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Optimization of preconception preparation in women with a disorder of menstrual function regularization in anamnesis

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Abstract

Literary data show that with a complicated premorbid background accompanied by endocrine dysfunction, the proportion of placental insufficiency and disorder of the prenatal development are increased; the number of perinatal complications, operative delivery and negative postnatal effects constantly grows. The purpose of the study is to develop a program of preconception preparation of patients with a disorder of menstrual function regularization and to assess its effectiveness in improving the hemodynamic potential of the uterus and ovaries at the preconception stage.

Materials and methods of the research: To evaluate the effectiveness of the proposed modified program of preconception preparation, all patients were divided at random into two groups – the main (40 patients), where the complex metabolic therapy with the use of L-arginine aspartate with vitamin B8 (inositol) was employed, as well as the comparison group (40 patients) with a standard approach to preconception preparation.

Results of the study and their discussion: The results of monitoring the level of growth factors in the cervical mucus of the patients in the main group showed the approximation of these criteria to the reference limits in 67.5% of observations, along with improvement of hemodynamics of the uterus in more than half of the examined women. Implementation and use of the modified protocol of preconception preparation in patients of the main group contributed to significantly higher indices of clinical pregnancy, its prolongation, and the birth of living children against the data of the comparison group. It should be noted that the proportion of early toxicosis was reduced by 2.2 times, retrochoric hematoma – 1.8 times; involuntary miscarriages and non-developing pregnancies, as well as the number of coagulation disorders, were also lower.

Conclusions: Assessment of the dynamics of the level of growth factors in cervical mucus even at the preconception stage gives an opportunity to predict deep injuries of the vascular endometrium and can be used to control the effectiveness of preventive measures in women at risk. The development and implementation of a comprehensive diagnostic system for the endometrial factor, an assessment of the mechanisms of the synthesis of growth factors, an optimized program of preconception preparation and pathogenetically arranged hormonal support have contributed to a reduction of early reproductive loss and prolongation of pregnancy in this category of patients.

Keywords: a disorder of menstrual function regularization, miscarriage, growth factors, nitric oxide donors, inositol

Introduction

Literary data show that with a complicated premorbid background accompanied by endocrine dysfunction, the proportion of placental insufficiency and disorder of the prenatal development are increased; the number of perinatal complications, operative delivery and negative postnatal effects grows^[1, 2]. Due to the immaturity of neuroendocrine regulation in women with a disorder of menstrual function regularization, insufficient secretion of gonadotropins, ovarian tissue dysfunction and disturbances in steroid hormonal secretion are observed, which may be one of the causes of hyperplasia or hypoplasia of the endometrium, increased vascular wall penetration, hemodynamic disorders of the vascular system of the uterus and ovaries, inferiority of its neuro-receptor apparatus^[5]. Actually, defective trophoblast invasion and disorders of remodeling of spiral arteries affect the placental perfusion and lead to the development of placental dysfunction even at the early stages of gestation^[2, 4-6]. It is known that proangiogenic and anti-angiogenic factors that directly influence the processes of migration and invasion of trophoblast cells are involved in controlling the growth and development of chorion and placenta^[2, 4-6]. During the course of physiological pregnancy, proangiogenic and anti-angiogenic factors are in the balance state, providing adequate

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implantation and placentation necessary for further prolongation of pregnancy. The severity of the imbalance of vascular factors that accompanies implantation disorder, the development of placental dysfunction and negative perinatal effects determine the depth of vascular disorders in the utero-placental complex, as well as the severity of placental disadaptation, which depend on the rate of development of this imbalance and compensatory and adaptive capabilities of the maternal organism [5, 7]. However, nowadays, scholars disagree on the role of certain growth factors regulating vascularization of the endometrium in the genesis of reproductive losses, and the lack of clear clinical practice guideline for the diagnosis and therapy of implantation dysfunction requires the search for new ways to correct the impaired preimplantation background in such patients, which, undoubtedly, would allow to develop more effectively the treatment programs for many pathological conditions of the reproductive system [1-3, 5]. All of the mentioned above stipulates the relevance of the practical aspect of the planned scientific research, since it will make sense to take a step closer to the development of new approaches to reducing the number of reproductive losses in patients with a disorder of the menstrual function regularization in anamnesis.

The Purpose of the Study is to develop a program of preconception preparation of patients with a disorder of menstrual function regularization and to assess its effectiveness in improving the hemodynamic potential of the uterus and implantation capacity of the endometrium at the preconception stage.

Materials and Methods of the Research.

