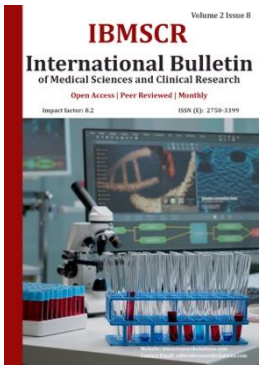

INFERTILITY PROBLEMS AND ENDOMETRIAL THINNESS

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Abstract. The endometrium is a unique structure of the female body designed for reproductive function. Full maturity of the endometrium, its receptivity, and the ability to engage in adequate "communication" with the product of fertilization is the key to the successful initiation of pregnancy and pregnancy. According to local and foreign authors, the prevalence of infertility reaches 10-15%, in some regions of Russia - 20%, and the frequency of spontaneous abortion in the first trimester of pregnancy remains at 16%. Based on this, the study of these problems is one of the urgent issues. This article provides the latest information on endometrial thinning and infertility.

Keywords: endometrial thinning, morphofunctional state, hormonal changes, infertility.

Introduction. The World Health Organization (WHO) estimates that infertility affects 10 to 25% (48 to 180 million) of reproductive-age couples worldwide. It is associated with adverse physical and mental health consequences of infertility, significant social stigma, increased risk of domestic violence, and marital instability. Although men and women are equally susceptible to infertility, women often bear the social burden of infertility, especially in societies where a woman's identity and social value is closely tied to her ability to bear children [10].

The endometrium is a unique structure of the female body designed for reproductive function. Full maturity of the endometrium, its receptivity, and the ability to engage in adequate "communication" with the product of fertilization is the key to the successful initiation of pregnancy and pregnancy. Impairment of implantation leads not only to long-term infertility and failure of in vitro fertilization but also to spontaneous abortions in the first trimester of pregnancy, increased risk of premature birth, and other serious complications (preeclampsia, fetal growth restriction syndrome). Currently, these complications are considered to be the result of insufficient invasion of trophoblasts, which are formed in the early stages of blastocyst implantation.

The morphofunctional state of the endometrium determines the probability of pregnancy, its successful course, and successful completion. One of the important causes of decreased fertility (infertility and abortion) is insufficient endometrial function, which is caused by both ovarian dysfunction and changes in the structure of the endometrium, often caused by inflammation [1, 6, 8, 13]. Restoring the sensitivity or receptivity (receptivity) of the endometrium is a more complex task than stimulating the activity of the ovaries or stimulating its hormonal exchange. Admittedly, this is far from a solution today. Hormonal, immunomodulating, metabolic, targeted therapy should be considered in the context of the causes of thin endometrial formation and have a complex, not competing, effect based on the understanding of the processes that occur in the endometrium during normal menstruation.

According to local and foreign authors, the prevalence of infertility reaches 10-15%, in some regions of Russia - 20%, and the frequency of spontaneous abortion in the first trimester of pregnancy remains at 16% [3, 4]. The decrease in female fertility has many causes, among which the percentage of infertility of the uterine factor in isolated or combined form is 24-62% [9]. It is known that pathological changes in the endometrium during infertility reach 88% [7] and with ineffective IVF attempts - 77.5% [4]. The presence of intrauterine pathology is an independent risk factor for infertility, increasing its probability four times. These data confirm the existing opinion about the main role of endometrium in implantation and placenta. Therefore, the need for morphofunctional evaluation in women with infertility and normal spontaneous abortion is clear.

Currently, there is no generally accepted definition of "thin endometrium". In various studies, the authors suggest considering different endometrial thickness as a prognostic criterion of implantation failure. Endometrial thickness during the "implantation window" of less than 8 mm is considered to provide minimal opportunities for effective conception. According to a systematic review and meta-analysis of studies evaluating clinically relevant endometrial thickness in ECU programs, thin endometrium (≤ 7 mm) was observed in only 2.4% of successful cycles leading to pregnancy. The probability of clinical pregnancy in cases with endometrial thickness ≤ 7 mm was significantly lower compared with endometrial thickness > 7 mm (23.3 and 48.1%, respectively) [11].

Endometrial deficiency can occur as a result of previous inflammatory diseases of the pelvic organs, changes in hormonal homeostasis, medical manipulations, and operations associated with damage to the basal layer of the endometrium. One of the most important reasons for the decrease in reproductive function is the chronic inflammatory process in the endometrium. This disease is characterized by disruption of intercellular interactions, sclerosis of the stroma around blood vessels, changes in tissue angioarchitecture, and ischemia [5]. Infertility (mostly secondary) is diagnosed in almost 50% of women with chronic endometritis, and 37% of patients have failed IVF attempts (an average of three attempts per patient). Long-term and often asymptomatic persistence of infectious agents in the endometrium leads to clear changes in the tissue structure, prevents normal implantation and placenta, forms a pathological response to pregnancy, and also causes a violation of the proliferation and normal cyclic transformation of the endometrium. The structural consequences of chronic endometritis are associated with the development of synechiae in the uterine cavity, the extreme degree of which is Asherman's syndrome.

