ritis coefficient the ethnic in group significantly differed in the activity of alkaline phosphatase , in the groups with high and low de Ritis coefficient important differences along with the activity alkaline phosphatase was high and LDH, γ-GT, KK, which indicates the intensity of energy metabolism. γ-GT is not only involved in the transport of amino acids, but also is an indicator of and a key enzyme of the antioxidant system – glutathione.

In the table 2 evidence shows that the coefficients atherogenic and de Ritis interrelated. The lower atherogenic coefficient was in group 2, where the de Ritis coefficient exceeded the normal value, and indicating to tension energy processes and the predominance of catabolic reactions in the body. Signs of disorders of lipid metabolism were observed in group 3, where the de Ritis coefficient was below normal values and testified about the depletion of the functional reserves of the organism.

As can be seen from table 2 in alien inhabitants of Yakutia in comparison with the indigenous people in all three groups, levels total cholesterol, triglycerides were high. Significantly high levels of triglycerides, cholesterol and LDL cholesterol in alien inhabitants of Yakutia in comparison with indigenous suggests they are in chronic stress and the body's energy needs are met by lipids.

The relatively low level of HDL cholesterol in the indigenous population than newcomers combined with significantly high levels of cholesterol in VLDL, possibly associated with changes in traditional diets and eating foods rich in carbohydrates.

The activity of enzymes that characterize the metabolic state of the organism, is correlated from atherogenic coefficient (table 3). In table 3, the statistically significant correlation of transaminases with atherogenic coefficient in men of Yakutia suggests that the values of these biochemical indices of the blood serum can reveal persons with signs of disorders of lipid metabolism. Preventive measures to restore metabolic balance is required among individuals with elevated energy costs, as long as «hard» adaptation to high latitudes conditions leads to exhaustion of the functional reserves of the organism, and any violation of

Table 1

Biochemical parameters of blood serum in men of Yakutia

Biochemical parameters	Indigenous (n=126)	Newcomer (n=174)	Reliability (p)
Lactate dehydrogenase, U / L	382, 37±8,38	352,03±5,87	0,000
Gamma-GT, U / L	48,71±3,67	39,30±3,42	0,001
Alkaline phosphatase, U / L	247,53±7,24	169,88±4,31	0,000
Creatine kinase, U/l	128,14±9,86	157,69±8,08	0,001
ALT, U / L	24,17±1,39	21,23±0,96	0,009
AST, U / L	30,12±1,85	31,26±1,29	-
Coefficient de Rytis	1,40±0,05	1,67±0,06	0,035
Triglycerides, mmol / l	0,94±0,04	1,12±0,03	0,000
Cholesterol, mmol / l	5,57±0,10	5,99±0,08	0,001
HDL-C, mmol / l	1,53±0,04	1,48±0,03	-
LDL-C, mmol / l	3,45±0,11	4,01±0,08	0,000
VLDL-C, mmol / l	0,57±0,07	0,51±0,01	0,000
Coeff. atherogenicity	2,96±0,13	3,29±0,09	0,004
Glucose, mmol / l	4,45±0,06	5,10±0,07	0,000

Table 2

Biochemical parameters of blood serum in men depending on the de Ritis coefficient

Biochemical parameters	I group		II group		III group	
	Indigenous (n=35)	Newcomer (n=42)	Indigenous (n=44)	Newcomer (n=76)	Indigenous (n=47)	Newcomer (n=64)
Lactate dehydrogenase, U / L	366,53±15,56	361,54±11,99	399,57±16,92	367,38±9,54*	379,92±11,28	348,76±9,11*
Gamma-GT, U / L	52,80±8,92	51,61±12,36	37,09±5,09	30,69±2,94	56,53±5,25	40,30±3,03*
Alkaline phosphatase, U / L	256,03±13,20	171,11±7,75*	225,88±12,86	188,37±7,43*	259,67±11,34	174,40±6,62*
Creatine kinase, U/l	136,86±22,34	156,34±13,16	137,69±22,37	167,67±16,26*	115,05±7,36	148,53±10,84*
ALT, U / L	24,86±2,88	20,36±1,39	16,23±1,97	14,97±1,02	31,08±1,96	29,03±1,96
AST, U / L	33,91±4,03	28,0±1,90	31,59±3,92	32,90±2,43	25,91±1,42	27,92±1,64
Coefficient de Rytis	1,37±0,01	1,38±0,01	2,0±0,06	2,26±0,07*	0,86±0,03	0,95±0,03*
Triglycerides, mmol / l	1,03±0,09	1,06±0,07	0,83±0,05	0,94±0,04*	0,99±0,07	1,20±0,06*
Cholesterol, mmol / l	5,38±0,21	5,81±0,18	5,52±0,16	5,78±0,12*	5,74±0,17	5,98±0,14
HDL-C, mmol / l	1,49±0,08	1,51±0,05	1,60±0,07	1,66±0,04	1,49±0,08	1,39±0,04
LDL-C, mmol / l	3,17±0,22	3,71±0,18	3,42±0,18	3,71±0,11*	3,68±0,18	3,96±0,14
VLDL-C, mmol / l	0,71±0,18	0,59±0,11*	0,49±0,08	0,42±0,02*	0,56±0,09	0,54±0,03*
Ka	2,93±0,28	2,96±0,13	2,67±0,17	2,61±0,09*	3,25±0,23	3,47±0,16

*- the reliability between indigenous and immigrant inhabitants.

metabolic balance are accompanied by the development of pathology.

CONCLUSION

1. The differences of biochemical parameters in blood serum at ethnic groups depended on the degree of adaptation to high latitudes conditions.

2. The transaminases ratio (de Ritis coefficient) can be used to assess the functional state of the organism and the formation of a group of persons with signs of disorders of lipid metabolism.

Table 3

Correlation between biochemical parameters and atherogenic coefficient

Biochemical parameters	Indigenous		Newcomer	
	Coeff. correlation (r)	Reliability	коэфф. корреляции (r)	достоверность (p)
(p)	Coeff. correlation (r)	Reliability (p)	0,255	0,001
ALT	0,358	0,000	0,255	0,001
AST	0,246	0,005	0,238	0,002

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FEATURES OF BIOPHYSICAL PROPERTIES AND COMPOSITION OF ORAL FLUID IN CHILDREN WITH CONNECTIVE TISSUE DYSPLASIA LIVING IN THE CONDITIONS OF HIGH LATITUDES

ABSTRACT

The complex clinical laboratory research of the children with connective tissue dysplasia (CTD) living in the North conditions has been done. The obtained data confirmed the existence of particular changes in structure and properties of oral fluid which promoted disturbance of structural homogeneity of solid tissues of teeth and decreased their caries resistance. The examined age groups of children showed biophysical properties of oral fluid characterized by the secretion rate reduction, the increase of saliva viscosity, the dominance of II and III types of microcrystallization, the decrease of remineralizing potential of oral fluid. The high-quality changes of common protein decrease concentration in children with a severe DCT form have been noted in children's saliva. Besides, the activity decrease of alkaline phosphatase irrespective of case severity has been revealed. The carried cationic and anionic spectral microanalysis of oral fluid has revealed the decrease in concentration of cations of magnesium and calcium which are important in teeth enamel saturation by mineral components of hydroxyapatite. Magnesium is a coenzyme of protein structures and generally concentrates in the bone tissue, dentine and enamel of teeth. Besides, it participates in formation of normal structure of connective tissue and its deficiency in prenatal development influences on the development of connective tissue dysplasia syndrome. The revealed features of structure and properties of oral fluid can be consider specific regional biological risk factors of the development of pathological processes of organs and tissues of oral cavity in children with DCT living in the North conditions that on the other hand has been confirmed by the obtained data of the high level of teeth caries in the examined age groups of school children and the high intensity level in key age group of 12-year-old children by WHO. In this regard, the complex treatment-and-prophylactic events and rehabilitation of children have to be organized taking into account the revealed biophysical features of properties and composition of oral fluid among school children with DCT living in the Republic of Sakha (Yakutia).

Keywords: dysplasia of connective tissue, organs and tissues of oral cavity, oral fluid, caries of teeth, prophylaxis of dental diseases.

INTRODUCTION

There is still high level of dental diseases among various age groups of the population [1, 2]. Aggressive factors of external and internal environment affect the development of dental diseases [3- 5]. Among the common risk factors, the congenital dysgenesis, which according to different authors has a high level of prevalence which indexes reach up to 80%, is an important value in pathogenesis of pathological processes of organs and tissues of oral cavity [6- 8]. Organs and tissues of the oral cavity have a connective tissue origin at the morphogenetic level [9, 10]. At the same time frequent phenotypical symptoms of the dysplasia of connective tissue (DCT) in the oral cavity are dentoalveolar anomalies, Gothic palate, caries of teeth, diseases of parodont and temporal - mandibular joint (TMJ), etc. [11, 12].

It should be noted that the organization and optimization of treatment-and-prophylactic actions among children with DCT is based on knowledge of its pathogenetic mechanisms and manifestations in organs and tissues of the oral cavity and also maxillofacial area. Taking it into account, we've made complex studying of properties and composition of oral fluid among children of school age with the proven diagnoses of DCT, especially there were not similar researches in the conditions of the Republic of Sakha (Yakutia).Research aim was studying of features of structure and properties of oral fluid among children with connective tissue dysplasia, living in the North conditions.

MATERIALS AND METHODS

The complex clinical laboratory research of children of school age from 10 to 14 years in educational institutions № 31 of "City Yakutsk", and also State Budgetary Institution of the Republic of Sakha (Yakutia) "Neurologic children's rehabilitation center" was made (Yakutsk). In total 494 children were examined. The affect of solid tissues of teeth caries was estimated by the indexes of relevance and intensity. The assessment card of the dental status was used for the research results (WHO, 1997). Intensity was determined by indexes of CFE and DC, teeth that were filled, extracted and affected with caries, and also their surfaces. The structure and properties of oral fluid were determined by indexes of salivary discharge (n=182); viscosities of oral fluid with application of viscosimeter VK-4 by N. V. Zimkin's method with coauthors (1955), (n=182); microcrystallization types by P. A. Leus's method (1977), (n=182); the acid-base equilibrium was studied on the device "713 pH Meter» of Metrohm company (Germany), (n=182); the cationic and anionic electrophoresis of the mixed saliva was carried out on the device of system of capillary electrophoresis «Kapel-104T» (Russia), (n=182); protein (n=494), alkaline phosphatase and relative density (n=182) on the device «Uriscan Optima» of the YD Diagnostics company (Korea). Statistical processing of clinical material was carried out with application of standard methods of variation statistics with calculation of standard mean square error by packages of the application programs «Microsoft Excel» 2007 (Microsoft Corporation). The received results were grouped in set of identical signs. A critical significance level when checking statistical hypotheses was $p \leq 0,05$.

RESULTS AND DISCUSSION

The analysis of the received results of study of biophysical properties of oral fluid in the examined age groups of children with DCT characterized the existence of their particular features (Tab. 1). So, the index of viscosity in age groups demonstrated its increase where data varied ranging from 3.03±0.05 to 3.31±0.07 units (optimum viscosity index – 4.16 units). It should be noted that the viscosity increase of oral fluid in turn reduces saliva rate (the best value of secretion rate – 0.40 ml/min.), and it was confirmed by the obtained data. Despite it, the acid-base balance in the oral cavity was in its optimum indexes (the best value of pH 6.5-7.5). It should be noted that the above changes of properties of oral fluid in children of school age to some extent make negative impact on microcrystallization types. III DCT type dominates in structure of microcrystallization types in children which made in average 62.47±0.53% that in turn, defined the unfavorable prognosis for the development of pathological processes of hard tissues of teeth of demineralizing character in the examined age groups of children. The revealed features of microcrystallization types affected the decrease of the remineralizing potential of oral fluid.

It is known that children with DCT determine the quantitative and qualitative changes of composition of oral fluid (Tab. 2). So, the particular tendency of changes of concentration of protein in saliva depending on DCT severity has been revealed. At the same time children with mild DCT form of all age groups had the concentration within reference values (3.37±0.38 to 5.39±0.17 g/l). These data were interpreted as the increase of protein of moderate severity in all age groups of the examined children (6.80±0.13 to 9.58±0.26 g/l). The most maximal changes of protein content in oral fluid were noted in children with severe DCT degree which were characterized as its decrease where indexes varied up to 1.43±0.08 g/l within digital values 1.25±0.04 (optimum content of the common protein in the mixed saliva 1.56-6.30 g/l). It should be noted that the alkaline phosphatase has important value in metabolic process of organs and tissues of the oral cavity. The indicators of alkaline phosphatase in oral fluid in the examined age groups of children with CTD characterized the decrease of its activity. So, minimum activity was defined by age group of 12-year-old children (31.9±0.69 units/l), and the maximal activity among 10-

Table 1

Properties of oral fluid among the examined age groups of children with CTD

Age, (years)	pH	Viscosity, (units)	Salivation speed, (ml/min)	Types of microcrystallisation, (%)		
				I	II	III
10 (n=37)	7,12±0,06	3,03±0,05	0,25±0,01	6,09±3,93	27,33±3,04	66,58±1,39
11 (n=34)	7,05±0,04	3,11±0,06	0,31±0,02	14,71±3,49	29,42±2,88	55,87±1,80
12 (n=37)	6,81±0,07	3,17±0,02	0,33±0,04	15,21±3,55	33,17±2,79	51,62±2,02
13 (n=39)	6,72±0,06	3,23±0,08	0,35±0,06	12,17±3,67	18,12±3,42	69,71±1,26
14 (n=35)	7,05±0,05	3,31±0,07	0,37±0,05	5,71±3,78	25,72±2,98	68,57±1,26
Average value	6,95±0,03	3,17±0,02	0,32±0,03	10,78±1,27	26,75±1,04	62,47±0,53

Table 2

Composition of oral fluid among children with connective tissue dysplasia living in the conditions of high latitudes

