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THE EFFECT OF PRP THERAPY ON CHRONIC ENDOMETRITIS AND THE RESULTS OF ASSISTED REPRODUCTIVE TECHNOLOGIES

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ABSTRACT

The aim of this study is to investigate the impact of chronic endometritis (CE) on the effectiveness of assisted reproductive technology (ART) programs. The article discusses the pathogenetic mechanisms of the impact of endometrial inflammation on uterine receptivity, implantation frequency, pregnancy onset, and pregnancy outcomes. Data from modern clinical studies and systematic reviews are presented. Emphasis is placed on the need for mandatory diagnosis and treatment of CE to improve the effectiveness of ART.

INTRODUCTION

Against the backdrop of continuous improvements in in vitro fertilization (IVF) technologies, the frequency of implantation failures remains high, reaching up to 60% even with the transfer of high-quality blastocysts. One of the reasons for the low effectiveness of ART is considered to be chronic endometritis — a hidden inflammation of the endometrium, which, according to various authors, occurs in 14–56% of patients with repeated implantation failures (Cicinelli et al., 2015; Kitaya et al., 2011).

Chronic endometritis (CE) is an inflammatory disease of the uterine lining that progresses subclinically over a long period of time and often remains undiagnosed. Despite the absence of obvious clinical symptoms, CE has a significant impact on a woman's reproductive function, being one of the common causes of implantation failure in assisted reproductive technology (ART) programs, pregnancy loss, premature birth, and placental disorders. At the same time, standard diagnostic methods, such as transvaginal ultrasound imaging, are not sensitive enough to detect chronic endometrial inflammation, which requires the use of more accurate methods, including immunohistochemical testing for plasma cell markers (CD138+).

Chronic inflammation disrupts the molecular mechanisms of endometrial receptivity, alters the expression of cell adhesion molecules, contributes to increased levels of pro-inflammatory cytokines and immune cell activation, which reduces the likelihood of successful embryo implantation and increases the risk of reproductive loss.

EH disrupts the physiological mechanisms of endometrial preparation for embryo implantation, alters the immune profile of the uterine environment, and contributes to the development of fibrotic changes in the stroma and impaired vascularization. These pathogenetic mechanisms increase the risk of failed implantation, early miscarriage, fetal growth retardation, premature birth, and placental formation disorders.

In modern conditions, given the active development of IVF technologies and the growing need to optimize ART outcomes, the problem of timely diagnosis and effective treatment of chronic endometritis is becoming particularly relevant. Given the impact of CE on the results of infertility treatment, the inclusion of diagnosis and correction of chronic endometrial inflammation in the standards of preimplantation preparation of patients is a necessary step to improve the overall effectiveness of reproductive programs.

Untimely diagnosis of CE leads to unjustified repeated attempts at ART and reduces the overall likelihood of pregnancy. Therefore, studying the role of chronic endometritis in the pathogenesis of reproductive failure and developing effective algorithms for its treatment are of high clinical importance.

Thus, studying the role of chronic endometritis in the pathogenesis of reproductive failure and developing algorithms for its diagnosis and treatment are the most important tasks of modern reproductive medicine.

1. The effect of PRP therapy on chronic endometritis.

PRP therapy is a method of local administration of autologous platelet-rich plasma, containing a high concentration of growth factors, into damaged tissues. In recent years, the use of PRP has been actively studied in the treatment of chronic endometritis, especially in women with implantation disorders and infertility.

Mechanisms of action of PRP in chronic endometritis:

1. Stimulation of endometrial regeneration.

The platelets contained in PRP release a variety of growth factors, including:

• placental growth factor (PGF),

• platelet-derived growth factor (PDGF),

• transforming growth factor β (TGF-β),

• vascular endothelial growth factor (VEGF),

• epidermal growth factor (EGF).

These factors activate the proliferation of endometrial cells, promote the restoration of the normal structure of the endometrium, and enhance its reparative processes.