In addition to the thickness of the endometrium, the most important indicator of its viability is the echographic characteristics, in particular, signs of a three-layer structure. It turned out that even if the thickness of the endometrium is less than 7 mm, the presence of a three-layered structure can ensure pregnancy (24.4%) and a low rate of pregnancy in the first trimester, while no pregnancy was observed in the absence of signs of pregnancy [13].

The gold standard for assessing the condition of the uterine cavity and mucous membrane is hysteroscopy with biopsy and subsequent histological examination of the endometrium [18]. At the same time, only structural changes in the uterine cavity and chronic endometritis are available for visual and morphological diagnosis, which limits the use of this method. Histological criteria for thin endometrium have not yet been developed. At the same time, immunohistochemical examination reveals several changes that characterize this pathological condition of the mucous membrane of the uterine body.

The pathophysiological characteristics of thin endometrium are insufficient growth of the glandular epithelium, high uterine blood flow resistance, decreased vascular endothelial growth factor, and poor vascular formation [9]. High blood flow resistance in the radial arteries can be a trigger that negatively affects the growth of the glandular epithelium, resulting in a decrease in the level of vascular endothelial growth factor in the endometrium. Low vascular endothelial growth factor causes impoverished angiogenesis, which further reduces vascular blood flow in the endometrium. This vicious circle leads to the formation of a thin endometrium, which in turn has a bad effect on receptivity. There is evidence that high resistance in blood flow of radial arteries at the beginning of the menstrual cycle may be a predictor of thin endometrium, but the mechanism of high resistance in uterine arteries is not yet clear.

One of the important reasons for the formation of thin endometrium is the loss of steroid hormone receptors. Classical genomic mechanisms of hormone action involve the activation of specific nuclear receptors, while faster biological effects are mediated by membrane-bound receptors, including G-protein-coupled receptors [10]. The presence of the latter in the endometrium has not been proven, and the expression of estrogen receptor alpha and estrogen receptor beta is high, with a predominance of estrogen receptor alpha, which is present both in the epithelium and in the stroma of the functional layer. In humans, estrogen receptor alpha density is highest during the proliferative phase but decreases during the secretory phase of the cycle. Epithelial estrogen receptor beta also decreases in the secretory phase and is not detected in the stroma, but is present in the vascular endothelium. Both subtypes are found in cells that line blood vessels. It is important that experimentally, the loss of estrogen receptor alpha leads to a loss of sensitivity of the endometrium to estrogens, while the loss of estrogen receptor beta is not accompanied by a change in its phenotype and a decrease in fertility [19].

The endometrium, like other tissues of the body, is characterized by a daily circadian rhythm of gene activity [12, 20, 22]. Desynchronization of ovarian and endometrial cycles can lead to loss of endometrial receptivity for no apparent reason. In general, it should be recognized that we are still very far from understanding the causes of disruption of the normal growth of the endometrium, and the treatment of this pathological condition is often empirical.

Conclusion. The problem of thin endometrium has not been solved today. The pathogenesis of the impaired growth of this organ, which is necessary for reproduction, is not clear, and the methods of normalizing proliferative processes are limited. The need to test existing methods, as well as to search for new therapeutic approaches, is clear because optimizing the treatment of thin endometrium is the key to restoring fertility in many women.

References:

1.Ata B. et al. Walking on thin endometrium //Current Opinion in Obstetrics and Gynecology. – 2024. – С. 10.1097.

2.Ergashev F. R. et al. Damage to the main bile ducts: the frequency and causes of their occurrence, risk factors, classification, diagnosis and surgical tactics (literature review) //International scientific review of the problems of natural sciences and medicine. – 2019. – С. 82-96.