Age	Protein, (g/L)			Number of examinees	Alkaline phosphatase, (units/l)	Relative density (specific gravity), g/ml
	DCT I stage	DCT II stage	DCT III stage			
10 (n=103)	4,53±0,01	9,58±0,03	1,25±0,03	n=37	51,5±0,07	1,005±0,08
11(n=98)	4,33±0,02	6,80±0,02	1,32±0,04	n=34	40,2±0,05	1,007±0,08
12 (n=96)	4,81±0,01	6,94±0,05	1,41±0,08	n=37	31,9±0,06	1,006±0,01
13(n=102)	5,39±0,01	6,89±0,06	1,37±0,07	n=39	43,8±0,07	1,007±0,06
14 (n=95)	3,37±0,04	7,42±0,04	1,43±0,08	n=35	46,2±0,08	1,007±0,06
Среднее значение	4,02±0,01	7,52±0,01	1,35±0,01	Среднее значение	30,1±0,16	1,006±0,01

Table 3

Cationic and anionic spectral microanalysis of oral fluid among the examined age groups of children with connective tissue dysplasia

Cations	Concentration, mmol/l				
	10 лет n=37	11 лет n=34	12 лет n=37	13 лет n=39	14 лет n=35
Ammonium	2,32±0,04	2,82±0,02	2,93±0,01	3,24±0,04	3,27±0,03
Potassium	5,79±0,04	6,18±0,02	6,23±0,02	5,89±0,03	6,27±0,02
Sodium	6,46±0,05	6,32±0,01	6,51±0,03	6,34±0,01	6,49±0,04
Lithium	0,021±0,02	0,023±0,01	0,024±0,01	0,023±0,01	0,025±0,03
Magnesium	0,48±0,08	0,51±0,04	0,55±0,01	0,54±0,04	0,52±0,03
Strontium	0,071±0,02	0,064±0,04	0,072±0,01	0,065±0,04	0,072±0,02
Barium	0,26±0,03	0,29±0,02	0,27±0,05	0,31±0,04	0,28±0.03
Calcium	0,36±0,02	0,37±0,07	0,36±0,09	0,37±0,08	0,35±0,7
Anionics	Concentration, mmol/l				
Chloride	2,35±0,02	2,38±0,01	2,36±0,03	2,33±0,03	2,39±0,07
Nitrite	0,005±0,002	0,007±0,008	0,006±0,001	0,006±0,001	0,008±0,004
Fluoride	0,03±0,01	0,04±0,08	0,03±0,01	0,05±0,004	0,03±0,01
Phosphate	7,45±0,07	7,53±0,03	7,37±0,01	7,40±0,09	7,39±0,03
Sulfate	0,13±0,01	0,14±0,03	0,13±0,01	0,15±0,04	0,13±0,01
Nitrate	0,025±0,008	0,025±0,008	0,026±0,004	0,026±0,004	0,024±0,001

year old children (51.5±0.71 units/l). At the same time the average index in the examined age groups of children was 30.1±0.42 units/l (optimum indicator of activity of alkaline phosphatase 54-114 units/l at pH 7.0 and above). The analysis of the obtained data by indexes of the relative density of oral fluid did not reveal features where data fluctuated within digital values from 1.005±0.08 g/ml to 1.007±0.06 g/ml, and the average value of groups was at the level of 1.006±0.01 g/ml (optimum index of the relative density 1.001-1.017 g/ml).

The saturation of oral fluid with various mineral components is important in the development of pathological processes of solid tissues of teeth of demineralizing character (Tab. 3). Taking it into account we carried out the cationic and anionic spectral analysis of oral fluid where the data characterizing the particular disbalance of micro and macroelements were obtained. So, the most maximal indexes of concentration were ammonium, potassium, sodium and they had on average 2,91±0,05, 6,07±0,02 and 6,42±0,01 mmol/l among cations. Further on concentration there were lithium (0,023±0,04), strontium (0,068±0,06) and barium (0,28±0,04 mmol/l).

It is known that children with undifferentiated form of connective tissue dysplasia in the oral fluid were characterized by decreased content of magnesium and calcium and to some extent it was a marker of the congenital dysgenesis. In our study children with CTD living in the conditions of high latitudes showed the decrease of cations concentration of magnesium, calcium in the oral fluid and they were on average in age groups 0,52±0,05 and 0,36±0,02 mmol/l (optimum index of magnesium 0,58 mmol/l; calcium – 1,45 mmol/l). The revealed features of decrease in concentration of these cations among children with DCT made negative impact on configurational regularity of hard tissues of teeth and reduced caries resistance.

The anionic composition of oral fluid did not reveal any special changes. So, the maximal concentration were revealed on average among chlorides (2.36±0.05) and phosphates (7.42±0.01 mmol/l).

It should be noted that the decrease of calcium concentration in the oral fluid contributed to the decrease of the activity of alkaline phosphatase which participated in maintaining calcium - phosphorus coefficient within its normal values. Besides, the revealed features of biophysical properties and composition of oral fluid are specific regional biological risk factors of the development of teeth caries that to some extent is confirmed by the high level of pathological processes of hard tissues of teeth of demineralizing character among the examined children (91.13+0.10%) and high level of caries intensity among 12-year-old children (5.78+0.21).

CONCLUSION

The received results of the complex clinical laboratory research of structure and properties of oral fluid in children with CTD characterize the reduction in the secretion rate, the increase of viscosity, the decrease in the remineralizing potential and activity of alkaline phosphatase, weakening of the common protein among children with severe degree, and also the poor content of cations (calcium, magnesium). These features of structure and properties of saliva in children with CTD are biological risk factors of the development of pathological processes of organs and tissues of the oral cavity which are important for complex treatment-and-prophylactic and rehabilitation work.

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SCIENTIFIC REVIEWS AND LECTURES

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THE ASPECTS OF USE OF AUTOLOGOUS DERMAL FIBROBLASTS

ABSTRACT

Methods of healing of skin injuries with the use of cell therapy have been approved all over the globe to be safe and effective. Many different cell types are used in clinical applications including keratinocytes, endothelial cells, bone marrow stem cells and iPS cells. However, skin fibroblasts are in the spotlight today due to their efficacy and ease of culturing.

At present, autologous dermal fibroblasts are widely used in cell therapy and have very promising perspectives in healing of skin defects and injuries. It was demonstrated that fibroblasts have high efficacy in healing such injuries as burns, chronic wounds, tendon regeneration and correction of age-related skin changes.

Keywords: cell therapy, autologous skin fibroblasts.

INTRODUCTION

Fibroblasts are mesenchymal cells located on a border of the epidermal and the dermal layers of the skin. Their main function is production of the extracellular matrix (ECM) that play structural role in the skin and also provide morphological and functional organization, as well as homeostasis of the skin in both normal and pathological states. Fibroblasts participate in restoration of skin integrity after damage, interact with other skin and blood cells that migrate to the lesion site, therefore functioning in both physiological and reparative histogenesis in the dermis. Depending on the location there are different subpopulations of fibroblasts each of which have unique features, influencing their regenerating abilities [2]. The deep understanding of differences between these subpopulations was used when developing new methods of treatment aimed for skin rejuvenation with the use of collagen.

The improper skin healing can affect its function and leads to deterioration in its appearance due to formation of scar tissue and ulcers that promotes development of a secondary infection and cause disturbance of the barrier function of the skin. Traditional methods of wound care promote the fastest epithelization, however skin function is not always restored. The new approach to skin regeneration is based on change of a local microenvironment of a wound by introduction to it or to its edges of human cells.

Fibroblasts, interacting with epithelial cells and producing growth factors, regulate epidermal morphgenesis, producing collagens and glycoproteins promote skin regeneration and rejuvenation [29]. Although there were positive results with the use of other cell types for skin regeneration, this review will be focused on the use of autologous fibroblasts in cell therapy.

At present, fibroblasts based cell technologies are established method in regenerative medicine, which not only effectively eliminates visual defects of the skin, but also reorganize it from within. Constantly growing experience in the field cell technology and its use in various medical spheres including treatment of dermal injuries, trophic ulcers, use in orthopedics, healing of wounds of different etiology and use in cosmetology indicate the importance of further research in this area.

Use of autologous fibroblasts in cell therapy

The deeper understanding of the role of fibroblasts in skin regeneration and rejuvenation led to extension of their use in cell therapy for treatment such conditions as: chronic wounds, dermal injuries, diabetic and trophic ulcers, age-related changes of face, neck and arms skin (decrease of thickness and elasticity of skin, wrinkles), cicatrixes of various etiology and alopecia. Recently, the use of cultured fibroblasts began to incorporate in medical practice after it was demonstrated that dermal fibroblasts maintain diploid karyotype, have limited life expectancy [2], and don't induce tumorogenesis after injections in laboratory animals [12].

Transplanted autologous dermal fibroblasts showed higher survival rates, faster epithelialization and adhesion to wounds as compared to allogenic skin fibroblasts. It is possibly related, to increased immune response to allogenic fibroblasts, and significant increase in scar tissue formation whereas autogenic dermal fibroblasts caused restoration of dermal function with the minimum formation of a scar tissue. Autologous dermal fibroblasts also improve healing of radiation-caused injuries, increasing the healing rate of wounds, tensile strength analyses also demonstrate higher density of cells as compared to the control group [5].

Dermal fibroblasts were also considered for restoration of other tissues. So, use of skin fibroblasts in combination with Bmp2 (bone morphogenetic protein-2) in gelatin scaffold resulted in complete regeneration of cranial seams in 4 weeks after engraftment. This method has potential as a therapy for patients with congenital disturbances of premature ossification of cranial seams [23]. Also other applications of dermal fibroblasts, such as regeneration of tendons, closing of pleural defects for sealing of respiratory tracts, restoration of a forward crucial ligament were considered.

Various methods are used for isolation of fibroblasts from skin biopsy these methods utilize mechanical or enzymatic treatment of tissue or combination of both. After cultivation isolated cells can be frozen or delivered to a medical institution for immediate use [9].

Fibroblasts based cell technologies have a huge potential and require further studying. Especially such areas as isolation from heterogeneous tissue homogeneous population of fibroblasts, technology of rapid

harvesting of necessary amount of cells with necessary functions, the optimal selection of biopsy site considering desirable medical effect, and also storage and transportation of fibroblasts to medical institutions.

Indications for use

Burns. The major goal at treatment of burns is restoration of barrier function of skin, prevention of secondary infection and scar tissue formation and disfiguration. Wound care materials and synthetic substitutes provide a temporary barrier to reduce the risks of infection.

The most effective approach for burn treatment is application of fibroblasts containing matrix material on the wound surface. Both synthetic and natural polymers are used for such matrices, as well as combination of two and their derivatives [8]. At present different types of skin substitutes are developed. It is heterogeneous group of therapeutic materials which differ in biological properties and methods of application. Long term storage and usability together with optimum price-effect ratio provided their universal availability [6]. The common principle that such materials all share, is creation of substitute that will mimic the structure of normal skin and have both dermis and epidermis layers. The base of the dermal component is usually represented by a three-dimensional collagen matrix containing mesenchymal cells. The epidermis layer is created on the surface of the dermal layer by growth and differentiation of keratinocytes. The composition of matrix proteins, cellular elements and methods of formation of the epidermis layer varies depending on the model [13]. There are multiple materials that combine cellular components and matrices. Skin equivalents containing autologous fibroblasts and keratinocytes were successfully developed and tested [18].

Quite recently spray system for delivery of cells directly to the wound area was developed. This system developed by Avita Medical (Northridge, LA, California) contains the mixture of patient's own cells and is sprayed directly to the wound area. Such treatment result in accelerated skin regeneration with less expressed scaring [20].

The possibility of use of artificial skin containing autologous fibroblasts and keratinocytes in other applications, except burns, was demonstrated by Llames *et al.* [16]. They used skin equivalents for treatment of patients with big wounds after removal of a giant nevus. These patients experienced epithelization in all cases without formation of bubbles and tightening of wound edges. These studies indicate that fibroblasts based cell therapy alone and in combination with skin equivalents is effective for treatment of burns and other serious injuries.

Fibroblasts in cosmetology. In 2011 FDA (Food and Drug Administration) approved the use of autologous skin fibroblasts in the form of injections for correction of nasolabial folds wrinkles of moderate and heavy degree in adults (LaViv technology, Fibrocell Technologies, Exton, PA) [14].

In studies involving therapeutic use of autologous fibroblasts significant improvement of the face contour after injection of autologous cells is shown. In addition to reduction of wrinkles, scaring after acne was also reduced. Side effects were not observed in these studies. Because of the early progress in use of autologous fibroblasts in treatment of nasolabial fold wrinkles and improvements of a face contour after fibroblasts application, the indications were extended also on esthetic medicine. The use of autologous fibroblasts is authorized also for treatment of post-acne scars and reduction of flabbiness of skin in the periorbitary region.

Fibroblasts in orthopedics. The Replicel Life Sciences Inc. has developed therapy on the basis of autologous fibroblasts from hair follicles for treatment of a chronic tendinitis. Autologous skin fibroblasts promote the activation of reparative processes in injured tendons [16]. Another orthopedic indication is the use of autologous fibroblasts in osseointegrated prostheses. Autologous fibroblasts reduce chances of skin infection and development of osteomyelitis, the most disturbing complications in the area of a prosthesis attachment [28].

Wound healing. Healing of surgical wounds is another sphere of autologous fibroblasts application. The wounds treated with autologous skin equivalents on the basis of hyaluronic acid undergo faster epithelialization and result with lesser scaring increasing the overall satisfaction of patients as compared to use of the skin transplant along. These results were obtained during studying of skin defects after removal of basal cell carcinoma [17].

Apligraf (Organogenesis, Canton, Ohio) is an allogenic skin equivalent consisting of 2 layers of skin obtained from fibroblasts and keratinocytes. This equivalent is approved by FDA for treatment of chronic wounds, such as trophic and diabetic ulcers of foot, so far more than 200 thousand patients were treated with this product [25]. Nevertheless it is an allogenic product and can provoke immune rejection. This problem can be solved by using autologous components of the skin consisting of fibroblasts and keratinocytes for production of individual two-layer equivalents for recovery and regeneration of the skin. The latest discoveries clearly demonstrate that chronic diabetic ulcers treated with a mixture of autologous fibroblasts and keratinocytes in fibrin suspension result in faster healing of ulcers without side effects [26].

Fibroblasts can be used in the form of suspension on a wound or ulcer. In case of a diabetic ulcer the patented mixture of keratinocytes and fibroblasts is suspended in fibrin glue and applied on a wound before applying of a bandage.

