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THE COMBINED PRENATAL SCREENING WITHIN THE PRIORITY NATIONAL «HEALTH» PROJECT FOR 2012 IN THE REPUBLIC OF SAKHA (YAKUTIA)

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Results of the biochemical screening I trimester are given in Yakutia within the Health national project. The obtained data confirm high efficiency of definition of biochemical markers in the I trimester of pregnancy of formation of group of risk of chromosomal anomalies and meets the requirements of early identification of pathology of a fetus.

Keywords: pregnancy, serum markers, ultrasonography of a fetus, invasive procedures, chromosomal anomalies.

Introduction. The problem of hereditary and congenital pathology, first of all the congenital developmental anomalies (CDA) and chromosomal illnesses, continues to remain actual. The quantity of FCA in structure of the reasons of a perinatal and infantile case rate and a mortality was significantly enlarged. Chromosomal syndromes have big specific gravity in structure of congenital diseases, and the most actual is Down syndrome prophylaxis, as most frequent chromosomal pathology. The indicator of the children's invalidism in most cases caused by congenital and hereditary pathology, shows a tendency to body height [2].

The combined ultrasonic and biochemical screening is surveyed now as an obligatory method of the prenatal diagnostics referred on identification of women of groups of high risk of the birth of children with chromosomal illnesses and developmental anomalies [4]. In 2010 within actions of the priority national Health project the new section "Prenatal Diagnostics of Disturbances of Development of the Child" with financial security at the expense of agents of the federal budget which was realized in the Moscow, Rostov and Tomsk areas is included.

The large-scale organization of prenatal screening in the Republic of Sakha (Yakutia) was begun in 2011. Within the Priority national Health project "Prenatal diagnostics of disturbances of development of the child" the mass combined screening of pregnant women in terms of 11-13 weeks 6 days is begun. According to the order Ministry of Health Republic of Sakha (Yakutia) am

No. 01-8/4-196a of 01.03.2011. "About carrying out prenatal diagnostics of disturbances of development of the child in the territory of the Republic of Sakha (Yakutia)" all pregnant women living in the territory of the republic, addressed for medical observation in healthcare institutions are subject to prenatal screening.

According to the literature, the combined ultrasonic and biochemical screening in the I trimester of pregnancy allows to tap 85% of fetuses with chromosomal pathology [3]. Biochemical screening includes definition of levels of serum markers in bloods of mother - PAPP-A (the plasma protein associated with pregnancy) and free β-CGH (free β-subunit of chorionic Gonadotropinum). PAPP-A - a glycoprotein synthesized of trophoblastomas throughout all pregnancy. In combination with other biological and clinical data the lowered PAPP-A values have prognostic value for detection of certain chromosomal anomalies of a fetus. Free β-CGH - a glycoprotein produced of trophoblastomas of a placenta. On an early duration of gestation St. β-CGH stimulates function of a yellow body for synthesis and secretion of placental steroids, estrogen and Progesteronum. Level free β-CGH quickly raises in the first two weeks after conception and reaches a maximum on the 9th week and gradually goes down during the 2nd and 3rd trimester of pregnancy. Research free β-CGH is used for Down syndrome screening.

Materials and research methods. For the immunofluorescent analysis of levels of serum markers Serums of women in the I trimester of pregnancy, in term from 11 weeks to 13 weeks 6 days inclusive were used. Samples of Serum were accompanied by the direction, a blood filled before a capture. The direction contained the following these patients: demographic data; information on a blood sampling; anamnesis; the weight of the pregnant woman measured in day of delivery of a blood; data of ultrasonography of a fetus: the coccyx - the parietal size of a fetus (CRL) has to be 45-84 mm, the thickness of collar space (NTT), existence and the size of a nasal ossicle, the frequency of cardiac reductions (HR) of a fetus, in addition venous duct, a tricuspid regurgitation.

In medico genetic consultation of PNTs State Budgetary Institution Republic of Sakha (Yakutia) RB No. 1-NTsM (PNC GBU RS (Y) RB N 1 NCM) within the national project in December, 2011 the biochemical KRYPTOR analyzer (BRAHMS, Germany), carrying out definition of the PAPP-A levels and free β-CGH in Serum of the pregnant woman is put. The system is founded on the TRACE technology in which the signal which is let out with a temporary delay by an immune complex is measured. All operations are completely automated. The TRACE technology differs high precision and specificity.