2. Reduction of inflammation.

The growth factors contained in PRP have an immunomodulatory effect:

• they reduce the level of pro-inflammatory cytokines (e.g., TNF-α, IL-6),

• they stimulate anti-inflammatory pathways,

• they promote the restoration of the normal immune profile of the endometrium.

3. Improvement of neoangiogenesis.

PRP stimulates the formation of new blood vessels in the endometrium through VEGF activation. This leads to improved vascularization and delivery of oxygen and nutrients, which is critical for restoring endometrial receptivity.

4. Fibrolytic effect.

Some components of PRP may contribute to the destruction of excessive fibrosis of the endometrial stroma, which is important in chronic inflammation and repeated trauma to the mucous membrane.

Clinical results of PRP use in CE:

• Studies show that intrauterine administration of PRP in women with chronic endometritis leads to a reduction in inflammatory changes in the endometrium, a decrease in the expression of inflammatory markers (CD138+), and restoration of normal endometrial thickness and structure.

• The use of PRP therapy is associated with an increase in the frequency of successful embryo implantation in ART cycles and an increase in the frequency of clinical pregnancies.

• In a number of studies (e.g., Zadehmodarres et al., 2020), a significant increase in endometrial thickness and improvement in the morphological characteristics of the uterine mucosa were noted after PRP therapy in patients with refractory endometritis and endometrial depletion.

Advantages of PRP therapy for chronic endometritis:

• Use of autologous plasma (eliminating the risk of immunological conflict or infection);

• Minimal invasiveness of the procedure;

• High biocompatibility;

• Possibility of repeated use within a single cycle of ART preparation.

Limitations and prospects.

Although PRP therapy shows promising results, it is important to note that:

• PRP preparation methods may vary, which affects its effectiveness.

• Large randomized studies are needed to standardize treatment protocols.

• The mechanisms of action of PRP in the endometrium have not yet been fully studied.

Nevertheless, PRP therapy is currently considered a promising method in the complex treatment of chronic endometritis, especially in combination with antibiotic therapy and immunomodulators.

Research objective

To evaluate the impact of chronic endometritis on the results of ART programs based on an analysis of current scientific publications. Research objectives:

• To study the pathogenetic mechanisms of implantation failure in chronic endometritis.

• To evaluate modern methods of diagnosing CE.

• To analyze the effectiveness of CE treatment in the context of preparing patients for ART.

• To formulate practical recommendations for the management of patients with HE.

Materials and Methods

An analytical review of publications in the PubMed, Scopus, and Web of Science databases for the period 2010–2024 was conducted. The selection included randomized clinical trials, meta-analyses, and systematic reviews that evaluated the impact of CE on ART outcomes.

Inclusion criteria:

• Articles devoted to the diagnosis of chronic endometritis;

• Studies analyzing ART outcomes in patients with and without signs of CE;

• Studies on the effectiveness of CE treatment.

A total of 38 publications were included in the final analysis.

Results and Discussion

Pathogenetic mechanisms. Chronic endometritis leads to disruption of key molecular events necessary for successful embryo implantation:

• Decreased expression of integrins αvβ3 and α4β1, which are involved in embryo attachment to the endometrial epithelium (Lessey et al., 2012).

• The production of leukemia inhibitory factor (LIF), which is critical for trophoblast invasion processes, is disrupted (Aghajanova et al., 2012).

• The activity of pro-inflammatory cytokines (TNF-α, IL-6) increases, leading to the activation of immune cells and a decrease in the tolerance of the endometrium to the embryo (Cicinelli et al., 2015).

Morphological changes include stromal edema, subepithelial fibrosis, and an increase in the number of CD138+ plasma cells.