One more sphere of autologous skin fibroblasts application is treatment of chronic wounds caused by vascular pathologies (atherosclerosis, thrombosis, varices), or physical impact (decubituses), harmful environmental effects (radiation). The use of skin equivalents promotes full epithelization of such lesions. However, since the main reason preventing wound epithelization is an obstruction of vessels, the complete healing is impossible without elimination of the main reason of a disease.

Also fibroblasts based cell therapy is effective method for treatment such dermatologic diseases as vitiligo, epidermolysis bullosa and pyoderma gangrenosum [24]. Fibrocell Science together with Intrexon Corp. is developing genetically modified skin fibroblasts for treatment of such orphan skin disease as epidermolysis bullosa

– a severe genetic disorder caused by the mutation in gene coding for collagen VII protein (COL7) [21]. The results of laboratory experiments and clinical trials indicate the possibility of collagen VII accumulation at the boundary of the dermis and the epidermis layers of the skin and healing of chronic skin defects in patients with epidermolysis bullosa using the method based on injection of allogenic fibroblasts [15].

Location-specific properties of fibroblasts

One of the most fascinating properties of the skin is its regional specificity. It is observed in many species and is an adaptive feature which is strictly followed. In human this phenomenon is represented by the presence of different types of hair. Also such divergence can be seen by the differences between the skin of palms, soles and face.

For studying of the location effect the experiments of substitution of the dermis and the epidermis layers were carried out on animals. This series of experiments showed that fibroblasts can determine a phenotype [19].

Clinical experiments have demonstrated similar results. When fibroblasts taken from hairy part of the head were transplanted to a hand this resulted in growth of a long hair as fibroblasts can "remember" their original location and determine the corresponding phenotype. It was shown that fibroblasts maintain the expression of specific genes (i.e. HOX gene) associated with their localization on the skin. Fibroblasts keep expressing them even after 35 cell divisions in culture. These studies revealed differences in gene expression pattern in fibroblasts taken from different areas of the skin that confirms the theory that fibroblasts shall be taken from sites suitable for further therapeutic application [27].

Thus, fibroblasts not simply play a supporting role. They have a great influence on determination of regional identity of skin. The role of fibroblasts in determination of skin phenotype is of great importance for development of cell therapy, and allows controlling the skin phenotype.

The idea to use autologous fibroblasts to help people with amputated limbs, decubituses and changes in the area of amputation [22]. Considering that skin diseases develop in 48% of cases in amputation area, the purpose of fibroblasts based cell therapy is to change skin phenotype in that area to promote better fixation of an orthopedic device.

Development of the therapy that would utilize autogenic fibroblasts is a very promising area, however there are difficulties related to material logistics, collection and transportation of material and production costs. Solving these issues will result in increase of perspective autologous fibroblasts based developments and products in the field of regenerative medicine.

Uniqueness of structure

In addition to regional differences of fibroblasts taken from various skin areas there are also structural and functional differences unique for each separate population. Fibroblasts isolated from reticular dermis and papillary dermis have different genetic markers and functional properties that show their regional uniqueness. Synthesis of collagen is a common feature of all types of fibroblasts, irrespective to their lineage, however reticular fibroblasts produce more procollagen. As for dermal equivalents, it was shown that papillary fibroblasts have higher differentiation and maturation rates and produce various soluble growth factors. Fibroblasts from reticular dermis produce various cytokines, such as keratinocyte grows factor and interleykin-6, and also suppress terminal differentiation of keratinocytes and formation of the basement membrane. Also they produce molecular targets which promote various rearrangements of glycosaminoglycans in collagen of the extracellular matrix. These data demonstrate that papillary and reticular dermis of skin contains different populations of fibroblasts. It was also shown that the upper population of fibroblast play role in formation of a hair follicles [20]. And the lower population is generally responsible for synthesis of the extracellular matrix, promotes wound healing that leads to development of ECM enriched tissue, but deprived of hair follicles. The data obtained in these studies can be used for anti-aging cell therapy based on autologous fibroblasts.

Domestic research

During the 1990th clinical trials were conducted at A.V. Vishnevsky Institute of Surgery on effective methods of skin restoration with the use of skin fibroblasts with further developing of these methods. In 1994 for the first time 3-day culture of allogenic skin fibroblasts was used for treatment of wound surfaces alone and in combination with autodermoplastics [11]. Later at the same institute the method of treatment of deep burns was developed, which include preliminary surgical treatment and combined autodermoplastics with the use of perforated dermal mesh and fibroblasts distributed in cell gel [1].

The studies carried out at Naval Clinical Hospital No. 1 (St. Petersburg) in 2008 demonstrated the efficiency of mesotherapy of dystrophic and destructive processes in skin with suspension of allogenic fibroblasts. The data suggests that use of cultured fibroblasts allows optimizing metabolic processes in skin [10].

During three year period of clinical trials of autologous dermal fibroblasts in correction of skin defects, carried-out in Ural State Medical University and Institute of Medical Cell Technologies (Yekaterinburg), all examinees experienced positive cosmetic effect in a problem area after introduction of autologous fibroblasts. Particularly they experienced a decrease of large and small wrinkles, decrease in dermal defects, and also the general improvement of face skin in the area of fibroblasts transplantation [9].

After clinical trials conducted in RGMU and V.N. Orekhovich Institute of Biomedical Chemistry of the Russian Academy of Medical Sciences, authors came out with a conclusion on safety and efficiency of cultured dermal autologous fibroblasts for treatment of age changes of a skin [5].

Today one technology that utilizes autologous dermal fibroblasts is officially recognized in Russia. The SPRS (Service for Personal Regeneration of Skin) therapy is personalized complex of diagnostic and therapeutic procedures for skin restoration developed by Human Stem Cells Institute (HSCI). In 2010 HSCI got permission from Federal Service for Supervision of Healthcare (Roszdravnadzor) to use of SPRS therapy for correction of age and cicatricle changes of a skin [2].

Russian researchers from the

Institute of Cytology of RAS developed a collagen-based dermal equivalent applied on a polylactide matrix and allogenic fibroblasts which was successfully tested as treatment of trophic ulcers and burns wounds in St. Petersburg's clinics [7]. It represents gel of the extracellular matrix proteins - collagen type I, or fibrinogen (commercially available substances prepared from plasma of a human blood) with the human dermal fibroblasts embedded in the gel. Toxicological tests have been performed in V.I.Shumakov Institute of Traumatology and Orthopedics and clinical tests were carried out in 3 clinics – Regional Burn Center of I.I. Dzhanelidze ambulance training Institute (St. Petersburg), Department of surgery of Academy of Military Medicine (St. Petersburg) and N.N. Burdenko Main Military Clinical Hospital (Moscow). According to the results of all tests carried out in 2006, Roszdravnadzor issued permission for production and a clinical use of the skin equivalent for a period of five years. Now, with the support of the Federal Agency for Scientific Organizations (FASO Russia), organizational and methodical approaches are being developed to introduce this effective method in clinical practice [3].

CONCLUSION

Thanks to their properties fibroblasts play an important role in regeneration processes. They are involved in formation of the extracellular matrix, synthesis of biologically active substances, initiation of migration and proliferation of various cell types after lesions. All these features make fibroblast very promising tool in various fields of medicine including: combustiology, dermatology, cosmetology, orthopedics, endocrinology and surgery. Differences in structural and functional features of fibroblasts depending on their localization and their role in development of a unique skin phenotype, open wide area for research on skin reprogramming, however it is necessary to consider the anatomic location of the biopsy site when locating the area of a skin where cell therapy will be carried out.

Proceeding from the above it is clear that clinical cell therapy develops very rapidly. The main directions were determined, safety and efficiency of this technology has been proved. Cell therapy with the use of autologous dermal fibroblasts has huge potential in the field of regenerative medicine. It offers safe, immunologically acceptable and simple option for tissue regeneration.

At present, in the Republic of Sakha (Yakutia) fibroblasts based cell therapy is not introduced. Though, considering climatic conditions of the region, the problem of treatment of patients with lesions and defects of skin belongs to one of the most urgent areas of medicine. For the last decade cell technologies achieved considerable success in the world. Broad clinical experience in effective and safe application of dermal fibroblasts for treatment of various skin defects has been accumulated. This experience demonstrates the importance of further development of this area.

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CAPABILITIES OF EXPERT SYSTEMS IN FORECASTING OPERATIONAL RISK FOR THE MOST COMMON INTERVENTIONS OF ABDOMINAL SURGERY (REVIEW)

ABSTRACT

Literature review is devoted to the actual problem of the use of expert medical systems in abdominal surgery. The article describes in details the existing models of support systems for medical decisions in patients with such common diseases as acute pancreatitis, acute cholecystitis and complicated peptic ulcer disease. The authors made a comparative analysis of modern expert systems and described the basic principles of their construction. The problems of existing systems, analysis of the structure and mechanisms, underlying the design of decision support systems (DSS), examples of various options for building a DSS designed for use in the practice of a surgeon with a description of their key differences, advantages and disadvantages are outlined in article.

Keywords: expert systems, pancreatitis, pancreatic necrosis, peritonitis, artificial neural networks.

The increasing importance of information provision of various medical technologies becomes one of the critical factors of development in all fields of knowledge at the moment [11]. An expert system in surgery can be used for differential diagnosis and selection of intervention techniques and the assessment of vital parameters in real-time. According to Kolesnikov, D. L., wound infection is about 12 - 25% of all nosocomial infections, being one of the most common complications among all postoperative infectious complications. Up to 42% of all additional costs surgical hospitals associated with the treatment of wound infections. A particularly large number of septic complications observed in abdominal surgery [14].In surgical practice when making medical decisions additionally should take into account such conditions as lack of time, high dynamics of the disease and other factors, significantly complicating the task of building computerized systems for decision support [18].However, the most specific reproduction of the surgical intervention process with its analysis has become a new strategy for prevention and early diagnosis of complications [5].

Despite the variety of existing medical expert systems to support medical decisions in the surgery, most of them consider the possibility of their use in narrow enough spectrum of surgical diseases, in particular, surgical pathology of the abdominal region [5, 12,13,15,16,17, 20,21,22, 26,29,31, 35]. The most frequently used model of these systems is the artificial neural network (ANN). The advantages of ANN are the ability to better classify the data to increase the specificity of the method, without reducing its sensitivity. This structure for the processing of cognitive information is based on the modeling of brain functions. The most important difference of ANN method is the possibility of constructing expert systems by a specialist, who can pass on their experience and the experience of colleagues, based on real clinical situations [11].One of the first expert systems in surgery, based on neural network method, was intended to predict the duration of stay in hospital of patients with acute pancreatitis (Pofahl, 1998), diagnosis of acute pancreatitis the level of enzymes (Kazmierczak , 1993), prediction of lethal outcome (Halonen, 2003) [21]. Development B. Andersson and co-authors was aimed at assessing the effectiveness of artificial neural networks to predict the severity of acute pancreatitis on the basis of the six most informative criteria: heart rate, pain intensity, serum creatinine, hemoglobin, ALT and blood leukocytes [42].

Evaluation of the effectiveness of artificial neural networks in surgical practice was performed also by russian researchers [15,27]. A rapidly developing surgery of the new technologies, in particular, expanding opportunities for laparoscopic interventions, promote the steady development of information technologies in support of medical decision-making in this area. At the same time, mortality in various forms of pancreatitis varies widely, reaching from 25 to 65% with infected pancreatic necrosis [30].In turn, the number of complications when performing laparoscopic procedures on an emergency basis is about 9%, and the informativeness of available rating scales (Ranson, SAPS, APACHE II), according to some authors, does not provide individual prognosis for each specific clinical case [1,25,32]. Meanwhile, automated systems in abdominal surgery are becoming increasingly common, in particular, to quantify the risk of postoperative complications [6,12,13,16,17,19,29] , evaluation of choice of method of surgical treatment [3,10,30], and also as a training system to study General surgery [8,24,28]. Key among the analyzed works is the development of Gurevich N. A. dedicated to the development of objective criteria to define and expand the limits of laparoscopic surgery with minimum risk of surgical complications. As the reasons of iatrogenic complications researchers have identified such factors as clinical and anatomic features (the severity of the inflammatory - infiltrative changes of pancreatoduodenal zone, atypical localization of vascular- ductal items), technical conditions, and experience of the surgeon. Presented software system allowed to improve intraoperative diagnosis and to avoid repeated interventions in a large sample of patients on the basis of the retrospective analysis of endoscopic images with the participation of surgeon-moderator [5]. The analysis of literature data allows to identify the most numerous group of informational developments in the field of pancreatology[5,13,16,19,20, 22, 29, 31, 35]. Despite these successes, the problem remains relevant because of the high frequency of hospitalization in emergency surgery [44]. According to some authors, the frequency of infectious complications after the intervention on the pancreas correlates with such indicators as duration of the disease, the lesion of the tissue of the

