



effect of progesterone can be achieved if you take progesterone from the luteal phase, and not after a positive pregnancy test.

In pregnant women in the first trimester dydrogesterone at the recommended doses has a teratogenic effect. In the study, conducted in Israel on the basis of Maccabi Healthcare Service, which retrospectively analyzed the data for 17 years, it has been established that dydrogesterone use in the first trimester is associated with an increased risk of hypospadias, congenital CCC defects, uninhabited Bataal duct, spina bifida, as well as hydrocephaly/

Since dydrogesterone is an orally active progesterone, the structure of which differs from natural progesterone, there is danger concerning its safety for offspring.

Thus, the data of modern world investigations confirm the high efficiency of progestins use (micronized progesterone, utrozhestan) both during preconception training in women, who have had previous miscarriages, and for the purpose of treatment.

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### **PREREQUISITES FOR THE DEVELOPMENT OF DISORDERS OF THE MESTRUAL CYCLE AGAINST THE BACKGROUND OF ENDOCRINE SYSTEM PATHOLOGY**

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In the structure of gynecological diseases in adolescents and young women, a significant place occupies functional disorders of the menstrual cycle, in particular against the background of thyroid pathology.

The purpose of the study is to establish thyroid pathology the frequency of alleles and genotypes of the GP IIIa polymorphism gene in the structure of puberty menorrhagia in girls with concomitant thyroid pathology and to identify risk factors for puberty menorrhagia based on genetic analysis.

70 teenage girls, patients with puberty menorrhagia, who were treated in the gynecological department of the city clinical maternity hospital №1 in Chernivtsi, were examined. Girls were divided into two groups: I (main) – 30 teenage girls diagnosed with puberty menorrhagia against the background of concomitant thyroid pathology, the second group (comparison) – 40 teenage girls diagnosed with puberty menorrhagia. Control group – 25 almost healthy teenage girls. GP IIIa gene polymorphism (PLA1/PLA2) was studied once, after patients were included in the study, by selecting genomic DNA.

The frequency of alleles and genotypes A1A2 of polymorphism of the GP IIIa gene was conducted in adolescents with menorrhagia, including thyroid pathology and in healthy teenage girls. It was found that the incidence of occurrence "wild" A1 allele of the GP IIIa gene in teenage girls with menorrhagia is 2.41 times greater than "mutant" A2 allele: 99 (70.7%) 41 (29.3%) cases of 140 allocated alleles ( $\chi^2=9.64$ ,  $p=0.002$ ). A similar trend was observed in the control group: A1 identified in 35 (70.0%) cases, which were 2.33 times more frequent than A2 alleles – 15 (30.0%) cases of 50 allocated alleles ( $\chi^2=5.63$ ,  $p=0.018$ ). The resulting distribution by observation groups mirrored the total in the surveyed population, where prevailed "wild" allele over the "mutant" in 2.39 times ( $\chi^2=9.01$ ,  $p=0.003$ ).

Genotype distribution thyroid pathology owed that A1A1-genotype is more likely to be registered in adolescents with puberty menorrhagia than 1.25 times ( $\chi^2=10.14$ ,  $p=0.001$ ). By contrast, the relative frequency of A1A2-genotype, on the contrary, prevailed in the control group of 1.45 times ( $\chi^2=12.03$ ,  $p<0.001$ ). Homozygote mutation A2A2 was registered only in teenage girls with menorrhagia – 8.6% ( $n=6$  people). The relative frequency of "wild" A1 allele probably prevailed over the A2A2 genotype at 7.5 times ( $\chi^2=45.6$ ,  $p<0.001$ ).