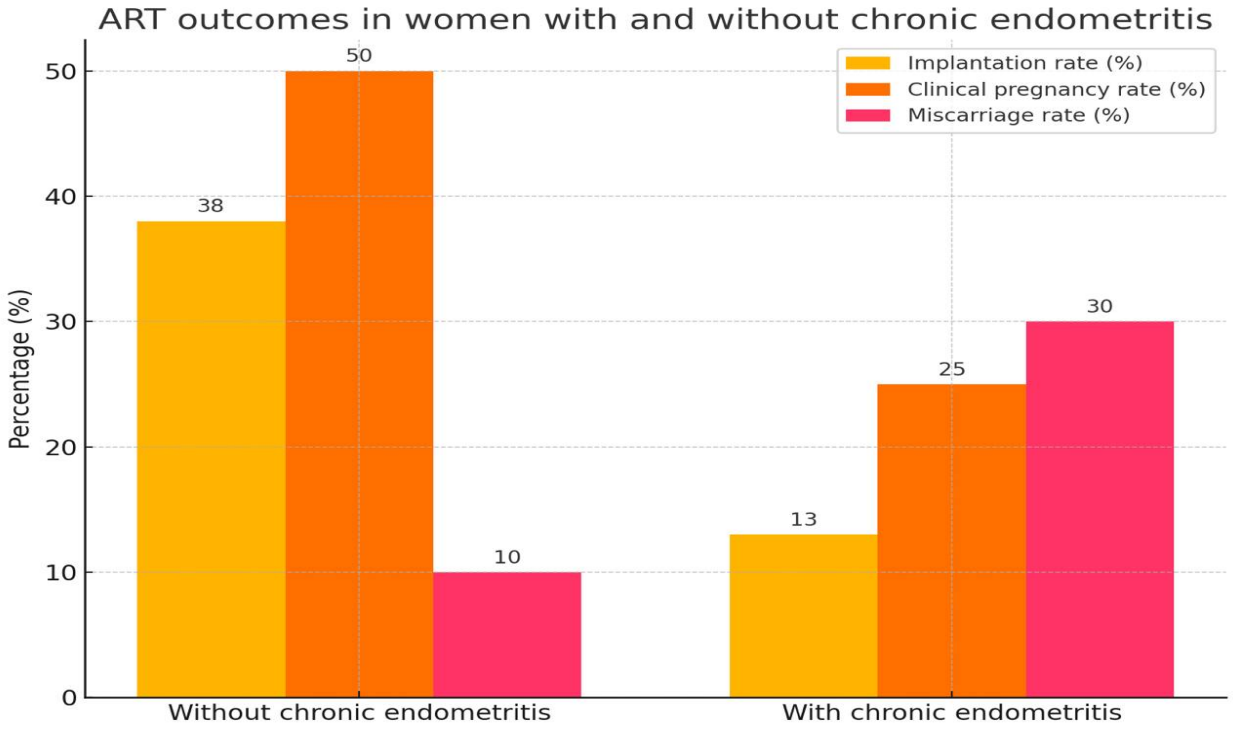
Prevalence and impact on ART outcomes. According to Johnston-MacAnanny et al. (2010), chronic endometritis is diagnosed in 45% of women with repeated implantation failures. At the same time:

• The frequency of pregnancy after ART in patients without signs of CE is about 50%,

• while in patients with CE — only 25–30%.

On average, the presence of chronic inflammation reduces the likelihood of clinical pregnancy by 2 times and increases the risk of early miscarriage by 2.5 times (Cicinelli et al., 2015). The results of pregnancy, birth rate, and miscarriage are shown in Figure 1.

Figure 1.



Diagnostic methods

The most reliable method for verifying HE is histological examination of the endometrium with immunohistochemical determination of plasma cells (CD138+). Hysteroscopy is also used to identify characteristic features: pinpoint hemorrhages, micropolyps, and mucosal edema.

Modern molecular methods, such as microbiota sequencing (Next-Generation Sequencing), open up new perspectives for the diagnosis of endometrial dysbiosis associated with HE (Moreno et al., 2016).