pancreas, the markers of systemic inflammation, type of surgical intervention [38,39,40,43]. The results of the microscopic and microbiological examinations of the material aspiration of pancreatic tissue ,peripancreatic tissue and fluid accumulations were put in the basis of the "System for prediction of infected pancreatic necrosis" [20]. As input parameters were used the retrospective clinical, laboratory and instrumental examinations of 398 patients. The main output parameter in accordance with the task of computer modeling was sterile or infected pancreatic necrosis. As a diagnostic biological substrates took place in the mathematical model for predicting acute pancreatitis by A.V. Ivanov and a team was a selected set of trace elements (copper, zinc and iron), determined by atomic emission spectroscopy. The concentration of them was considered in conjunction with the electric resistance of biologically active points, connected with the disease "pancreatitis" [13]. The method of multivariate analysis using logistic regression was applied to the program "Automated accounting system of injuries of the pancreas" [35]. The authors have analyzed 109 35 quantitative and qualitative indicators, the key of which was demographic data, type and mechanism of injury, severity of the patient's condition, the number of damaged organs, blood loss, method of surgical treatment, complications, mortality. Distinctive characteristics of this development were the records of medical errors such as diagnostic delay (operation), technical mistakes (inadequate hemostasis), tactical mistakes (the the increase in surgical intervention, inadequate drainage). Determinant factors in the development of specific postoperative complications have been identified by researchers (age characteristics of patients, mechanism of injury, tactical mistakes, type of intervention, exceeding the limits of laboratory values). The prognostic efficiency of this development was about 88.9%. A number of earlier authors when constructing predictive models of expert systems used as prognostic criteria the disturbance of cytokine regulation in acute pancreatitis and deviation of parameters of cellular immunity [9,23,33]. The main feature of the method of predicting acute suppurative pancreatitis, developed byHrachkov V. V., is a kind of "dynamic" models and the possibility of verification of current data with the regulatory indicators for the entire diagnostic and treatment process [34]. The system of criteria of severity used by Yudin V. N. (2009), divides all the prognostic signs into 3 classes based on their combination with the clinical picture of acute pacreatitis [37]. The basis of neuron-network model ofVinnik Yu. S. is set of examples with input parameters and pre-formulated answers with the indication of the forecast of pancreatic necrosis [2]. More recent work on the application SPVR during surgical interventions on the pancreas focused on the choice of method of surgical intervention, method of completion, risk assessment relaparotomy [3,13,16]. The risk of repeated surgery interventions in acute pancreatitis is about 10-40% of cases [7].The forecasting system of re-intervention in the surgical treatment of severe acute pancreatitis using the method of sequential analysis of A. Wald developed by Krichmar, A. M. and coauthors. The index of forecast re-intervention is defined as sum of diagnostic factors. According to the developers, the greatest prognostic value belongs to indicators of systemic inflammatory reaction (leukocytosis of blood, PCT, LDH, CRP), presence of fluid collections or infiltration according to the ultrasound examination, hemorrhage in the peripancreatic tissue, the presence (or absence) of sequesters in the packing bag, the presence of devitalized areas in the pancreas by visual inspection and localization of the inflammatory process (lesion of pancreas head). [16]. An integral part of decision making in surgery is the qualifications of the doctor and his ability to assess the surgical risk. Consequently, modern expert systems should take into account not only objective clinical and laboratory parameters of surgical risk, but the level of professional standard of a surgeon. A rating of a surgeon is one of the basic components of a modern system of support of decision-making in abdominal surgery "Automated system for evaluation of treatment outcomes of patients with acute surgical pathology of abdominal organs" [3]. The authors of this expert system identified three factors influencing the risk of surgical intervention: the patient's condition, complexity of the surgical intervention, level of experience of surgeon. The ranking surgeon was determined by two groups of parameters, which included formal characteristics (such as experience, qualification, academic degree etc.) and the actual results of the interventions.The choice of method of surgical approach, postoperative peritonitis is implemented in the "Computer expert system for prediction of the postoperative peritonitis" ofZharikov A. N. and co-authors. The program used 25 common options, consolidated into 4 groups of diagnostic criteria, reflecting the functional state of vitally important systems of homeostasis. According to the degree of deviation of these parameters the software allows to draw conclusions about the trends of the postoperative peritonitis in real time. The final forecast is calculated as a percentage of participation for each group of criteria and identifies 4 kinds of possible ways to address the adverse outcomes (sanationrelaparotomy, the elimination of anastomotic failure or refusal of their application, removing enterostomy, the creation of decompressive laparoscopy) [10]. The evaluation scale of the state of the abdominal organs presented in the development of Savelyev V. S., referred to as "the Index of the abdomen." The basis of the method was 7 groups of factors, the main of which was the prevalence of peritonitis, the character of the exudate, the presence of adhesive process, the condition of the intestine and as a source of peritonitis.These indicators were used to select the indications for the choice of tactics of conducting the patient with peritonitis in mode laparotomy "on demand" or "program". In the framework of the expert system the authors developed quantitative assessment of bacterial and fungal infections of peritoneal exudates by flow cytometry. On the basis of comparison of results of microbiological analysis and the extent of involvement of the abdominal organs a pattern of conformity have established for the abdominal index and number of microorganisms in 1 ml. of exudate [30].A free-standing problem in abdominal surgery is the estimation of surgical risk on the organs of the hepatobiliary zone. In the structure of acute surgical pathology as the complications of choledocholithiasis is included an acute cholecystitis with paravesical infiltrate, abscess,

perforation, obstructive jaundice, cholangitis, external or internal biliary fistula. During emergency interventions, the mortality due to complications of cholelithiasis reaches 12 %, when planned and delayed interventions - up to 1 % [36]. The practical application of existing assessment scales predict outcomes of surgical intervention in this disease is difficult because there is no possibility to integrate the results of scores of various clinical and diagnostic parameters in a single system and extrapolate them to the specific clinical situation [17].

In the modern system «Automated system for quantitative assessment of interventional risk» probability - statistical and neural network models are used. They aimed at the assessment of the preoperations severity in patients with cholelithiasis.

The result of processing the incoming data in the development is a “computer image” of the patient, which shows the relationship of the clinical picture with the empirical medico-biological data. The integration of these parameters is achieved by the possibility to quantify the severity of the clinical situation and the risk of surgical intervention [6]. In the framework of the study the results of laparoscopic cholecystectomy (LCE) were used by V.V.Zvyagintsev and coauthors to develop an expert system based on mathematical forecasting models, designed to predict the difficulty of the upcoming intervention, to change the composition of the operating team, to choose the technique of laparoscopic cholecystectomy and to prevent possible complications. These functions are combined in a computer system, predicting the complexity of the operation, containing as the basic principle encoding of the following characteristics: anamnestic data, ultrasound characteristics, clinical symptoms, laboratory data.

The purpose of this expert system is the ability to obtain information about the possibility of performing intervention, the complexity of the intervention, its expected duration, possible technical difficulties, and also to personalize the recommendations for more effective intervention based on the characteristics of the patient [12]. The task of predicting and evaluating the severity of acute cholecystitis based on fuzzy logic decision-making is implemented in the program of Korenevskiy N. and others. This model of the expert system is based on the observation of significant changes in the quantitative composition of the trace element composition in blood of patients with acute cholecystitis. Revealed trends allowed the authors along with other useful features (clinical data, age, presence of comorbidity, the data of instrumental examination, laboratory data) to use quantitative cuprum, zinc and cobalt content in the blood for the predicting the occurrence, early diagnosis and severity of acute cholecystitis. [15]. Does not lose its relevance in the context of intra-abdominal interventions such a widespread problem as gastroduodenal bleeding (GDB) of various etiology. The proportion of peptic ulcer bleeding in the structure of GDB according to Holster I. L. and authors is 31-67% [41]. Bleeding of ulcer etiology, in turn, have the greatest chance of surgical treatment compared with GDB non-ulcer etiology [4]. The main factors of adverse outcomes of this disease are currently the frequent relapses, the patient’s age and severe comorbidity. Data systematic review of Potakhin S. N. and co-authors suggest about the imperfection of the existing developments in the software developed to predict the risk of re-GDK. The programme of risk assessment used at the present stage, represented by a set of scales, based on the interpretation of endoscopic picture of the disease, or based solely on laboratory and clinical parameters.The sensitivity of these methods reaches about 99%, whereas the specificity is not beyond 30%, which inevitably increases the risk of hyperdiagnostics. The evolution of re-bleeding -risk evaluating methods observed in the predictive indices “Baylor Bleeding Score” and “Cedars – Sinai” (2012).

Despite the large number of review papers on the subject of comparative studies there are not enough Russian developments until recently as already today there are about 100 different scoring risk scales of recurrence of GDB, part of which is implemented in the form of computer programs. However, according to the author, none of the options does not meet the requirements of real clinical practice. In particular, existing assessment scales take into account a specific set of signs which not all cases can be public. The methodology needs to be simplified and easy to use and also have the opportunity to be integrated into electronic medical records [26]. Thus, based on the data presented, we can confidently speak of a steadily evolving process of informatization of medical-diagnostic process in medicine in general and surgery in particular. The observed intensive informatization of medical institutions is an integral part of the development of personalised medicine, aimed at minimizing complications and risks, which is the cornerstone of successful intervention in surgical specialty.

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CLINICAL CASE

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CLINICAL CASE OF CYSTIC FIBROSIS WITH THE DEVELOPMENT OF CYSTIC FIBROSIS-RELATED DIABETES IN A 14 YEARS OLD BOY

ABSTRACT

The paper presents a clinical case of cystic fibrosis mixed form, severe, combined with cystic fibrosis-related diabetes, in a fourteen-year old boy.

Objective: demonstration of the clinical case of cystic fibrosis, combined with cystic fibrosis-related diabetes, a boy of 14 years.

Materials and methods

The analysis of the cystic fibrosis-related diabetes patient's observations. The patient is the oldest patient among those diagnosed with cystic fibrosis.

Conclusion

Thus, the feature of the case of cystic fibrosis (CF), a boy of 14 years, is a complicated course with chronic Pseudomonas aeruginosa infection and persistent connection cystic fibrosis-related diabetes.

Keywords: cystic fibrosis, North, children.

INTRODUCTION

Cystic fibrosis (CF) (Cystic Fibrosis) - the most common genetic abnormality, caused by a mutation of the gene CFTR (cystic fibrosis transmembrane conductance regulator), causing a violation of transportation of chlorine ions, sodium and bicarbonate in the epithelial cells, which causes progressive damage to the exocrine glands vital organs [1] . CF frequency varies among Europeoids from 1: 600 to 1: 17,000 births. The RF frequency of cystic fibrosis is according FGBU Medical Genetic Research Center 1: 10,000 newborns [2]. According to the Ministry of Health YARMIATS of Sakha (Yakutia) is registered in 13 patients with cystic fibrosis. Cystic fibrosis-related diabetes prevalence varies depending on diagnostic criteria and screening. In Minnesota found 9% of 5-9-year-olds, 26% of 10-20 year olds and 50% of 30 years and above [5]. In recent years, the life expectancy of CF patients has been steadily increasing, at the same time increases the frequency of complications in these patients, such as diabetes mellitus (DM), accounting for a variety of data from 2.5 to 32%. In clinical practice cystic fibrosis-related diabetes (MZSD) is often diagnosed only when the manifestation of carbohydrate metabolism disorders [3]. Diabetes in cystic fibrosis (CFRD - cystic fibrosis-related diabetes) affects approximately 20% of adolescents and 40-50% of adults with cystic fibrosis. Since adolescence, the incidence is 3%, with a certain predominance of the female gender. According to Russian scientists, impaired glucose tolerance (IGT) occurs in 50-75% of adult patients with cystic fibrosis and clinical diabetes mellitus (DM) manifests in 5-15% of cases. In 2006, at the Russian Centre of cystic fibrosis IGT was found in 53% of patients (aged from 2 months to 18 years), and insulin-dependent diabetes (type cystic fibrosis-related diabetes) as manifest forms of endocrine lesions of the pancreas, - 1% of patients [4].

Objective: demonstration of the clinical case of cystic fibrosis, combined with cystic fibrosis-related diabetes, a boy of 14 years.

MATERIALS AND METHODS

The analysis of the cystic fibrosis-related diabetes patient's observations. The patient is the oldest patient among those diagnosed with cystic fibrosis.

THE RESULTS AND DISCUSSION

Child is from the 2nd pregnancy, with toxicosis at the first half, the 2nd delivery. Age of mother during pregnancy 23 years. Self- delivery, in time. He was born with a weight - 2820 growth - 51 cm. Breastfeeding - up to 1 month. Psychomotor development with a lag: the child began to keep a head in 4 months, to sit - from 9 months, to go - from 1 year 9 months. From the first days of life there was frequent (5-6 times a day), mushy stool. From 3 months frequent colds, there is a constant nasal congestion, at 6 and 9 months, he suffered pneumonia. From the day of birth body mass gain is poor. In 2002, cystic fibrosis was diagnosed. He was examined in the Center of cystic fibrosis (Moscow) in 2003, the diagnosis was confirmed. Basic therapy: Creon 75 thousand units x 4 times a day, while snacking addition to 400 thousand units per day, Pulmozyme 2.5 mL x 2 times daily. The patient is a carrier of a chronic Pseudomonas aeruginosa infection; 4 times a year is admitted to the Department of Pediatric Pulmonology center RBN№1 - NCM routinely for antimicrobial therapy. Consistently receives Pulmozyme, inhaled colistin. Last admission from 4 to 18 July 2016.

Complaints on admission: cough with muco-purulent sputum and wheezing, nasal stuffiness.

When having an objective medical examination his height was 162 cm, the body mass was 41 kg. The condition of the patient was very severe and he had a hyposthenic physique. The cutaneous integument and mucous membrane had a natural colour, moderate humidity. The peripheral lymph nodes were multiple, matted and painless, the size is up to 0.8 cm. The fingers were like «drumsticks», the nail coatings were like «hour glasses». The shape of the chest was correct. The frequency of respiratory movements was 28 in a minute and there was a mixed pattern of breathing. The percussion sound on the lungs was bandbox. When auscultation in lungs, the breathing was tough, mosaically weakened, carried out in all area, humid small- and medium bubbly sounds on both sides, more on the right. There was dry humming wheezing when

forced expiration. The nasal breath is moderately complicated, the discharge was mucous. Heart rate was 116 in 1 min. The tones were clear, rhythmical. The tongue was moist laid over by a whitish-yellow coating.

The stomach was painless. The liver performed at 1 cm from under the costal arch, the pancreas was not palpable. The boy urinated freely. There was a formed stool twice a day.

Here are data of laboratory instrumental studies: monocytosis (14,3%)- general blood test dated from 12.01.16, monocytosis remained on the 21.01.16 (12,6%) , subcompensated respiratory acidosis (pH 7,279, pCO2 52,4, pO2 32,1, sO2 51,9, FCOHb 0,3, FO2Hb 51,3, FMetHb 0,8, cBase -2,0 mmol/L, cHCO3 19,8 mmol/L, K+ 4,4 mmol/L, Na+ 137 mmol/L, Ca2+ 0,64 mmol/L, Cl 105 mmol/L) was in the parameters of the venous blood acid-basic state dated from 12.01.16 . A urine screen test was within normal limits dated from 21.01.16: 80.0, the colour was light yellow, transparent, specific gravity was 1025, urine was acidic, no protein, sugar +++, acetone was negative. Biochemical blood test dated from 12.01.16 shows reduction of urea level (0.4 mmol/L) and growing of alkaline phosphatase (922.9 u/l), atherogenic index was 2,19. In the second medical examination dated from 21.01.16 it was found a hypoglycemia (18.3 mmol/L). Antistreptolysin O 196,9 IU / ml (Russia index) was negative.