In this study, at the preconception stage and in the 6-12 weeks of pregnancy, an examination was carried out on 80 women with a disorder of menstrual function regularization in their case histories. To assess the effectiveness of the proposed modified program of preconception preparation, all patients were divided at random into two groups – the main (40 patients), and the comparison group (40 patients), depending on the treatment program that was applied. The key points of the modified preconception program were metabolic therapy aimed at improving microcirculation, trophics and hemodynamics of the uterus and endometrium (L-arginine aspartate, a vitamin-mineral complex containing a therapeutic dose of folate, polyunsaturated fatty acids in a complex with vitamin B8 (inositol). A prerequisite for using the proposed complex was the following principle. In the last decade, a significant role has been given to myo-inositol in most metabolic processes, and the number of publications on the study of its biological, metabolic, pharmacological and clinical uses in various fields of medicine is approaching 40,000. The main pharmacological positive effects appropriate at the stage of preconception preparation in this category of patients are normalization of cholesterol, decreased tendency to thrombophilia, activation of egg division, normalization of lipid metabolism, prevention of atherosclerosis, antidepressant and adaptive effect [8]. The use of the aforementioned complex and hormonal support was based on existing data obtained as a result of the literary analysis [3, 4, 7]. In the comparison group at the preconception stage, recommendations have been used in accordance with the national standards of the Ministry of Health of Ukraine. In the course of scientific research we have used general-clinical, functional and instrumental methods of examination,

assessment of the pelvic organ blood circulation, echographic markers of endometrium, and also the investigation of the level of proangiogenic growth factors in cervical mucus – vascular endothelial growth factor A (VEGA) and placental growth factor (PIGF) as markers of implantation impairment [5-7] by immunoassay using test kits BIOSOURCE (USA) on a MULTILABEL COUNTER 1420 (Denmark) photometer. For an objective judgment about the degree of validity of the results of the study, a variational-statistical method for analyzing the obtained results using the application and the package STATISTICA for Windows®-6.0 has been used.

Results of the Study and Their Discussion

The study of growth factors in women with a disorder of menstrual function regularization in their case histories showed the low secretion of these transmitters, along with the impairment of hemodynamics in the uterine vessels, which undoubtedly plays a significant role in the pathogenesis of probable early reproductive losses, the number of which in this category of patients was 2.6 times higher than control data. In this group of women, there was a disturbance of the production of angiogenesis markers, starting with the preconceptional phase, by 4.0 times compared with control, moreover, such tendency is noted in the dynamics of the whole monitoring during the first trimester of pregnancy ($p < 0.05$).

Estimation of hemodynamic parameters of the uterus revealed that the visualization of the main branches of the uterine, radial and basal arteries was recorded in 83.75% of cases and in 16.25% of observations only the spiral arteries of the venous type were detected. A comparative assessment of the blood flow in the uterine arteries revealed the marked changes in the form of retrograde early diastolic blood flow in 17.5% of women, moreover, these changes were bilateral, and in basal and spiral arteries there was the increase of vascular resistance rates in 26.25% of cases. Ultrasound scan of the terminal branches of the uterine arteries revealed a direct relationship between the thickness of the endometrium and the blood flow profile in the spiral and basal arteries.

Results of the monitoring of the growth factors level in the cervical mucus of the patients in the main group at the preconception stage and in the first trimester of pregnancy showed the approximation of the criteria to the reference limits in 67.5% of cases, along with the improvement of the hemodynamics of the uterus in more than half of the examined women, which allows to propose the mentioned methods of the research to assess the resulting quality of preventive measures and the effectiveness of preconception preparation in this category of women.

It should also be noted that as a result of the introduction and use of the modified protocol of preconception preparation in patients of the main group, there were probably higher rates of the clinical pregnancy onset, its prolongation and the delivery of living children compared to the comparison group that received standard protocols without additional metabolic, antioxidant and an gioprotective influence ($p < 0.01$).

The analysis of the first trimester of pregnancy allowed to register a significant proportion of complications; involuntary miscarriage, non-developing pregnancy and anembryony were noted only in the comparison group, the proportion of early toxicosis was 2.2 times lower and the retrochoric hematoma – 1.8 times compared to the data in the comparison group ($p < 0.05$), the reduced proportion of coagulation disorders should also be mentioned. These positive points should be

explained as an adequate approach to hormonal support using droidogestron, which has an immunomodulating effect capable of normalizing the embryo-endometrial dialogue, as well as improving implantation potential and adaptation of trophoblastic transformation and implantation through correction of endothelial dysfunction.

Conclusions

Thus, the assessment of the dynamics of growth factors level even at the preconception stage in cervical mucus provides an opportunity to predict deep injuries of the vascular membrane of the endometrium and can be used to control the effectiveness of preventive measures and preconception preparation in women at risk.

Summing up and summarizing the results of the conducted research, it can be concluded that the development and implementation of a comprehensive diagnostic system for the endometrial factor, the evaluation of mechanisms for the synthesis of growth factors, optimized preconception preparation program and pathogenetically arranged hormonal support contributed to reducing the number of early reproductive loss and prolongation of pregnancy in this category of patients.

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