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# Chronic Endometritis in Terms of the Results ofiIn Vitro Fertilization Programs

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**Abstract**: The frequency of cholecystectomy in unsuccessful pregnancies in the IVF and PE program is 51.8%, of which 81.3% are patients with tuboperitoneal factor infertility.

The sensitivity and specificity of anamnestic risk factors are compared with the data of hysteroscopic examination with separate diagnostic curettage and histological examination of the contents of the uterine cavity as methods of examination of CE in combination with ultrasound diagnostic methods and tubular biopsy of the uterine cavity. .

The microbial landscape of the uterine cavity in patients with a history of unsuccessful pregnancy in the IVF and ET program against the background of cholecystectomy is mainly represented by associations of opportunistic microorganisms and viruses. However, in the group of patients with a history of implantation failure in the IVF program, bacterial contamination in the uterine cavity and in the cervical canal ($p = 0.091$) was 5.6% and 1.5%, respectively. it was 48.6% and 16.4% ($p < 0.001$).

Based on the microbial landscape of the uterine cavity, the state of the receptor apparatus, the thickness of the endometrium and the state of blood flow in the endometrial vessels, the algorithm of recommended medical actions in patients with implantation failure in IVF. In the background of cholecystectomy, the program allows to increase the effectiveness of subsequent ART programs.

**Key words:** Monoclonal antibodies to estrogen and progesterone receptors, Van Gieson, Mycoplasma genitalium, cytomegalovirus.

For all patients in this group, anamnestic data was collected, examination was carried out, including: assessment of the microbial landscape of the vagina and cervical canal using smear microscopy, polymerase chain reaction (PCR) test for the presence of Chlamydia trachomatis, Ureaplasma. urealyticum, Ureaplasma parvum, Mycoplasma genitalium in the cervical canal,

cytomegalovirus, Herpes simplex virus types 1 and 2, study of the quality of the endometrium and the composition of the uterine cavity by hysteroscopy, endometrial biopsy, followed by histological, immunohistochemical analysis of the endometrial scraping, bacteriological examination. Hysteroscopy was performed on days 5-10 of the menstrual cycle using a Storz hysteroscope according to standard methods. Endoscopic criteria for the diagnosis of "chronic endometritis" are local or diffuse hyperemia of the endometrial surface, against the background of which white foci located in the center and endometrial tumors are detected. After separate diagnostic curettage of the uterine cavity and cervical canal, hysteroscopy was performed. Endometrial biopsy was performed on days 5-10 of the menstrual cycle as a method of assessing the quality of CE therapy. There is no need to expand the cervical canal to insert the tube into the uterine cavity, the procedure is atraumatic, painless and performed on an outpatient basis; Thus, aspiration tube biopsy of the endometrium has several advantages over diagnostic curettage of the uterine cavity. The contents of the uterine cavity, obtained by the above two methods, were sent for histological examination, after appropriate processing and paraffin embedding of sections stained with hematoxylin and eosin and Van Gieson. Morphological criteria for the diagnosis of "chronic endometritis" depending on the characteristics of general and tissue reactivity, the duration of the disease, the presence of exacerbations and their severity [10]:

Inflammatory infiltrates, consisting mainly of lymphocytes, neutrophilic leukocytes, are often located around glands and blood vessels, less common;

presence of plasma cells;

changes in the endometrial stroma.

Immunohistochemical examination of endometrial tissue was also performed using monoclonal antibodies to estrogen and progesterone receptors (Novocastra, UK; DAKO, Denmark; Epitomics, USA). Detection systems LSAB2 (DAKO, Denmark), KP-500 (Diagnostics BioSystems, USA). The following quantitative criteria (level) were used: absence of positively labeled cells - 0, up to 20% - 1, up to 40% - 2, up to 60% - 3, up to 80% - 4, up to 100% - 5. In addition, according to the level of staining intensity: low, medium, high intensity.

All patients in the study group underwent ultrasound examination to determine blood flow in endometrial vessels (Voluson 730 Expert device, resistance indices (RI) of basal, spiral, arcuate and uterine arteries were evaluated in 3D mode).

According to the results of histological examination of the contents of the uterine cavity, the main group (group Ia) of 72 patients diagnosed with CE was determined, its etiology and the state of receptors of the endometrium were determined. 67 patients with a history of unsuccessful embryo implantation in the IVF program, who did not suffer from chronic endometritis, formed the control group (group Ib).

An algorithm for examination, treatment and preparation for conception of patients with a history of failed embryo implantation in the IVF program against the background of cholecystectomy was developed. At the same time, 41 patients who made up the main group (IIa) underwent etiotropic treatment (if necessary), control hysteroscopy or pipel biopsy of the endometrium and a complex of preparation for conception before entering the next IVF protocol.

The control group consisted of 31 patients (IIb) who had one or more failed IVF attempts against the background of cholecystectomy, who refused treatment or underwent a standard course of anti-inflammatory therapy.

**Results and its discussion**

After histological examination of the contents of the uterine cavity after hysteroscopy, as a "golden" standard for the diagnosis of CE, its frequency was 51.8% of patients with a history of unsuccessful embryo implantation in the IVF program. Infertility factors were also analyzed in patients in the study group, in this group the tuboperitoneal factor was 81.3%; In the group of patients with a history of unsuccessful embryo implantation in the IVF program, the diagnostic sensitivity of pipette biopsy after histological examination for the diagnosis of CE is 98.6% and the specificity is 97.0%. Thus, pipette biopsy after histological examination with high sensitivity and specificity can be used to diagnose CE. All patients underwent ultrasound examination to determine the blood flow in the endometrial vessels during the expected implantation window (5-6 days after ovulation). 78.5 ± 5.0% of non-CE patients had intact blood flow, while 43.7 ± 5.8% ($p < 0.001$) of CE had affected blood flow. In addition, in this group of patients, the decrease in blood flow in the basal arteries was 56.3 ± 5.8%, in the control group it was 21.5 ± 5.0% ($p < 0.001$) (Fig.