Immunosorbent assay of hepatitis antigen dated from 18.01.16 was negative. On direct microscopic sputum examination dated from 22.12.15 there was a massive growth of Pseudomonas aeruginosa, sensitive to ciprofloxacin, metallo-beta-lactamases, resistant to amikacin, gentamicin, piperacillin, ticarcillin, Candida albicans. Sweat test dated from 13.01.16 is 119,74 meq / l. Urine amylase dated from 12.01.16 was 61 u/l. Helico test is Hp (-) dated from 18.01.16 . Blood on glycated hemoglobin dated from 25.01.16 was 9%. Here are data of immunosorbent assay of hepatitis antigen dated from 18.01.16: HBsAg was not found, Anti-HBcor was not found, anti-HCV result was uncertain 1,24, HCV IgG/ IgM was not confirmed, HCV-cor IgG/ IgM п/т, HCV-ns IgG/ IgM п/т – were not found. Glycemic profile dated from 23.01.16: at 7 a.m - 8,7 mmol/L, at11 a.m - 11,98, at 4 p.m. - 19,1, at 20p.m. - 13,4, at 03 a.m. - 19,6 , at 7 a.m - 13,2. There is a daily urine dated from 25.01.16: protein was 0,04 g/l and acetone, glucose were negative. There is a microscopy of sputum dated from 20.01.16: yeast-like fungu was positive. ECG dated from 12.01.16 had a sinus rhythm with heart rate 80 beats per minute. Electrical axis of heart had normal position. Incomplete right bundle branch block. Voltage of left ventricular complex was raised .There is the bronchoscopy dated from 13.01.16: 2-sided catarrhal bronchitis. Fiberoptic gastroduodenoscopy dated from 14.01.16: incompetence of cardia. Duodeno gastric reflex. P esophagitis. Congestive expressed gastroduodenopathy. A chest computer tomography (20.01.16): uneven broaden on both sides, deformations of bronchi.

The walls of the bronchi are thick. Part of clearance was filled with discharge. Earlier spot changes are not defined. Lung interstices were sealed diffusely irregularly. Effusions in pleural was not defined. Increasing signs of intrathoracic lymph nodes were not noted. There was an abdominal and retroperitoneal space computer tomography dated from 20.01.16: liver and pancreas have grown up moderately, contours were equal. The structure of parenchyma was homogeneous, indices were within the normal range. Intrahepatic bile ducts were not expanded. The gallbladder was reduced, there were hyperdensive concretions in the body cavity. The lymph nodes remain in a gastrohepatic omentum of a porta of hepar. Pancreas was with signs of atrophy of the parenchyma, tail and body density of pancreas was reduced. The kidneys were located typically, not enlarged, contours were equal, renal cortex was sealed. Pelvis of kidneys were not expanded. Enlarged mesenteric lymph nodes with small calcifications were remained. Effusions in abdominal was not defined. Medical report: lipophanerosis of pancreas. There were gallstones in the bladder. It was noted the increasing of lymph nodes of abdomen.

There is a medical report of a Color Flow Doppler Mapping echocardiography dated from 21.01.16: Ectopic mount MK chords with minimal regurgitation. Regurgitation was on tricuspid valve 0 - 1 st. The cavities of the heart were not expanded. Ejection fraction - 68%. He was consulted by a gastroenterologist, and an endocrinologist.

Clinical diagnosis: Cystic Fibrosis, mixed form, severe. Chronic purulent bronchitis.

Bilateral mixed bronchiectasis of lower lobes. Chronic persistent pseudomonas infection. Chronic respiratory failure.

Chronic pancreatic insufficiency. Cholelithiasis. Chronic maxillary sinusitis. Chronic superficial gastritis common, active stage. Duodeno-gastric reflux with reflux esophagitis 1st class distal to the deficiency of the cardia rosette. Diabetes, first identified. A deviated septum of the nose to the right, without breaking the nasal breathing.

Treatment: sulperazon, ciprofloxacin, cefepime, inhalation of colistin, pulmozim, creon, ursodez, acetylcysteine, flomax, flukorus, linex, omeprazole, motilium, fluconazole.

Physiotherapy: ultraviolet irradiation № 7 on the chest, therapeutic physical training, bioptron № 4 on the chest. Replacement insulinotherapy was given: Apidra- breakfast – 3 units, lunch – 3 units, dinner – 3 units (for glucose above 14 mmol / l 1 U). Lantus: 10 p.m.- 7 units. Discharged 27.01.16.

CONCLUSION

Thus, the feature of the case of cystic fibrosis (CF) in a 14 year old boy is a complicated course with chronic *PSEUDOMONAS AERUGINOSA* infection and persistent connection of Cystic Fibrosis-related diabetes.

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EXPERIENCE EXCHANGE

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THE DYNAMICS OF THE LIVER FUNCTIONAL STATUS IN PATIENTS WITH ODONTOGENIC PURULENT-INFLAMMATORY DISEASES OF THE MAXILLOFACIAL REGION, COMPLICATED BY SEPSIS

ABSTRACT

To assess the degree of hepatic function disorder in patients with widespread phlegmons of the maxillofacial area, complicated by sepsis, the researchers studied blood levels of cytolytic enzymes alanine aminotransferase and aspartate aminotransferase. It is established that at the widespread phlegmons of maxillofacial area complicated by a sepsis the concentration augmentation in blood serum of transaminases is observed, and degree of their augmentation corresponds to the standard criteria of expression of pathological process. Including in a complex of medical actions of intravenous laser radiation of blood in a combination with sodium hypochlorite, especially a combination of ultra-violet radiation of a blood with a double irrigation of wounds by sodium hypochlorite, contributes to normalization of cytolytic enzymes indicators by 6-7 days from treatment initiation.

Keywords: odontogenic pyoinflammatory diseases, sepsis, maxilla-facial phlegmon, odontogenic infection, sodium hypochlorite, ultra-violet radiation of a blood.

At patients with acute odontogenous pyoinflammatory processes of maxillofacial area complicated by a sepsis often functions of internals and their systems, including a liver [2,4,5,8] are broken that often leads to serious disorders of a regulation of metabolic processes and change of a metabolism in an organism in general [7,9,10,12]. These circumstances dictate need of carrying out complex assessment of the general and local disorders, and also development of

Table 1

Distribution of patients on gender and age, persons

Group of a research		Age						total
		Young 18-44 years		Average 45-59 years		Elderly and senile 60 and more years		
		M	W	M	W	M	W	
Control group		5	5	5	5	5	5	30
Primary group	1 subgroup of a research	2	5	4	3	1	2	17
	2 subgroup	5	2	3	4	3	2	19
	3 subgroup	3	2	1	3	-	-	9
	4 subgroup	3	3	4	3	-	1	14

new pathogenetically reasonable effective methods of treatment of acute odontogenous pyoinflammatory diseases of maxillofacial area with the complicated current, such patients promoting a favorable outcome at after treatment [1,3,6,11].

Research objective: to study a functional condition of a liver at patients with the acute odontogenous pyoinflammatory processes of maxillofacial area complicated by a sepsis by test of definition in a blood of maintenance of an alaninaminotranspherase (ALT), an aspartate aminotransferase (nuclear heating plant) when performing complex etiopathogenetic therapy.

MATERIAL AND METHODS

The research was conducted with participation of 89 patients aged from 27 up to 72 years which came according to urgent indications to specialized maxillofacial unit of a versatile hospital with the widespread odontogenous phlegmons of maxillofacial area complicated by a sepsis (tab. 1).

The control group included 30 people, aged from 21 up to 72 years without symptoms of acute odontogenous inflammatory diseases and changes from internals.

Depending on the carried-out treatment patients of the main group were divided into 4 subgroups. To all patients of the main group of a research the standard complex therapy of a basic disease was carried out. In addition, the patient of 1 subgroup carried out a daily disposable irrigation of a postoperative wound by freshly cooked solution of sodium hypochlorite, in the second subgroup in a complex of treatment included the intravenous laser radiation of a blood (ILRB), in the third subgroup the daily two times irrigation of a postoperative wound was carried out by freshly cooked solution of sodium hypochlorite, in the 4th subgroup besides a two times irrigation sodium hypochlorite applied ultra-violet radiation of a blood (UVRB). From 17 patients of the first subgroup at the 4th pathological process extended to two, and at 13 to three the cells of space. The second subgroup was made by 19 patients. At 2 of them phlegmon extended to two and at 17 to three anatomo-topographical areas of the person. Among 9 patients allocated in the third subgroup at 5-acute pyoinflammatory process occupied three and at 4 more than three cellular of spaces. The fourth subgroup was made 14 are sick among which occupied three the 6th phlegmon, and at 8 patients - 4 and more anatomy topographical areas of the person. At all patients in day of entering the general state was regarded as serious and extremely serious. After preliminary preparation the surgical grant in volume of opening and drainage the near gnathic of phlegmons was carried out. Operations were performed under intravenous anesthesia. Along with surgical treatment carried out the complex intensive care including the antibacterial, desensitizing, disintoxication, immunocorrective and antiinflammatory drugs.

The maintenance of ALT and nuclear heating plant determined by the standard technique on a biochemical autoanalyzer of Impact-400 (Gillord, USA) by means of standard sets. The obtained data were compared to indicators of faces of control group and entered in tables and databases of a software package Microsoft Access. Statistical processing was made with use of a software package of Statistica for Windows v. 7.0.

Table 2

Studying of dynamics of maintenance alanine and asparagine transaminases in blood serum in the course of complex treatment of phlegmons of maxillofacial area

Group of patients		Observation terms	ALT	Nuclear heating plant
Control group		Healthy	0,40±0,022	0,20±0,012
Basic group	1 subgroup	Basic data	3,45±0,195***	2,02±0,072***
		6-7 days	2,10±0,147***^^^	1,53±0,048***^^^
		At an extract	1,3±0,072***^^^°°°	1,11±0,038***^^^°°°
	2 subgroup	Basic data	3,49±0,128***	2,50±0,062***
		6-7th days	1,90±0,066***^^^	2,12±0,054***^^^
		At an extract	0,80±0,035***^^^°°°	0,4±0,014***^^^°°°
	3 subgroup	Basic data	3,75±0,097***	2,62±0,075***
		6-7th days	2,54±0,044***^^^	1,54±0,063***^^^
		At an extract	2,11±0,034***^^^°°°	1,01±0,029***^^^°°°
	4 subgroup	Basic data	3,86±0,073***	2,71±0,073***
		6-7th days	0,59±0,013***^^^°°°	0,26±0,008***^^^
		At an extract	0,40±0,010^^^	0,22±0,008^^^°°

Note: * - distinctions rather this groups of healthy are significant (* - p<0,05, ** - p<0,01, *** - p<0,001); ^ - distinctions of rather basic data are significant (^ - p<0,05, ^^ - p<0,01, ^^^ - p<0,001); ° - distinctions are significant rather these 6-7 days (° - p<0,05, °° - p<0,01, °°° - p<0,001)

RESULTS AND DISCUSSION

At patients with the complicated course of widespread phlegmons of maxillofacial area authentically expressed rising of maintenance of ALT and nuclear heating plant in blood serum became perceptible.

At 17 patients with widespread phlegmons of maxillofacial area (1 group of a research) complicated by a sepsis, in day of entering in a hospital rising of ALT by 8,6 times (p 0,01), nuclear heating plant - in 10,1 times (p 0,001) in comparison with indicators of healthy faces of control group (tab. 2) was observed. At a repeated research for the 6-7th days of complex treatment with a disposable irrigation of wounds freshly cooked solution of sodium hypochlorite noted depression of the studied indicators, but they all the same were above values of control group in 5,3 (p 0,05) and by 7,7 times (p 0,05) respectively. At research ALT and nuclear Heating Plant at the final stage of complex treatment further depression is noted though all of them still considerably exceeded indicators of control group (p <0,05). In the second group of a research (at 19 patients

with the widespread phlegmons of maxillofacial area complicated by a sepsis) the maintenance of ALT and nuclear heating plant in day of entering was reliable above in 8,7 controls and by 12,5 times respectively. For the 6-7th days of complex treatment with including in a complex courses of the intravenous laser radiation of a blood (ILRB) and a disposable irrigation of wounds solution of sodium hypochlorite observed appreciable depression of concentration of ALT and nuclear heating plant in blood serum in comparison with the previous term of a research, but they in 4,8 (p 0,05) and by 10,6 times (p 0,001) respectively, exceeded indicators of control group. Further treatment of patients with use with VLOK and a local irrigation of wounds with solution of sodium hypochlorite promoted distinct reliable depression of maintenance of ALT and nuclear heating plant, but it was higher, than at patients of control group. In the third group of a research (9 patients with the widespread phlegmons of maxillofacial area complicated by a severe form of a sepsis) when entering blood ALT nuclear heating plant indicators in 9,4 and by 3,1 times, respectively, exceeded values of control group. In this group of patients besides complex therapy the two times irrigation of a wound surface was applied by freshly cooked solution of sodium hypochlorite At a repeated blood analysis for the 6-7th days and at the end of complex treatment (for 9-10 days) in this group of ALT and nuclear Heating Plant value progressively decreased, but were much higher than indicators of control group (p 0,001). At a research of concentration of cytolytic enzymes in blood serum in the 4th studied group (to 14 patients with the widespread phlegmons of maxillofacial area complicated by a severe form of a sepsis) authentically expressed rising of indicators of maintenance of ALT in 9,7 and nuclear heating plant by 13,6 times in comparison with indicators of control group is also taped.At a repeated research for the 6-7th days of complex treatment with including of a double irrigation of wounds solution of sodium hypochlorite and ultra-violet radiation of a blood (UVRB) noted distinct depression of concentration of ALT and nuclear heating plant which slightly exceeded indicators of control group (p<0,05). Continuation of complex therapy promoted further depression of maintenance of ALT and nuclear heating plant, and by the time of an extract didn't differ from indicators of control group (p<0,05).

CONCLUSION

Thus, increase in concentration transaminases by ALT and nuclear heating plant in blood serums is observed at widespread phlegmons of the maxillofacial area complicated by sepsis, extent of their increase corresponds to the standard criteria of expressiveness of pathological process. Inclusion in a complex of medical actions of ILRB in combinations with one-time irrigation of wounds promotes distinct decrease in concentration of cytolytic enzymes in blood serums. At a combination of complex therapy by double irrigation of wounds solution of sodium hypochlorite and UVRBU the maintenance of ALT and nuclear heating plant for the 6-7th days decrease to control indicators.