Epidemiological analysis of the risk of puberty menorrhagia against the background of pathology of thyroid depending on genotypes and alleled state of the GP IIIa gene thyroid pathology owed an incorrect increase in the likelihood of their appearance in carriers A2A2-, A1A2-genotypes and A2 allele in 1.33, 1.24 and 1.27 times, respectively (OR=1.37-1.46,  $p\geq 0.05$ ), for the lowest chances of menorrhagia in adolescents without the disease (OR=0.69-0.73,  $p\geq 0.05$ ). Instead, A1A1-



genotype and A1 allele was associated with puberty menorrhagia without concomitant pathology of the thyroid (OR=1.60 and OR=1.40,  $p>0.05$ ), with a low probability of their occurrence against the background of diseases (OR=0.63,  $p>0.05$ ).

In adolescents with menorrhagia without thyroid disease, the A1A1 genotype occurs 11.7% more frequently than those with thyroid disease ( $\chi^2=4.01$ ,  $p=0.041$ ) and 15.0% more frequent than in the control group ( $\chi^2=4.54$ ,  $p=0.033$ ). Whereas in girls with menorrhagia and thyroid pathology, the relative frequency of A1A2-genotype is 9.2% ( $\chi^2=3.97$ ,  $p=0.052$ ) and A2A2 genotype by 2.5% ( $p>0.05$ ) above these in adolescent groups. Among girls with puberty menorrhagia, menorrhagia is 10.0% more likely to occur carriers of A1A1-genotype, control ( $\chi^2=9.86$ ,  $p=0.002$ ), while controlling 18.6% more heterozygote carriers A1A2-genotype than in both surveyed groups ( $\chi^2=12.03$ ,  $p<0.001$ ).

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### **EVALUATION OF SPECIFIC PREGNANCY PROTEINS FOR PREDICTING EARLY REPRODUCTIVE LOSSES IN WOMEN INCLUDED IN THE ASSISTED REPRODUCT PROGRAM**

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Among the main causes of reproductive losses in patients with infertility included in the program of assisted reproductive technologies an important place belongs to the local premature detachment of the chorion accompanied by the development of placental dysfunction, involuntary termination of pregnancy and with its preservation - a high frequency of fetal distress, intrauterine growth retardation and perinatal morbidity and mortality.

The aim of the study was to assess the levels of specific pregnancy proteins (free estriol,  $\beta$ -chorionic gonadotropin and PPAR-A) in the serum of patients with induced pregnancy complicated by local non-progressive chorionic detachment and their fluctuations during the first trimester of pregnancy.

We conducted a clinical-laboratory and ultrasound examination of 60 patients with infertility included in the program of assisted reproductive technologies and with clinical signs of non-progressive retrochorial hematoma during gestation from 6 to 16 weeks of pregnancy (main group). The control group was consisted of 30 women without a complicated gestational period. Serum hormonal studies for placental proteins of free estriol,  $\beta$ -chorionic gonadotropin and pregnancy-associated plasma protein-A were performed in the dynamics of pregnancy at 9-12 weeks and 16-18 weeks using the method of enzyme-linked immunosorbent assay.

According to the results obtained in the dynamics of the first half in women with physiological pregnancy, significant deviations should be considered only in relation to the level of free estriol, which increased by 31.2% in the dynamics of the first trimester of pregnancy. In 69.5% of women in the main group at 8-9 weeks of pregnancy, the concentration of PPAR-A pregnancy protein increased 2.1 times against the control data, and the concentration of free estriol and  $\beta$ -chorionic gonadotropin levels remained virtually unchanged.

Evidence of the above changes is the data of ultrasound evaluation of embryonic structures in this category of women. The following echographic signs of pathology of embryonic structures were revealed: amniotic hypoplasia in 12.8% of patients, chorionic hypoplasia in 17%, fragmented chorion in 9.65%, chorionic presentation in 36.82%, uniform echogenicity of extraembryonic cavities - in 2.8%. The presence of unidirectional changes in the concentration of major markers during the physiological course of pregnancy, while multidirectional changes, primarily PPAP-A and  $\beta$ -chorionic gonadotropin, can predict a complicated course of pregnancy.

The most important for predicting a satisfactory course of pregnancy in the first trimester are ultrasound markers of pathology of the embryo and extraembryonic structures in combination with data from the biochemical panel of pregnancy proteins.