

Pregravid preparation of women with chronic endometritis in IVF cycles

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ABSTRACT

Aim: of our study was to improve the pregravid preparation of women with chronic endometritis to develop individual approaches to overcoming infertility, taking into account the state of endometrium.

Materials and Methods: The study included 90 women (main group, n=90), 28 to 38 years with an anatomically normal uterus and chronic endometritis (CE). Patients were divided into 2 groups: group I – 45 women with CE who received conventional treatment; group II – 45 women with CE who received pregravid preparation by subendometrial injections of Platelet-Rich Plasma (PRP).

Results: At the first stage of study, the ART statistical reports from 2015 to 2022 were analyzed at the Medical Center of Reproductive Health «Damia», (Ivano-Frankivsk). Analysis of the vaginal flora parameters before treatment at the first stage revealed the presence of conditionally pathogenic flora in culture from the cervical canal (*Candida albicans* – 2.4%, *Escherihia coli* – 4.8%, *Staphylococcus epidermidis* – 6.2% *Enterococcus faecalis* – 6.9%), and was evidence of a possible recurrence of inflammation during gestation. In the age category, the groups of patients were homogeneous, with no significant differences by the level of AMH and the level of CD 138. Biochemical pregnancy be present in 20 patients (44.4%) of group I and 28 (62.2%) of group II. Fertility within a year after the end of therapy was restored with the proposed method of therapy in most women (51.1%), in the comparison group this number was 11.1% lower. Pregnancy rate between the groups (I and II) did not differ significantly. The number of live births in group II — 19 births (42.2%) — was 2 times higher than I group (9 (20.0%), $P<0.05$). The most common complication for women in the comparison groups was early pregnancy loss. Among 18 (40.0%) clinical pregnancies of group I, 8 women (17.8%) had early miscarriage, 1 ectopic pregnancy (2.2%), while in group II clinical pregnancy be present in 23 women (51.1%). The number of terminated pregnancies was two times lower than in the first group (8.9% vs. 17.8%, $P<0.05$).

Conclusions: Chronic endometritis is one of the main causes of pregnancy loss after in vitro fertilization. Patients of the second group were treated with the proposed method of subendometrial injections with Platelet-Rich Plasma (PRP), prepared from autologous blood, is an effective method of preparing the endometrium for embryo transfer and can increase the number of live births in patients with chronic endometritis.

KEY WORDS: chronic endometritis, Platelet-Rich Plasma, miscarriage, CD 138

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INTRODUCTION

Infertility, miscarriage, especially in the early stages, have a leading place in the causes of low birth rates associated with medical problems. The frequency of this pathology does not tend to decrease and, conversely, during wartime it becomes not only a medical, but also a global social problem of Ukraine [1].

One of the main tasks of the Health Service of Ukraine during the war and economic problems is to preserve every desired pregnancy and the birth of a healthy child. In 2023, the number of pregnancies decreased by 2 times. Infertility, miscarriage, especially in the early stages, have a leading place in the causes of low fertility associated with medical problems. The frequency of this pathology does not tend to decrease, and conversely,

during wartime, the divorces of young couples, military losses of young men of reproductive age, forced emigration of young women abroad, the problem of preserving each pregnancy and creating conditions for its development becomes not only a medical but also a global social problem of Ukraine.

Health of the maternal organism and uterine cavity itself, — the site of the first meeting of the embryo and pregravid endometrium, is extremely important for the normal development of gestational sac. Today, chronic endometritis (CE) is one of the leading causes of unsuccessful ART, the causes of silent miscarriage in the early stages [2].

According to world studies [2, 3, 4], CE is the result of bacterial-viral contamination of the endometrium

and loss of the ability of local immunity and specific and nonspecific defenses of the woman's body to resist pathogens. The last decades are characterized not only a change of genital infection pathogens (viral infection and opportunistic microflora took the first place), but also a change in the clinic of inflammatory processes (primary latent course without clinical manifestations) [5]. Treatment of infertility in patients with chronic endometritis is accompanied by disorders of the morpho-functional state of the endometrium, which requires the development of minimally invasive diagnostic methods and an individualized treatment method for pregravid preparation of the endometrium for embryo transfer, a means to increase the live births in this category of patients.

In reproductive medicine, there are known facts about the effect of Platelet-Rich Plasma (PRP) on endometrial proliferation. The effectiveness of PRP therapy for endometrial proliferation in chronic endometritis remains very interesting. The question of the effectiveness of PRP therapy for endometrial proliferation in chronic endometritis remains very interesting [1, 5, 6, 7].

Due to platelet activation in PRP, growth factors such as vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), platelet-derived growth factor (PDGF), transforming growth factor (TGF), and cytokines become biologically active and are secreted within 10 minutes of clotting [8, 9, 10, 11].

All of the above biologically active substances stimulate the growth and transformation of endometrial cells, participate in tissue regeneration; in the regulatory cell migration, reconstruction of the extracellular matrix; in cell proliferation and cell differentiation; in angiogenesis [6, 8, 9, 12, 13].

Since PRPs are derived from autologous blood, is minimized the risk of disease transmission, immunogenic reactions. Platelet-Rich Plasma has already become widespread in ophthalmology, orthopedics and surgery for wound healing [1, 4, 7, 11, 12, 14, 15].

AIM

The aim of our study was to improve the pregravid preparation of women with chronic endometritis to develop individual approaches to overcoming infertility, taking into account the state of endometrium.