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RESULTS OF KIDNEY RESEARCH OF PATIENTS WITH VISCEROPTOSIS

ABSTRACT

The article presents the results of research and analysis. According to the results of a comprehensive survey in the visceroptosis patients in 24.8% of them nephroptosis of varying degrees was diagnosed. Diagnostic studies included an objective examination, renal ultrasonography, excretory urography and urinalysis data. The features of the nephroptosis diagnosis in visceroptosis patients, the relationship of renal ptosis with omission of the colon are sshown.

Keywords: nephroptosis, colonnephroptosis, visceroptosis, excretory urography, pyelonephritis, chronic colonic stasis.

INTRODUCTION

The urgency of the problem of Nephroptosis treating underlines the high incidence of this disease and mostly the young and able-bodied persons. According to contemporary authors nephroptosis is 2.65% among urological patients [1].

The question is whether nephroptosis distinct disease or visceroptosis part still is not been resolved. The lack of a common view on the etiology, pathogenesis Nephroptosis led to the problem of treatment. Conservative treatment Nephroptosis, unfortunately, proved to be ineffective. All this testifies to the great social and economic significance of this problem.

MATERIALS AND METHODS

Kidney Research was conducted in 387 (71.7%) patients with visceroptosis. Changes identified based on physical examination, renal ultrasonography, excretory urography and urinalysis data (Table 1).

The table above shows that nephroptosis identified by us in 96 (24.8%) patients examined, including the right-hand - in 41 (10.6%), left-handed - in 2 (0.5%), two-way - 53 (13. 7%) patients. It should be noted that 49 (51%) of 96 patients with kidney nephroptosis mobility was detected initially and then investigated the gastrointestinal tract and thus all patients diagnosed visceroptosis in various embodiments. In all 96 cases nephroptosis combined with the omission of the colon, and the left-sided nephroptosis - only the left-hand and two-way - two-way colonoptosis.

Many researchers regarded nephroptosis as an isolated disease, but a combination of renal ptosis with omission of the stomach, colon, uterus, and other organs to explain the overall weakness of the connective tissue, and in particular the weakness of its fascial plates [1, 3, 5]. We agree with their opinion, but I would like to emphasize the role of mobility in the pathogenesis of colon Nephroptosis. Kidney Mobility limited number of issues, of which the main role is played by the vascular pedicle, renal fascia and abdominal pressure. Kidney Vessels may be extended under the influence of frequent tensions or long her shift. The kidney is surrounded by a sheath of leaflets pre- and behind the kidney fascia, which are spliced on the lateral margin and form tapering downwards socket. Founded fascia cavity is adipose tissue (adipose capsule) and is penetrated by thin connective webs between the sheets of fascia and fibrous capsule of the kidney. The

Table 1

Kidney changes identified in patients with visceroptosis

Infractions	Total n, 387	
	Abs.	%
Right nephroptosis	41	10,6
Bilateral nephroptosis	53	13,6
Left nephroptosis	2	0,5
Chronic pyelonephritis	213	55,0
Kidney Cyst	12	3,1
Oxaluria	59	15,2
Uraturia	15	3,9

Fig. 1. Bilateral nephroptosis

funnel shape of the fascial box, normal tone of fascial sheets and sufficient development of perinephric fat also limit the mobility of the kidney. In our opinion, the normal (mezoperitoneal) location of ascending and descending colon departments also has value as a stabilizing factor in limiting the mobility of the kidney. When intraperitoneal location of these sections of the colon, and they have the mesentery, in our opinion, is released retroperitoneal cellular spaces in the lumbar region to the right or to the left, which leads to a decrease in the tone of fascial sheets and creates favorable conditions for the omission of the kidneys and the development of its mobility. The combination of the omission of the kidneys in 100% of cases with prolapse of the colon indicates the relationship of these processes.

Diagnosis Nephroptosis has its own characteristics. Examination of patients should be carried out polypositional. As a rule, an objective examination of the patients in a horizontal position, the kidney takes a normal anatomic position, and identify its mobility is not possible. In a standing position at palpable nephroptosis lower pole or all of the movable kidney. Determination of mobile kidney difficult when panvistseroptosis when lowered liver covers the internal organs. To confirm the diagnosis necessarily an ultrasound and excretory urography, which allow to identify both the anatomical position of the kidneys, and changes in their functional state. At excretory urography performed in 96 patients (Fig. 1), nephroptosis I degree was detected in 12 (12.5%), grade II - in 54 (56.3%), and grade III - in 30 (31.2%) patients.

Reducing the concentration ability of the kidneys, delayed release of the radiopaque substance was detected in 47 (48.9%), the deformation of the cups and pelvis - in 29 (30.2%) patients with nephroptosis. Changes indicative of inflammation, such as increasing the number of leukocytes, presence of mucus, bacteria urinalysis were reported in 82 (85.4%) of 96 patients with nephroptosis. Ultrasound examination revealed renal parenchyma seal them, and in most cases mobile suffered kidney. Right-sided pyelonephritis was diagnosed in 38 (39.6%), left-handed - in 2 (2.1%), double-sided - in 42 (43.7%) patients with nephroptosis.

Impairment of renal function in patients with chronic colonic stasis, say many researchers. S.N. Navruzov (1988) highlights the renal form of chronic colonic stasis and V.G. Us (1988) highlights the kidney shape visceroptosis [2, 4]. The authors believe the changes in primary colon, and the phenomenon of chronic pyelonephritis explain endogenous intoxication. In our studies, chronic pyelonephritis was diagnosed in 213 (55%) of 387 examined patients, which was confirmed by ultrasonography, and urinalysis. It is noted the dependence of the frequency of detection of chronic pyelonephritis on the degree of chronic colonic stasis. Patients with HTS compensation detected in step 27 (7%) patients with a XTC subcompensation stage in 84 (21.7%) with a XTC decompensation in step 102 (26.3%) cases.

Causes of pyelonephritis, in our opinion, in some cases are due to nephroptosis caused by violations of urine outflow, and the other - chronic endogenous intoxication caused by prolonged delay in intestinal contents, and, moreover, the complex of these factors.

CONCLUSION

High resolution of excretory intravenous urography and ultrasound allows us to consider them major and reliable diagnostic methods of nephroptosis at which we were able to identify the displacement of the kidneys down in 100% of the cases of all patients. A comprehensive, well-grounded approach to the performance of diagnostic tests at colononephroptosis improves the efficiency of the surgical treatment.

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CURRENT STATUS OF DIAGNOSIS AND SURGICAL TREATMENT OF RENAL CELL CARCINOMA

ABSTRACT

The article presents a review of the prevalence of renal cell carcinoma, used at the moment of classification of the disease. The instrumental methods of diagnosis of renal cell carcinoma and surgical treatment at the present stage of development of medicine are shown. Various methods of surgical interventions and approaches to the choice of a method of surgical treatment of the disease and therefore different results are described. The authors gave the analysis of results of surgical treatment of renal cell carcinoma based on data published in the current medical literature, including the use of laparoscopic techniques.

Keywords: renal cell carcinoma, diagnosis of kidney tumors, laparoscopic partial nephrectomy, open partial nephrectomy.

INTRODUCTION

Renal cell carcinoma (RCC), it is one of the especially significant in urology oncological diseases due to the high frequency of morbidity and mortality. In the world of renal malignancies are gaining growth rate. So in Russia according to the monograph V.I.Chissova et al. provided Statistics 2010, which revealed 516.874 new cases of malignant kidney education, women 54.0%, and men 46.0%. The absolute number of men newly diagnosed with RCC diagnosed 2000-2010 was increased from 7646 to 10286 people, women from 5959 to 8437. The average age of patients was 61.7 years (60.4 for men, 63.1 for women) [6] . In men, kidney cancer occurs in 2 times more often than women. [7] The structure of mortality from cancers to share RCC worldwide accounts for 2.7% of men and 2.1% for women [56]. In Russia, the number of deaths from 2000-2010, the RCC with men from 4450 to 5223, women from 2822 to 3030. In other words the death rate from kidney cancer rose from 5.01 to 6.01 per 100 thousand. Population, the percentage of growth in 17, 38% [52]. According to Siegel R.L. over the past five years (2007-2011 y.), the overall death rate from cancer has decreased from 215.1 in 1991 to 168.7 per 100 thousand. population decreased by 22% in 2011. The subsequent reduction in mortality from RCC can be accelerated by the widespread use of new knowledge in the field of cancer control in all strata of the population [45]. Siegel R., et al write identification 58240 new cases of kidney cancer and 13,040 deaths from RCC recorded in the US in 2010 [45].

Classification. To date, the practice of using multiple types of classifications of kidney cancer. Historically, Russia is widely used classification of renal tumors, the proposed NA Krajewski et al. (1981) [24]. In this classification, the following types of RCC on the histological structure: clear cell RCC - 73.7%, granular cell (dark cell) SIC - 17.5%, Spindle (sarcomatoid) RCC - 3.7%, ferrous RCC - 5.1%. However, in 1996 the idea of the morphological structure of kidney tumors has been revised (Heidelberg) and adopted by the working classification, called “Heidelberg” or “Maynts”. It is based on cytogenetics and kidney tumors at early classification W. Thoenes (1986) [13]. 1. The clear cell RCC, RCC chromophilic 2. 3. papillary RCC, chromophobe RCC 4., 5. oncocytomas 6. cancer of the ducts of Bellini, 7. neuroendocrine cancer.

Known as the TNM system (2009), describes the anatomy of the spread of destruction and consists of three parts (TNM).

The classification of malignant tumors in the so-called “stage” of the process is based on the postulate that high survival for localized tumors than than the common beyond the organ lesions [9].

In 1981, S.A. Fuhrman et al. proposed a classification system tumors, which take into account the index of the cell nucleus, the degree of differentiation of tumor cells Fuhrman system [1].

- Grade 1 (G1) - high-grade tumors;
- Grade 2 (G2) - moderately differentiated tumor;
- Grade 3-4 (G 3-4) - low-grade tumor.

Diagnosis. Currently, there are various methods of diagnosis of RCC. Non-invasive diagnostic methods of our time as ultrasound and CT, MRI led to a change in the method of examination of patients with RCC, in addition, to increase the detection rate of the earlier stages of the disease [32,27]. Ultrasound is a common screening methods of radiation diagnosis of renal neoplasms [47]. CT is the most valuable diagnostic value, which is the main and the main method of diagnosis of kidney structures. The most common solid and solid-cystic tumor types that occur regardless of the lower or upper pole. The existence of a cystic component, due to the presence of hemorrhage and necrosis areas that clearly differentiated with the help of CT. Typical fibrous renal capsule as hyperechogenic rim at the periphery of the tumor, clearly delineating the tumor and normal kidney tissue. However, at low tumor cell differentiations kidney fibrous capsule can be infiltrated and inflamed. During the CT scan with contrast may diagnose a tumor the size of 0.5 mm. determine the location in relation to the segments, boundaries and goal kidney [16]. Practice shows that CT also allows you to see an increase in regional lymph nodes along the aorta and inferior vena cava, blood clots in the hollow and renal veins, and distant metastases. How to write Zagoria R.J. and Wolfman N.T. doubts about the results of CT scans occur only when non-directional search for renal tumors [56]. Implementation of multiplanar and three-dimensional reconstructions allows the doctor to evaluate complex vascular architecture

of the kidneys and urinary tract. ICB renal cancer patients compared to standard CT can more accurately determine the stage of the disease and metastasis, provides information for determining the amount and the method of surgical treatment [23]. Patients suffering from intolerance to iodinated contrast agents, MRI is an excellent alternative. [26] Take into account that an MRI scan about 24% of kidney tumors reserves without differentiation [56]. Unlike CT MRI worse displaying tumor calcification, which can lead to diagnostic errors. However, MP angiography is considered to be an accurate method for the detection of venous tumor invasion [33]. As the data of other studies of MRI in the detection sensitivity of the inferior vena cava thrombosis reaches 80-100%, which corresponds angiography with selective catheterization of the inferior vena cava [53]. Taking into account the peculiarities of metastasis, a set of mandatory surveys for staging contains X-ray light, and with a reasonable suspicion of metastases in the lungs to do CT chest. Radioisotope scan skeleton renografiya radionuclide that can play a major role in addressing the many issues in the further treatment.

Treatment. Surgery is the only effective treatment for kidney cancer. To date, use these types of surgery: combined, by extension, radical nephrectomy and simple. When choosing a need to take into account the fact that access must be less traumatic, and more, provide access to the object operation [1]. As is known, the standard treatment for localized renal cell carcinoma is radical removal of kidneys from the time of its introduction (S.J. Robson et al., 1963). In domestic medicine nephrectomy for renal tumor performed the first SP Fedorov in 1923. The principles of the operation have not changed since the days of C.S. Robson and typically include early bandaging a. renalis, subsequent ligation v. renalis and their intersection, kidney removal is Gerota fascia, along with the surrounding perirenal fiber, removing the ipsilateral adrenal gland. However, the choice of access execution lymphadenectomy currently remain controversial [55]. Advanced kidney removal involves almost the same amount of transactions that radical removal. However, it a regional lymphadenectomy is performed after diagnosis of metastatic lymph node.

Laparoscopic radical nephrectomy (LRN). Laparoscopy remained exclusively a diagnostic method for a long time, until in 1983, Z. Kurt et al. I not made a laparoscopic appendectomy, since laparoscopic surgery has been gaining a place in the different surgical specialties. In 1990, Clayman first realized laparoscopic nephrectomy at oncocytomas [56]. The terms of use of laparoscopic surgery in the treatment of urological diseases each year continues to grow [48]. Sor1soa1 et a1. (1991) published the results of the first radical laparoscopic nephrectomy in RCC [14]. Over the past decade known urologists around the world have repeatedly demonstrated that laparoscopic nephrectomy in RCC is feasible and most preferable than open surgery. Today more and more evidence that the T1 and T2 laparoscopic nephrectomy is becoming a serious alternative to open surgery [56]. In 1999 Cervais et al. raised the bar even higher with laparoscopic nephrectomy in patients with T3a and T3b tumors even as cytoreductive surgical intervention prior to immunotherapy. It was found that these patients recovered significantly better than similar patients who underwent open surgery, as they were able to start a course of immunotherapy for 1 month before [50]. The results of 64 patients after laparoscopic radical nephrectomy and 69 - after open radical nephrectomy. In this retrospective multicenter survey shows that the 5-year survival rate after LRN is the same after the traditional open surgery [35]. According to the same Permpongkosol S et al. (2005), a ten-year survival rate after laparoscopic radical nephrectomy was significantly higher than with conventional surgical approach. [36] At this time, the treatment of RCC by means of open and laparoscopic techniques. The greatest number of successful operations obtained by laparoscopic surgery, but they have drawbacks such as the need for pneumoperitoneum.