Treatment

The basis of therapy is broad-spectrum antibiotic therapy aimed at eradicating the bacterial pathogen. The most commonly used regimens are doxycycline and metronidazole, sometimes with the addition of ofloxacin or amoxicillin/clavulanate.

The effectiveness of treatment is confirmed by a decrease in the level of CD138+ cells in the endometrium and the restoration of normal receptivity. According to Cicinelli et al. (2018), a course of antibiotic therapy led to an increase in the frequency of pregnancy in IVF programs from 20% to 56%.

Figure 2.

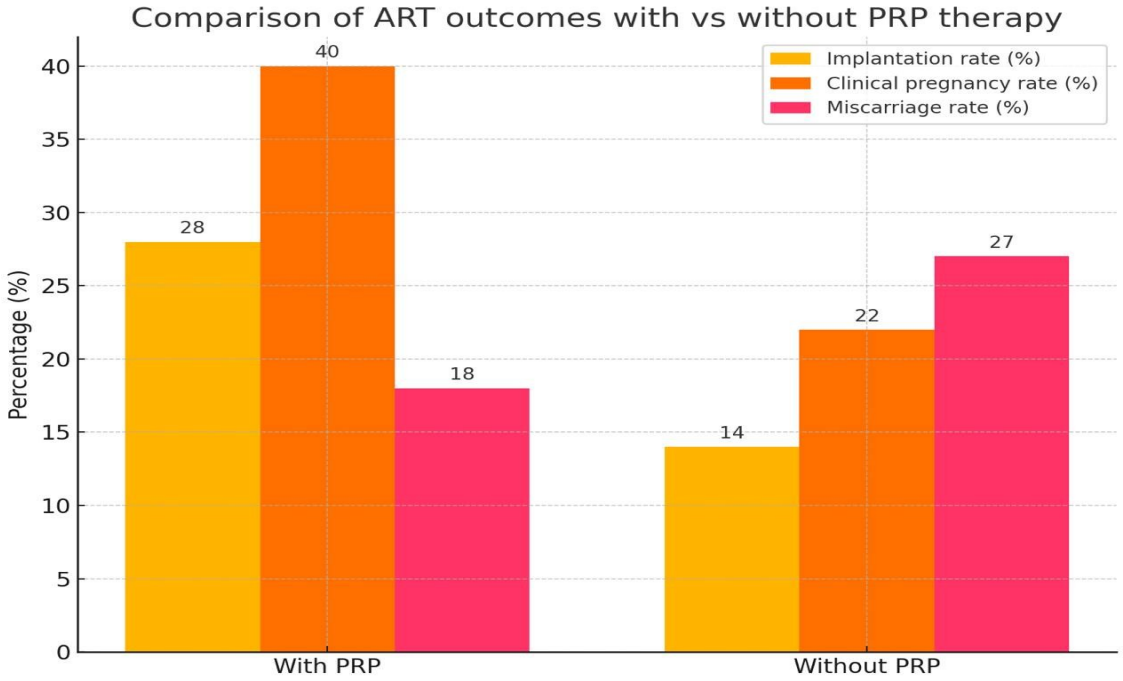


Figure 2. Comparison of ART outcomes with and without intrauterine PRP therapy. Literature data demonstrate that PRP application is associated with an increase in implantation and clinical pregnancy rates, as well as a reduction in miscarriage rates compared to standard ART protocols without PRP [10]

CONCLUSION

Chronic endometritis is an important and often underestimated factor in reproductive failure when using ART. Pathological changes against a background of chronic inflammation lead to a decrease in endometrial receptivity and an increased risk of miscarriage.

Mandatory testing for chronic endometritis should be included in the algorithm for preparing patients for ART procedures, especially in cases of repeated implantation failures. Timely treatment of chronic endometritis significantly improves the chances of successful conception and a favorable pregnancy outcome.

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