The specialized software of "Astraia" (obstetric and gynecologic database) allows to calculate the combined risk of anomalies of a fetation (a Down syndrome (a trisomy 21), Edwards (a trisomy 18), Patau (a trisomy 13) taking into account the biochemical indicators defined in the double test of the

first trimester and results of ultrasonography, 11-13,6 weeks of pregnancy made in terms. Such test is called as the double test of the first trimester of pregnancy combined with NTT or the triad test of the first trimester of pregnancy. Results of calculation of the risks, received by means of the combined double dough, are much more exact, than risk calculations only on the basis of biochemical indicators or only on the basis of ultrasonography.

The software of "Astraia" is based on the algorithms developed by Fetal Medicine Foundation (FMF) and Fund of medicine of a fetus (London). The software considers qualification of experts of ultrasonic diagnostics on the basis of FMF certificate, allows conducting audit of all indicators, and also conducts a database on researches. The accounting of qualification of experts of ultrasonography theoretically excludes false hit of the pregnant woman in group of high risk that involves need of carrying out in this case unreasonable, economically expensive, having 1-2% of complications of invasive diagnostic manipulation.

The first level of prenatal screening begins with ultrasonic research and a blood sampling. Receiving a biomaterial for the first level of screening is carried out by means of vacuum test tubes for unit of Serum of Vacutainer system or similar. Then the biomaterial together with accompanying documentation is transported in medicogenetic laboratory where definition of level of serumal markers and calculation of the combined risk of chromosomal anomalies is made.

At the first stage of calculation of risk of value of concentration of PAPP-A and free β-CGH are transferred to the so-called MoM (multiple of median) characterizing degree of a deviation of this or that indicator from a median. At the following stage of calculation MoM amendment on various factors (mass of a body of the woman, an ethnic origin, existence of some diseases, smoking, multifetal pregnancy, etc.) is made. As a result so-called corrected MoM turn out. At the third stage of calculation the corrected MoM are used for calculation of risks. It allows to create group of risk and with the greatest accuracy to define individual risk. Pregnant groups of high genetic risk are referred on complex inspection to medico genetic consultation of PNTs RB No. 1-NTsM (PNC RB N 1 NCM). The prenatal medico genetic consultation, specifying diagnostics is carried out to MGC to pregnant women with use of ultrasonic research, invasive prenatal diagnostics (amniocentesis, horionbiopsiya, cordocentesis), cytogenetic researches, molecular and genetic diagnostics.

Results and discussion. In laboratory of prenatal diagnostics of MGC for 2012 it is surveyed according to the program of the combined screening of 6726 pregnant women, from them 3542 (52,7 %) are referred from districts and 3184 (43,3 %) - from Yakutsk. 1069 (15,9 %) pregnant women are aged more senior than 35 years. 246 (3,7 %) women are aged more senior than 39 years. 70 pregnant women had two at a birth. Into group of high risk entered 153 (2,3 %) pregnant women. From them 68 (44,4 %) women are aged more senior than 35 years.

Efficiency of screening is defined by its sensitivity (identification level) and specificity (level of false positive and false-negative results). Because the number of necessary invasive procedures depends on level of false positive results, this indicator isn't less important, than detectability in an assessment of efficiency of screening.

77 invasive procedures were carried out. By results of a karyotyping 17 fetuses with chromosomal pathology, including syndromes of the Down (8), Edwards (6), Shereshevsky-Turner (2), Patau (1) were taped. Thus, identification of pathology made 22%. At all ultrasonic markers were noted: NTT augmentation, hypoplasia or lack of a nasal bone.

The false-negative result was observed at one pregnant woman from Yakutsk in term of 12 weeks, results of ultrasonography and biochemical screening in norm. In the II trimester echographical markers of chromosomal anomaly of a fetus are taped, the pregnant woman refused invasive diagnostics, the child was born with a regular form of a Down syndrome.

In all cases of existence of a syndrome of Edwards at a fetus level of markers in a blood of mother was lowered and averaged 0,35 MoM for PAPP-A and 0,21 MoM for free β-CGH. It is necessary to notice that 9 (53 %) women from 17 with chromosomal pathology of a fetus of an age category were more senior than 35 years. At women at whom fetuses with Shereshevsky-Turner's syndrome were taped, the age made 21 and 22 years, respectively.

In 2012 15 children with chromosomal pathology were born, from them 14 travailled women didn't pass the combined prenatal screening (two from Yakutsk, two from Neryungri, two from the Aldan ulus, also on one of Tattinsky, Vilyuysky, Namsky, Churapchinsky, Olyokma, Ust-Aldansky, Eveno – Bytantaysky uluses). From these 14 travailled women 8 were at the age of 35-46 years.

It should be noted the high frequency of chromosomal pathology in the southern districts of Yakutia (Neryungrinsky, Aldan uluses) in recent years, frequency made nearly 1: 200 labors (on the average the frequency of chromosomal pathology makes across Russia 1: 600 labors).