MATERIALS AND METHODS

The study included 90 women (main group, n = 90), 28 to 38 years with an anatomically normal uterus and chronic endometritis (CE). Diagnostic criteria for CE in infertility women were a hysteroscopic picture of

endometrial micropolyps, local or diffuse endometrial hyperemia, «strawberry symptom» [4] and expression of the CD 138 proliferation marker according to the results of an immunohistochemical study of endometrial biopsy.

Patients were divided into 2 groups: group I – 45 women with CE who received conventional treatment; group II – 45 women with CE who received the proposed treatment. The patients of the second group were treated with the proposed method of administering Platelet-Rich Plasma (PRP) by subendometrial injections using a Kitazato OPU needle 325 mm through the operating channel of the Bettocchi 5 mm hysteroscope in first half of the proliferative phase of the cycle (4–6 injections). Platelet-Rich Plasma was prepared from autologous blood. Blood was drawn from the peripheral vein into an anticoagulant tube and processed by separating different blood components by a modified two-stage centrifugation method [3]. Patients of the second group were familiarized with the treatment method and signed a voluntary informed consent to the procedure.

The control group consist of 25 healthy women at the preparation for motherhood with a male factor of infertility.

Statistical analysis was performed using Statistica 10.0.

RESULTS AND DISCUSSION

At the first stage of the study, the ART statistical reports from 2015 to 2022 were analyzed at the Medical Center of Reproductive Health «Damia», (Ivano-Frankivsk). 600 cycles in women who underwent artificial insemination in vitro were analyzed. The main group of women who had confirmed chronic endometritis was identified.

All patients of the main group underwent antibacterial treatment to correct the microbial biotope of the vagina, depending on the identified pathogens. As antibacterial therapy, classical schemes of combination of broad-spectrum antibiotics with metronidazole and (or) clindamycin with presence of an anaerobic component were used.

Analysis of the vaginal flora before treatment at the first stage revealed the presence of conditionally pathogenic flora in culture from the cervical canal (*Candida albicans* – 2.4%, *Escherihia coli* – 4.8%, *Staphylococcus epidermidis* – 6.2% *Enterococcus faecalis* – 6.9%), and was evidence of a possible recurrence of inflammation during gestation. Conventional treatments have been shown to effect. In the endometrial aspirates from women of the main group, the pathogens was not found, which indicates a good effect of the proposed preventive and therapeutic method.

Table 1. Clinical results of in vitro fertilization in women with chronic endometritis after embryo transfer depending on the pregravid preparation of the endometrium

Group	Clinical pregnancy		Live birth		Miscarriage		Ectopic pregnancy	
	Abs.	%	Abs.	%	Abs.	%	Abs.	%
Group I (n=45)	18	40.0	9	20.0*	8	17.8*	1	2.2
Group II (n=45)	23	51.1	19	42.2	4	8.9	0	0
Control group (n=25)	25	100	24	96.0	5	20.0	1	4.0

Note: * - $P < 0.05$ – the significance of differences between indicators of groups I and II

Pregravid preparation of the second group patients began in the absence of sexually transmitted infections, and included, besides the traditional use of folates, PRP therapy by subendometrial injections for the immunomodulatory, antiviral action and blocking production of anti-inflammatory cytokines.

Patient reproductive history questionnaires were evaluated prior to pregravid preparation.

The groups of patients were homogeneous in the age category, with no significant differences by the levels of AMH and CD138. Biochemical pregnancy occurred in 20 patients (44.4%) of group I and 28 (62.2%) of group II. Embryo transfer was performed, respectively, one cycle after subendometrial injections with Platelet-Rich Plasma (PRP) in a standard endometrial preparation protocol prior to transfer of cryopreserved embryos: transdermal estradiol at 1 g per day from Day 5 of the cycle, ultrasound was performed from Day 10 to Day 13, if the endometrium reached a size of ≥ 7 mm, 250 μ g chorion gonadotropin alfa was administered once. Micronized progesterone 800 mg from the next day. On the day of administration of chorion gonadotropin alfa and day of embryo transfer, the blood progesterone level was measured. 5-day-old good quality embryos by a morphological scale were transferred into the uterine cavity. All hormone therapy was administered before the day of the pregnancy test, i.e. 2 weeks from the date of embryo transfer until fetal imaging.

The reproductive results in patients with CE were evaluated depending on the method of pregravid preparation of the endometrium before thawed embryos transfer (Table 1).

Analyzing the data, it can be noted that fertility within a year after the end of therapy was restored with the proposed method of therapy in most women (51.1%), in the comparison group this number was 11.1% lower. Pregnancy rate between the groups (I and II) did not differ significantly.

The number of live births in group II — 19 (42.2%) — was 2 times higher than I group (9 (20.0%)), $P < 0.05$). The increase in the absolute benefit (therapeutic benefit) of the proposed method of pregravid preparation was 22.2% (95% CI 5.16-46.35%).

The most common complication for women in the comparison groups was early pregnancy loss. Among 18 (40.0%) clinical pregnancies of group I, 8 women (17.8%) had early miscarriage, 1 ectopic pregnancy (2.2%), while in group II clinical pregnancy be present in 23 women (51.1%). The number of terminated pregnancies was two times lower than in the first group (8.9% vs. 17.8%, $P < 0.05$).

CONCLUSIONS

Chronic endometritis is one of the main causes of pregnancy loss after in vitro fertilization. Patients of the second group were treated with the proposed method of subendometrial injections with Platelet-Rich Plasma (PRP), prepared from autologous blood. This is an effective method of preparing the endometrium for embryo transfer and can increase the number of live births in patients with chronic endometritis.

The data indicate the effectiveness of the proposed improved algorithm for pregravid preparation of women with chronic endometritis in ART cycles.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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