Laparoscopic assisted radical nephrectomy (LARN) - a version of the standard laparoscopic surgery. With this operation, it uses standard laparoscopic instruments, first create a pneumoperitoneum and a laparoscope is inserted. After an additional incision in the abdominal cavity is entered free hand surgeon, thereby reducing the risk of iatrogenic damage of tissue dissection and retrektsii bodies [41]. In 1996, Dr. Nacada performed the first laparoscopic-assisted nephrectomy. In the same year in the United States approved the use of the first hand-held laparoscopic port, which later became the most popular. [33]

Laparoscopic assisted radical nephrectomy for renal cell carcinoma T2N0M0 in our country for the first time performed a professor OV Teodorovich in 2002 at the Department of endoscopic urology RMAPO [17]. Methods of assisted laparoscopy (AL) suited to laparoscopic surgery, which require an intact removal of a relatively large volume of tissue, which in the case of the classical method would entail an extension of the operational section of the trocar [44]. Positive moment assisted surgery is that the surgeon's hand helps in localization of structures and instruments of governance in the three-dimensional space, whereas in conventional laparoscopic surgery is often lost focus. Moreover, at the surgeon can control AL situations that may require open conversion, for example, massive bleeding. AL may also be used as an alternative, which is preferred transition from open to laparoscopic surgery [38]. AL surgery usually requires less trocars and working tools than traditional laparoscopy. A number of other advantages, the introduction of the hand into the abdominal cavity, which enables the operator to the tactile sense of the ability to carry out palpation of the kidneys and other tissues, excretion blunt manner, control bleeding, and so on. According Nakada et al. (2001), the average time assisted laparoscopic nephrectomy in 18 patients was 220.5 minutes, while traditional open radical nephrectomy -. 117.8 min [34]. However, the average stay (3.9 days after laparoscopy assisted nephrectomy versus 5.1 days after open radical nephrectomy), stay on a piece of disability (26.8 days after nephrectomy laparoscopically assisted versus 52.2 days after traditional open nephrectomy), the average duration of return to normal working life (28 days after nephrectomy laparoscopically assisted versus 150 days after open radical nephrectomy) speak in favor of laparoscopically

assisted radical nephrectomy. Lee SE et al. (2003) compares the results of the open nephrectomy and laparoscopic nephrectomy assisted 104 patients. According to him the length of laparoscopically assisted surgery was 194.9 minutes. against 180.7 minutes. with traditional open nephrectomy. The volume of blood loss higher in open surgery (262.8 ml versus 182.8 mL), were also observed significantly good performance early postoperative period: the start of feeding (2.6 vs. 3.2 days), the duration of an insurance drainage (2.6 day compared to 3.2) and the average length of hospital days (6.8 days vs. 8.9 at LARN after open surgery) [20]. As a result, the use of fewer ports and cleavage with cut muscles may reduce unwanted surgical complications.

Open partial nephrectomy. The world's first operation of partial nephrectomy (PN) is fixed and performed by Dr. Simon in 1870, a patient with hydronephrosis, and later Dr. Vizenz Czerny first performed RP over the tumor [18]. PN was originally proposed as an alternative method of choice of surgical treatment of patients with a single kidney tumors, congenital anomalies, systemic disease, with a reduction in filtration and excretory functions, as well as with bilateral kidney damage. The analysis of clinical and diagnostic information 14647 patients, which for the period from 1988 to 2001. performed surgical treatment due to the size of RCC with less than 7 cm Education found that conserving surgery was performed only in 1401 (9.6%) patients. Worth to note that the number of execution times in the ER increased from 1988 to 2001 (4.6% and 17.6%, respectively, p <0.001). In the period 1988-1999 gg. tumor having a size of 2 cm. RP was performed in 14% of cases, and from 2000-2001. in 42% of cases. When tumor size of 2 to 4 cm. The performance of nephron-sparing surgery has increased from 5% to 20%, respectively, analogical period [31]. After the data is carried out retrospective studies, as well as their frequency of decreased PN, organ surgery for localized forms of cancer has become the standard of care [37,10] have shown. The highlight of partial nephrectomy is the clamping of the renal artery, which time has a major role in the future of kidney function. In assessing the complexity of the surgical technique of resection depend on the location of the tumor, the presence of tumor in the middle segment or have kidney gate increases during ischemia (55 min. To 34 min. In patients with the presence of tumor in the upper and lower segments (p <0.05) . Fergany according to data in 2000 on the basis of the research results of a 10-year follow-up of patients with PN was performed. of the 107 patients, 96 (90%) surgery was performed on absolute grounds, in 42 (39%) preoperative period revealed a decrease in kidney function. 5 and 10 year survival rates were 88.2% and 73%, respectively. In 52 patients (49%) had stable renal function for the weight of the observation period [17]. According to the data analysis in 1454 patients in which the PN produced or PAD, no reliable differences recurrent survival was not found in the group of patients with a tumor size of up to 4.0 cm., and in patients with tumor sizes ranging from 4.0 to 7.0 cm. Mortality at step T1a turned 2,2% and 2,6% in the PPR and PH (p = 0.8), respectively, at step T1b - 6,2% and 9%, respectively (p = 0.6). During the RRP for a long time was considered the standard in the art partial nephrectomy, it is indented 1 cm. From the edge of the tumor, to achieve intaknogo surgical margins [11].

Currently, the question of the distance from the tumor to the resection margin still remains debated. In retrospective studies conducted in 69 patients who underwent RRP was performed, Castilla et al. an 8-year period of observation it was found out that the creation of a negative surgical margin is sufficient to achieve the appearance of recurrence, regardless of its width [15]. Piper et al. write that the observed 67 patients for 60 months, which proves to achieve absence of local recurrence of the tumor enough to indent the edge of 1 mm. [38]. At present, the existing clinical guidelines of the European Association of Urology partial nephrectomy in RCC indicated for all patients with clinical stage T1, with minimal surgical indented [28].

Laparoscopic partial nephrectomy. The first partial nephrectomy using endovideosurgical technology (LPN) was performed Winfield et al. In 1992, a patient with a kidney stone. While argon coagulator was used, the operation was carried out for 6 hours. In the course of LPN noted easier postoperative period, in comparison with standard access [54]. A year later, a group of authors led by McDougall described with the first laparoscopic partial nephrectomy performed for RCC [30]. Janetschek G et al. in 2000 we conducted the OSR analysis, namely comparison of OSR (n = 73) and wedge laparoscopic partial nephrectomy (n = 25) performed 98 patients diagnosed with RCC. The average age of patients 62.3 years, median tumor - 3.8 cm in the group OSR and 1.9 cm in the group of laparoscopic partial nephrectomy wedge... According to the data presented in the group OSR average time duration of surgery was 142 minutes (86 minutes - 230 min), the average amount of blood loss - 170 ml. (0 ml - 1500 ml.), Postoperative complications - 8.0%. In the group of laparoscopic wedge resection average time duration of the operation was 163.5 minutes. (90 minutes - 300 min), the average amount of blood loss - 287 ml. (20 ml - 800 ml), postoperative complications were observed in 8% of patients. According to the histopathological study of RCC was diagnosed in 87 patients, 2 patients - oncocytomas, from 1 - kidney adenoma, and 1 unknown -metastaz other malignant tumors, in 4 - multylokulare cyst, and 1 - kidney abscess. For up to 22 months. OSR observation group and laparoscopic wedge resection not been a local recurrence without distant metastases [21]. Stifelman et al. We proposed a method for the LRS using "hands" assisted operations, based on the experience of this procedure in 11 patients. The average operation time 273 min., The average amount of blood loss 319 ml. All operations were carried out without warm ischemia, harmonic scalpel was used in conjunction with argon coagulation. The average volume of the tumor was 1.9 cm. According to the Pathology Report angiomyolipoma in 7 patients, and 4 RCC [51]. In 2003, the published data of the comparative analysis of early postoperative complications following LPN (n = 100) and RN (n = 100), 200 patients completed RCC tumor is not more than 7 cm. At the Cleveland Clinic. Mean tumor size was 2.8 cm. In the group of LRP and 3.3 cm.

In the LPN group and in the latter group was significantly greater in patients with tumors greater than 4 cm (p <0.001), with the defeat of the only kidney (p = 0.002) , more malignancies were detected (p = 0.002). Mean operative time was 3 hours and 3.9 hours in the LPN group and PN, respectively (p <0,001), blood loss - 125 ml. and 250 ml. (p <0,001), and during ischemia renal parenchyma - 27.8 minutes. and 17.5 min. (p <0.001), respectively. Functional results in both groups were comparable, the mean preoperative serum creatinine level was 1.0 mg / dL (88.4 mmol / L) and 1.0 mg / dl (88.4 mmol / L) (p = 0,52) and the average serum creatinine levels after the operation - 1.1 mg / dl (97.24 mmol / l) and 1.2 mg / dL (106.08 mmol / l) (p = 0.65) and Group PFU LPN respectively. LPN was associated with a higher frequency of intraoperative complications (5% vs. 0%, p = 0.1). According to the frequency of postoperative complications did not differ between groups (11% in the LPN group versus 2% in the PN group, p = 0.01), however, urological complications (urinary drip, kidney hematoma, haematuria) were more frequent in the LPN group [20]. In addition a group of authors led by Simmons shows that carefully selected patients with clinical stage T1b-T3a and tumors greater than 4 cm., LRS allows to achieve oncologic outcomes comparable with those after the PN. In the period from April 2001 to December 2005, 75 patients performed LPN, PN - 35 patients. Mean tumor size was larger in the group of PN (5.3 cm. Against 4.9 cm., P = 0.03), this group often detected tumor spread beyond the kidney capsule (33% vs. 9%, p = 0.006) . Median follow-up was 57 months (27 months - 79 months) in the PN and 44 months (27 months - 85 months) in the group of LPN (P = 0.1). General and tumor - specific survival in both groups were the same and amounted to 89% and 97%. Relapse-free survival was 97% in the LA group and 94% in the group of LRP (p = 0.43). Functional results were better after LPN and the average decline in glomerular filtration rate was 13 ml / min to 24 ml / min PN group (p = 0.03) [46].

CONCLUSION

Thus, the analysis of the literature shows that laparoscopic surgery technique in RCC is effective and minimally invasive techniques compared to traditional surgery. Also, the advantages of laparoscopic nephrectomy methods compared with traditional methods are a minimal incision of the anterior abdominal wall, shorter hospital stay, faster recovery and all this significantly expands the indications for treatment of volumetric endosurgical kidney structures. RP provides the best long-term results in patients with local renal cell carcinoma. Compared with radical nephrectomy preservation of renal parenchyma eliminates the inconveniences associated with the duration of survival. The most important arguments for conserving surgery for kidney cancer are clearly increasing number of small renal tumors diagnosed sizes, operative technique conserving surgery is well designed, which allows to minimize the number of complications or avoid them completely. But despite the success of surgical treatment, kidney cancer is still quite a complex disease, in diagnostic and in therapeutic terms.

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THE APPLICATION EXPERIENCE OF SIMPONI (GOLIMUMAB) IN THE SECOND LINE OF BIOLOGICAL THERAPY (AFTER INFLIXIMAB) IN THE PATIENT WITH ULCERATIVE COLITIS

ABSTRACT

The article presents the clinical case analysis of the patient with diagnosis: ulcerative colitis of overall affection with clinical-laboratory results. The effect of baseline therapy with transition to genetically engineered biological therapy with the medicine “infliximab”. The development of secondary resistance to the medicine “infliximab” and prescription of “golimumab” in the second line of biological therapy.

Keywords: ulcerative colitis, infliximab, golimumab.

INTRODUCTION

The relevance of inflammatory bowel disease (further IBD) in different regions of the world considerably varies. So, the frequency of ulcerative colitis (further UC) according to different researchers makes from 21 to 268 cases, and the Crown disease (further CD) from 9 to 199 cases per 100 thousand population, reaching the maximal indicators in the countries of Scandinavia, North America, Canada, Israel. The incidence increase of UC is 5-20 cases a year, CD - 5-15 cases a year per 100 thousand population. According to epidemiological researches abundance of IBD in the European part of Russia makes 20,4 per 100 thousand population for UC and 3,7 per 100 thousand population for CD.

It is important to note that IBD develop mainly at the young age (mean age of the patients - 20-40 years).

The peculiarity of disease incidence in our country is a triple dominance of the severe complicated IBD forms with a high lethality due to late diagnostics. IBD within the first year of the disease is diagnosed only in 25% of cases, in other cases the diagnosis was made 3-12 years since the beginning of clinical symptoms. The frequency of complications makes 55% for CD diagnosis during the period up to three years, for later diagnostics — in 100% of cases. Heavy complications develop in 29% of cases at late diagnostics of UC.

IBD is diagnosed on the basis of assessment of complaints, anamnesis, clinical picture of disease, data of a complex of endoscopic, radiological, histologic and laboratory tests.

For many years the treatment of IBD

was limited by the use of the following medicines of baseline therapy: aminosalicylates - it is sulfasalazine and derivative of 5-aminosalicylic acid (5-ASA), glucocorticosteroids (GCS), immunosupressors of both chemical and biological nature. However, approximately 35% of cases showed the steroid-resistant or steroid-dependent current of IBD and also resistance not only to hormones, but also to immunosupressive medicines is developed that leads to heavy complications, operative measures and disability of people of young working-age.

The introduction of biological medicines in the scheme of treatment of IBD allowed increasing considerably a share of the patients reaching stable remission in short terms.

MATERIALS AND RESEARCH METHODS

The patient MTV, 55 years old with the diagnosis: ulcerative colitis, overall affection of colon, at clinical remission stage.

Extraintestinal joint manifestations (polyarthritis). Nephropathy. Ambiopia OD. Incomplete complicated cataract. Astigmatism left.