It is important to notice that the combined screening in the I trimester effectively taps not only chromosomal pathology, but also group of high risk on the fetus congenital developmental anomalies (CDA). So, by our results, at a normal karyotype of fetuses, at 2 fetuses congenital heart disease and at 1 fetus – congenital developmental anomaly of the person was taped. At the level of municipal medical institutions the following problems were taped:

insufficient coverage by ultrasonic research in demanded terms with the subsequent blood sampling;

the personnel base (doctors of BRIDLES) is insufficient for continuous work of the national project taking into account territorial features;

inaccuracies in NTT and CRL assessment (NTT measurement – the equipment has to be

standardized);

non-compliance with a technique of a blood sampling at pregnant women;

mistakes in biomaterial processing;

difficulties of the organization "Cold chain" when transporting blood serum in laboratory of prenatal diagnostics of MGC.

Indicators of coverage of pregnant women are given by screening research of the main biomarkers in the table. In 2012 Momsky, Oleneksky, Oymyakonsky and Eveno-Bytantaysky districts didn't participate in screening, the lowest coverage was observed in Abyysky, Allaikhovsky, Nizhnekolymsky, Ust-Maysky, Ust-Yansky uluses. Due to the above, a larger problem in carrying out prenatal screening at the Arctic uluses in connection with the remoteness, the difficult transport scheme, insufficient personnel base.

Thus, our data prove need not only accumulation of own results for definition of normal level of markers in a blood of pregnant women of surveyed population, but also correction of MoM taking into account regional features as in the software of "Astraia" the ethnic origin of the pregnant woman on which final calculation of risk depends is considered. In the I trimester strict correlation between a duration of gestation and level of each marker [1] therefore drawing up in each laboratory of the table of measurements of indicators on a certain week of pregnancy for calculation of own values of a median is necessary is proved.

Conclusion. For rising of efficiency of prenatal screening it is necessary:

The correct organization of processes of inspection on places in the presence of the qualified experts;

24. Equipment of offices of ultrasonic diagnostics by the equipment of high and expert level.

25. Training of experts of BRIDLES and obtaining FMF certificate by them. Training and external audit according to the FMF program allows unifying methodology of ultrasonography and gives the chance to consider reliable results of the fetometers which is carried out by these experts. It finally defines accuracy of calculation of individual risk of congenital disturbances of development in the child.

26. Regional values of a median have to form a basis for calculation of individual risk of the birth of the child with chromosomal pathology.

27. Coverage by screening has to be not less than 80% of the pregnant women who were registered on pregnancies till 13 weeks.

The received results well confirm high efficiency of definition of biochemical markers in the I trimester of pregnancy. The further complex analysis is necessary for elaboration of own strategy of inspection of pregnant women. However it is already clear that prenatal screening in the I-st

trimester of pregnancy is an effective method of formation of group of risk of chromosomal anomalies and meets the requirements of early identification of pathology of a fetus.

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Number of the surveyed pregnant women on the combined screening for 2012

Referrals	Biochemical markersPAPP-A and free β-CGH
Abyskyy	6
Aldansky	186
Aldayhovsky	6
Amginsky	166
Anabarsky	23
Bulunsky	42
Vilyusky	204
Verkhnevilyusky	158
Verkhoyansky	45
Verkhnekolimsky	12
Gorniy	85
Jigansky	42
Kobyaysky	22
Lenskiy	208
Megino-Khangalassky	129
Mirninskiy	339
Momsky	0
Namskiy	232
Nijnekolimsky	4
Neryungrinsky	529
Nyurbinsky	221
Oleneksky	0
Olyokminsky	47
Oymakonsky	0
Suntarsky	146
Srednekolimsky	19
Tattinsky	113
Tomponsky	19
Khangalassky	162
Churapchinsky	215
Ust-Aldansky	156
Ust-Maysky	2
Ust-Yansky	4
Eveno-Bitantaysky	0
Total , areas	**3542**
G/O PNC RB N 1 NCM	31
KRTch PNC RH N 1 NCM	15
MGC PNC RH N 1 NCM	410
G/K PNC RH N 1 NCM	41
Polyclinic N 1	645
Yakutian State Hospital N 2	212
Yakutian State Hospital N 3	573
Yakutian State Hospital N 4	287
Yakutian State Hospital N 5	326
Polyclinic N 5	204

FGBUZ DVOMC FMBA	112
Hospital YNC SO RAMN	73
FKUZ MCC MVD	87
Other clinics	168
Total , in Yakutsk	**3184**

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