The state of blood flow in patients in the main and control groups of the study

In the comparative assessment of the microbial landscape of the uterine cavity in the main study group, chlamydial contamination of the uterine cavity was 8.3 ± 3.3%, and none of the patients in the control group had chlamydia in the uterine cavity. . this was also statistically significant ($p < 0.01$). During bacteriological examination of the contents of the uterine cavity, bacterial contamination in patients with CE was 48.6 ± 5.9%, in patients without CE - 16.4 ± 4.5% ($p < 0.001$). In addition, contamination with enterococci prevailed (30.2%) in patients of the main group, while Enterococcus faecalis and Staphylococcus epidermidis were detected with equal frequency in 26.7% of patients without CE. No statistically significant differences were found between the intensity of proliferation of progesterone (PR) and estrogen (ER) receptors in stroma and glands in patients in the main and control groups of the study. But when using the correlation method of the study using the Spearman coefficient, a direct average correlation was found between the preserved blood flow in the endometrial vessels and the intensity of distribution of ER in the glands and stroma of the endometrium, as well as the intensity. distribution of PR in the stroma (+0.421, +0.475 and +0.514, respectively). With a decrease in blood flow in the basal vessels of the endometrium, an inverse correlation of the average strength with the scattering intensity of ER and PR in the endometrial stroma (-0.421 and -0.475, respectively) was revealed,

as well as weakness. correlation with the intensity of distribution of ER in endometrial glands is -0.296.

Based on the summarized literature data on the use of antibacterial therapy, infusion therapy [6], physiotherapy [7], ozone therapy [8], acupuncture [9] for patients with CE [5] in this category of patients. , as well as the results of research, and It has the effect of a number of anamnestic data, the state of the microbial landscape of the uterine cavity, the receptivity and vascularization of the endometrium according to the ultrasound examination, and the development of CE. Developed a pre-conception training program for patients with a history of failed embryo implantation in the IVF program.

**Choosing a method of hormone therapy**

In patients with a thickness of the endometrium after ovulation (more than 8 mm) and for patients with normal blood flow in the endometrial vessels, IR is not more than 0.48 in basal arteries, 0.38 in spiral arteries, IR 0.64 in arcuate arteries, IQ in the uterine artery. 0. 8) when conducting Doppler measurements on days 20-22 of the menstrual cycle, dydrogesterone was prescribed 10 mg orally 2 times a day on days 16-25 of menstruation as a preconception preparation).

In patients with a decrease in endometrial thickness (less than 6-8 mm) after ovulation, the drugs of choice are Femoston 2/10 orally for 28 days from the 1st day of the menstrual cycle, 1 tablet once a day with the addition of dydrogesterone. 10 mg 1 time per day from 16 1 to 25 days of the menstrual cycle or phase hormone therapy with drugs: oral estradiol 2 mg 1 time per day from 1 to 15 days of the menstrual cycle and dydrogesterone 10 mg 2 times per day. 16-25 days of the menstrual cycle.

Patients with a combination of a decrease in the thickness of the endometrium and a decrease in blood flow in the vessels of the endometrium due to hormone replacement therapy were prescribed an acupuncture course, as well as a complex, with the selection of acupuncture points aimed at improving blood flow in the uterus. metabolic therapy.

Patients in the comparison group were prescribed oral contraceptives 1 tablet once a day from the 1st day of the menstrual cycle for 21 days during the pre-contraceptive preparation phase.

Metabolic therapy for CE is aimed at improving tissue metabolism, activating energy processes in cells, eliminating the consequences of tissue hypoxia, including the transition from anaerobic to aerobic glycolysis [2].

Intravenous administration of 5% - 5.0 ml of Riboxin with 2% - 10.0 ml of glucose 5% - 200 μm of ascorbic acid is used as metabolic therapy. Deproteinized hemoderivative of calf blood (Actovegin) 5.0 ml (200 mg) intravenously in 200 ml of physiological solution for 5 procedures daily. Then, as a second step, Actovegin tablets (200 mg) were prescribed 3 times a day until the result was obtained in the IVF protocol. Our experience has shown that the use of Actovegin in patients with cholecystitis can increase the efficiency of IVF programs due to its metabolic effect, that is, increasing the transport and use of glucose and oxygen by tissue cells.

All patients with unsuccessful pregnancy in the IVF and ET program against the background of cholecystectomy were divided into two groups. IIa - the main group of 41 patients with cholecystectomy, who underwent the recommended preconception program before the second attempt at IVF and PE; IIb - the control group, which included 31 patients who had one or more failed attempts at IVF and PE due to chronic endometritis and refused or opted for the recommended therapy. The efficiency of the second attempt at IVF and ET was evaluated after the detection of a fertilized egg in the uterine cavity and was 92.7 ± 5.6% in group IIa, and 26.7 ± 6.1% in group IIb , which is statistically significant ( $p < 0.001$). The implemented complex of preparations for conception had a 46.61% ($\alpha < 0.01$) effect on the efficiency of repeated attempts in IVF and PE: 8.56% ($\alpha < 0.01$) with the use of complex metabolic therapy.

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