From the anamnesis it is known that for the first time bloody stool with mucilage, pains and burning in anus and rectum developed after the delivery in 1981. She received conservative treatment concerning chronic anal fissure, without effect. In 1994 she was operated concerning chronic hemorrhoids, chronic back anal fissure, rectum polyp. After surgical treatment the patient noted health improvement. Since 1994 to 2000 she felt well. Since 1999 to 2000 - a personal stressful situation. In 2000 within 2 months she used tea to weight loss. The complaints of bloody stool 15 times a day appeared on the background of weight loss. The treatment of acute intestinal infection with short-term effect was carried out in central republican hospital.

In 2002 the patient's complaints were bloody stool with mucilage to 8 times a day, IBD was suspected. The patient was sent to clinical-consultation department of Republican hospital No.1 where ulcerative colitis was diagnosed (examination results were not saved). The treatment was sulfasalazine. Since 2002 to 2011 – periodic exacerbations of the disease: about 5 times a year - in the form bloody stool with mucilage, abdominal pains, weakness. She began to receive the fissile treatment since 2011 - hormonal therapy, medicines 5-ASA, periodically was hospitalized. In April, 2012 the patient was given the 3rd group of disability.

Since August 16, 2012 the patient was administered genetic-engineering therapy: infliximab (Remicade) in 300 mg introduction dose (inductive course according to the instruction – 0-2-6 week, then maintenance therapy each 8 weeks), acceptability was satisfactory.

The patient felt improvement of health on the background of the therapy – formed stool was 2-3 times a day without pathological admixtures. Rectosigmocolonoscopy at 22.11.12 after the inductive course of biological therapy: examination was done to the hepatic angle. There were liquid stool masses in the colon. Mucous transverse colon was pink, vascular pattern was traced, haustration was kept. Mucous of the descending colon was hyperemic. Mucous of the sigmoid colon was hyperemic, moderately hydropic, irregular erosive, more expressed in distal departments, no folding. Rectum mucous was hydropic, hyperemic, covered with irregular sores, fibrin, tender in contact.

Clinical remission was recorded after a year therapy of infliximab. According to rectosigmocolonoscopy data at 1.08.13: ulcerative colitis of the left colon part, moderate activity (the device was carried into the caecum head. Bauhin's valve was of lip form. The moderate liquid feces complicating detailed examination were found in the lumen of the right part of intestine. The expressed vascular pattern was throughout colon mucous, moderately hyperemic. Mucous of sigmoid colon was hyperemic, moderately hydropic, centers of ulcers and erosion remain with fibrin imposing. Rectum mucous was hydropic, hyperemic). Since January, 2014 after 11 infusions of infliximab – bleedings in the mornings, during the day – bloody stool to 8 times a day. According to the emergency symptoms the patient was hospitalized to State Budgetary Institution of the Republic of Sakha (Yakutia) Republic hospital №2, coloproctology department where the exacerbation of ulcerative colitis was diagnosed. Anti-inflammatory treatment was carried out (prednisolone, 5-ASA, azathioprine). The patient noted improvement of health (stool 3-4 times a day), dose increase of infliximab up to 10 mg/kg was recommended. The patient felt well after infliximab increased dose. Since May, 2014 the patient noted stool acceleration to 6 times a day, blood impurity, deterioration of endoscopic picture without histologic material was also noted. Medicine infliximab was cancelled due to its developed secondary inefficiency. Date of the last infusion was at 30.04.2014.

The experts concilium made the decision to change biological medicine - golimumab was chosen (Simponi) – completely human monoclonal antibody. PURSUIT research data proved its effectiveness in bionaive patients with ulcerative colitis, and also golimumab safety for patients with rhematoid and psoriatic arthritis in the second, third or fourth line of biological therapy. Injections of inductive course of 200 mg dose subcutaneously were done at 11.07.2014 and 25.07.2014. No allergic reactions to medicine were recorded.

Then golimumab was injected 100 mg subcutaneously every month, patient's acceptability was good, without undesirable reactions. There were no complaints after inductive course, stool was 1-2 times a day, without blood and mucilage. Clinical-endoscopic remission was recorded after 4 injections.

In 1,5 years of therapy there weren't complaints, formed stool was 1-2 times a day without pathological impurity. According to rectosigmocolonoscopy data at 1.12.2015 – there were a moderate degree of activity: examination was done to the descending part of colon. Folds were routine, colon tone was normal. Mucous sigmoid and rectum were 30 cm from anus hydropic, hyperemic, dim, vascular pattern was not traced with multiple subepithelial hemorrhages and surface ulcer defects were covered with fibrin, sizes from 0,2 to 0,5 cm. Multiple pseudopolyps were to 0,3 cm size in rectum.

After 19 injections of golimumab in December, 2015 the compelled break was made in biological treatment, in connection with the long-lived traumatology hospitalization of the patient (spine injury and 2,5 months of treatment). All this time clinical laboratory remission of the disease remained: stool was 1-2 times a day, without pathological impurity, blood tests without inflammatory changes.

According to the instruction of medical use of Simponi even after the miss of injection, a repeated induction was not provided therefore treatment was continued as the supporting course, the next injection was carried out on March 8, 2016, the patient felt well. Further injection was planned monthly subcutaneously in 100 mg dose.

Total 20 injections of golimumab with the considerable improvement of activity indexes of ulcerative colitis, good drug tolerance were carried out.

CONCLUSION

This clinical case shows the effectiveness of golimumab (Simponi) in the 2 line of biological therapy (after Infliximab) in patient with ulcerative colitis. The two-month break in therapy did not cause a clinical exacerbation of the disease.

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ACTUAL PROBLEMS OF THE URGENT ENDOSCOPIC TYPES OF EXAMINATION

ABSTRACT

Medical activity is impossible without organizational efforts, as well as without the information field, in organizational and tactical-strategic area, in the diagnostic phase of care. High-tech instrumental methods of examination are important in the diagnostic phase of emergency medical care. At this stage of empowerment and improving the safety of endoscopic methods of examination that contributes to effective use of existing equipment, reduce medical errors and improve the quality of the activities of health care.

In order to improve the quality of the diagnostic phase of emergency medical care, improve and enhance the safety of medical and surgical endoscopic technique we examined the possibility of urgent endoscopy in case of insufficient local training of the patient. Based on these results, algorithms and urgent fibrogastroscopy and fibrocolonoscopy we developed ways to improve the safety of medical and surgical intracavitary endoscopic procedures.

Keywords: urgency, safety, quality, endoscopy.

Topicality. Endoscopic methods of the examination of the upper and lower digestive tracts, upper and lower respiratory tracts are now widely used in medical practice. There are some instrumental methods that are used in the first place for the diagnosis of acute surgical diseases - X-ray, ultrasound, endoscopy. It is possible to do therapeutic and operational manipulations during diagnostic endoscopy that allows you to do EMF palliative or curative treatment during the diagnostic phase. Instrumental methods of examination (among other

methods) allow us exhibit the clinical diagnosis of patients with acute surgical disease in the time interval of up to 1-2 hours after treatment. The diagnosis should be accurate, complete and in time. "It is in the use of emergency diagnostic and therapeutic endoscopy, we see an opportunity to improve the results of treatment of acute diseases and their complications" (1).

Purpose of the study. 1. To develop algorithms of emergency endoscopic methods. 2. To improve (optimize) medical and operative endoscopic examinations. 3. Improve the quality of EMF hospital.

MATERIALS AND METHODS

We used fibrogastroscopes, bronchoscopes, «Olympus» company duodenofibroscopes and tools to them, electrosurgical unit. The analysis of the performance of endoscopic types of examination from 2000 to 2014 was made during our research. There are 5300 fibroezofagogastroduodenoskopies (FEGDS), 3000 bronchoscopies (FBS), 270 fibrocolonoscopies (FCC) examinations are made per year according to the research. We created the methodical recommendations "Algorithm of the endoscopist's emergency FEGDS actions" ("The algorithm of emergency FEGDS") and "Scheduled and emergency fibrocolonoscopy" and improved therapeutic endoscopic and operative manipulation.

RESULTS AND DISCUSSION

The most commonly used method was FEGDS, the total number of FEGDS on emergency indications averaged 68%. Factors leading to delay emergency FEGDS were the lack of local training and emetic syndrome. Under the provisions of "The algorithm of emergency FEGDS" it is usually performed even with insufficient local preparation with a gradual examination of the esophagus, stomach and duodenum (KDP). At the risk of aspiration of gastric contents examinations stops at any stage and the patient is sent to a gastric lavage. Thus, the endoscopist doctor assigns gastric lavage reasonably and selectively. There are 80% of cases with insufficient preparation but successful examination of the small curvature of the middle and lower third of the stomach, duodenum, and during the initial emergency FEGDS perform therapeutic and surgical methods of hemostasis in detecting ulcers complicated by bleeding lesions WOCAT. Also we could successfully remove foreign bodies and stop the bleeding from esophageal varices (esophageal varices). Timely final stop of the bleeding from the digestive tract (WOCAT) gives an opportunity of the patient's short time healing. Temporary stop of the bleeding from the WOCAT allows preparation for abdominal surgery in the most optimal conditions. Doctor does primary emergency FEGDS with WOCAT parts phased examination after the psychoprophylactic preparation of the patient in case of emetic syndrome, and in the presence of severe or uncontrollable vomiting at any stage of examination of the study is terminated and recommended the implementation of emergency FEGDS after premedication solution Cerucalum or Sibazon. Thus, the endoscopist choses the medicine which will be used next time during the second emergency FEGDS. The delay of FEGDS due to the uncontrollable emetic syndrome gives a danger of critical consequences such as heart disorders.

To improve the efficiency of providing EMI we improved therapeutic and surgical methods of endoscopic research. Based on clinical observations revealed that the most common site of intense (inkjet) bleeding from esophageal varices is a rear - left wall n / 3 of the esophagus (about 70% of cases). Knowledge of this fact allows a focused inspection, identify the source of bleeding and perform hemostasis during the initial emergency FEGDS in conditions of insufficient preparation. Ink bleeding from esophageal varices or stopped intravascular and paravasal injection of 0.7% aethoxysklerol to 1.5 ml with the subsequent installation of the probe Blackmore. In all cases, bleeding from the digestive tract (bleeding stream or jet) are performed therapeutic and surgical methods of hemostasis.

The main reason leading to the delay of emergency endoscopy in acute diseases of the colon, was the lack of local training. For a number of objective reasons (hypotension colon bowel ptosis, elongation of sigmoid, partial colonic obstruction, etc.) to spend quality local training in a short period of time is impossible. When the primary emergency FCC applied the principle of "hydrocolumns", further washed the colon through fibrocolonoscopy water to 3 liters. The use of additional washing of the colon through fibrocolonoscopy managed to significantly improve the quality of diagnosis, medical and surgical manipulation for primary emergency FCC. Also, a decrease of general intoxication, succeeded in a relatively short time to spend quality local training colon before emergency abdominal surgery, significantly reduced the need for repeated emergency preparations for colon endoscopy. The quality of the colon was evaluated by a certain scale.

Relatively often emergency indications treated patients with destructive pulmonary diseases of bacterial origin, complicated by bronchopleural fistulas. We have improved the method of Rafinsky, temporary occlusion of bronchoscopy under local anesthesia segment or segments of the bronchi with a piece of foam rubber (synthetic sponge), with bronchopleural fistulas. The main provisions Rafinsky advanced techniques were the need to soak a piece of foam rubber, folded several times and captured biopsy forceps, secret bronchi for about 15-20 seconds. When impregnating bronchus secret piece of a sealed, takes a certain shape and occlusion of the bronchial segment is performed without technical difficulties. So, along with the rubber valve bronchial blocker significantly improve the quality of treatment abscessed pneumonia, complicated by bronchopleural fistulas.

To improve the quality of intracavitary electrosurgical operations in the

digestive tract, the tracheobronchial tree, paid special attention to the power parameters and operating modes of the electrosurgical unit. When removing benign depending on the size and density of the different modes used (isolated mode “cutting” and “coagulation” or simultaneous cutting and coagulation mode - “mixed”) varied coagulation and cutting power and from 3 to 5 watts. When performing endoscopic papillosphincterotomy (EPST) the optimal parameters were the following: Mode - “mixed”, power - 3.5 watts. Observance of optimal mode of power and high-frequency current cutting (ORIMR HDTV) succeeded in carrying out an order EPST reduce bleeding from the incision area of the roof longitudinal fold BDS (according to the literature is found in an average of 2% of cases). When performing EPST not intensive bleeding venous flow were observed up to 1% of the time and were stopped irrigation solution aminocaproic acid 5% or diathermocoagulation. Perforations WPC wall were noted. Significant reduction of danger EPST complications wall perforation and duodenal bleeding, possible to expand the indications for use of the complex emergency (with the implementation of medical and surgical manipulation), endoscopic retrograde cholangiopancreatography (ERPHG). Application of the complex emergency in a timely manner to eliminate ERPHG could block the distal common bile duct and restore the passage of bile.

The most frequent localization of foreign bodies of the digestive tract was observed in the area of the upper esophageal sphincter (75% of cases). Foreign body size over 1 cm are large. The safest and less traumatic for the extraction tool is not large-sized foreign bodies (fish, meat bones) from the area of the upper esophageal sphincter is the capture of the “biped”. When removing foreign bodies of large size used clamps of various types and diathermy loop.

CONCLUSIONS

Thus, the improvement of endoscopic types of research, it was possible:

1. To expand the indications for performing emergency endoscopy of the digestive tract in case of insufficient local training of the patient (reducing failures and delays in the examination of patients).

2. Reduce the number of unwarranted prescriptions gastric lavage and, accordingly, the delay performance of the main work of the staff of the receiving department.

3. Improve the timeliness of diagnosis of acute surgical diseases (reduction of delays and failures in the hospitalized patients in the profile of the disease).

4. Improve the safety of medical and surgical endoscopy.

5. To expand the indications for use of emergency medical and surgical endoscopy patients severe category (older age, presence of concomitant diseases and competing, heavy general condition due to the development of the main complications of the disease, severe anemia with impaired hemodynamic performance of the intense jet bleeding esophageal varices and ulcers digestive tract, etc.).

6. To create conditions for qualitative preparation of patients for abdominal surgery.

7. Enhance the effectiveness of existing endoscopic equipment.

8. Reduce the timing of recovery of patients due to the palliative and curative treatment of acute surgical diseases in the diagnostic phase of the EMF and therefore improve the overall quality of care hospitals operating in emergency mode.

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