3.Gharibeh N. et al. Cell-based therapy in thin endometrium and Asherman syndrome //Stem Cell Research & Therapy. – 2022. – Т. 13. – №. 1. – С. 33.
4.Kurbaniyazova F., Sodikova O. OPTIMIZING PRECONCEPTION PREPARATION FOR WOMEN WITH CHRONIC HYPOPLASTIC ENDOMETRITIS //Modern Science and Research. – 2024. – Т. 3. – №. 2. – С. 129-132.
5.Lv H. et al. Deciphering the endometrial niche of human thin endometrium at single-cell resolution //Proceedings of the National Academy of Sciences. – 2022. – Т. 119. – №. 8. – С. e2115912119.
6.Li X. et al. Effect of sildenafil citrate on treatment of infertility in women with a thin endometrium: a systematic review and meta-analysis //Journal of International Medical Research. – 2020. – Т. 48. – №. 11. – С. 0300060520969584.
7.Афян А. И., Долгушина Н. В. Тонкий эндометрий в клинике вспомогательных репродуктивных технологий (обзор литературы) //Гинекология. – 2014. – Т. 16. – №. 5. – С. 78-83.
8.Боярский К. Ю., Гайдуков С. Н., Пальченко Н. А. Современный взгляд на проблему рецептивности и тонкого эндометрия в программах ВРТ (обзор литературы) //Проблемы репродукции. – 2013. – Т. 19. – №. 4. – С. 51-60.
9.Кулбаева, С., Yadav, М., Салимбаева, Б. , Штобза, О. , Джантаева, З. и Борибаева, Д. 2024. Современный взгляд на проблему бесплодного брака: обзор литературы. Репродуктивная медицина. 1 (апр. 2024), 147–157. DOI:https://doi.org/10.37800/RM.1.2024.147-157.
10.Кузнецова И. В. и др. Проблема тонкого эндометрия и возможные пути ее решения //Эффективная фармакотерапия. – 2015. – Т. 5. – С. 42-9.
11.Куликова Г. В. и др. Рецептивность" тонкого" эндометрия у пациенток в программах вспомогательных репродуктивных технологий //Акушерство и гинекология. – 2019. – №. 10. – С. 100-107.
12.Краснопольская К. В., Ершова И. Ю., Федоров А. А. Тонкий эндометрий //Лечение бесплодия у женщин с гипоплазией эндометрия. М.: ГЭОТАР-Медиа. – 2020. – Т. 112.
13.Курбаниязова Ф. СОВЕРШЕНСТВОВАНИЕ ДИАГНОСТИКИ АНОМАЛЬНЫХ МАТОЧНЫХ КРОВОТЕЧЕНИЙ У ЖЕНЩИН РЕПРОДУКТИВНОГО ВОЗРАСТА //Евразийский журнал медицинских и естественных наук. – 2023. – Т. 3. – №. 9. – С. 57-61.
14.Оразов М. Р. и др. " Тонкий" эндометрий-современный взгляд на проблему //Фарматека. – 2018. – №. 6. – С. 15-22.
15.Оразов М. Р. и др. Тайны репродуктивных неудач:«тонкий» эндометрий //Репродуктивная медицина. – 2018. – №. 2. – С. 7-17.
16.Попова М. В. и др. Тонкий эндометрий как причина репродуктивных потерь и неудачных попыток ЭКО (обзор литературы) //Медико-социальные проблемы семьи. – 2020. – Т. 25. – №. 1. – С. 86-89.
17.Толибова Г. Х., Траль Т. Г., Коган И. Ю. Морфологическая оценка гипопластичного (тонкого) эндометрия у женщин с неэффективными протоколами вспомогательных репродуктивных технологий //Журнал акушерства и женских болезней. – 2020. – Т. 69. – №. 5. – С. 39.
18.Худоярова Д. Р., Турсунов Н. Б. «ОСТРЫЙ ЖИВОТ» В ГИНЕКОЛОГИИ: СОВРЕМЕННЫЕ ВОЗМОЖНОСТИ.

19.Худоярова Д., Зубайдуллоева З., Хайитбоев Д. ОБЩАЯ КЛИНИЧЕСКАЯ ХАРАКТЕРИСТИКА ОБСЛЕДОВАННЫХ БЕРЕМЕННЫХ //Евразийский журнал медицинских и естественных наук. – 2024. – Т. 4. – №. 2. – С. 57-61.
20.Шнейдерман М. Г. и др. Проблема тонкого эндометрия: возможности комбинированного негормонального лечения при подготовке к процедуре экстракорпорального оплодотворения //Гинекология. – 2014. – Т. 16. – №. 3. – С. 67-71.
21.Шнейдерман М. Г. и др. Новый способ прегравидарной подготовки" тонкого" эндометрия-альтернатива гормональному лечению //Акушерство и гинекология. – 2015. – №. 1. – С. 51-57.
22.Эфендиева З. Н., Аполихина И. А., Калинина Е. А. " Тонкий" эндометрий в аспекте репродуктивных неудач: современная проблема или гипердиагностика? //Акушерство и гинекология. – 2019. – №. 9. – С. 32-38..