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STRATEGIES FOR PRESERVING REPRODUCTIVE POTENTIAL IN WOMEN WITH ENDOMETRIOSIS.

Jumaeva DR

Asia International University

Abstract: Endometriosis is a leading cause of female infertility due to decreased ovarian reserve, inflammation, adhesion formation, and surgical treatment affecting ovarian tissue. Timely implementation of modern strategies for preserving reproductive potential minimizes the risk of premature ovarian failure and improves fertility prognosis. This article discusses key approaches to protecting ovarian reserve: early diagnosis, organ-preserving surgery, drug therapy, assisted reproductive technologies, cryopreservation methods , and individualized patient management strategies.

Key words : endometriosis, ovarian reserve, fertility, cryopreservation , IVF, AMH, AFC.

Endometriosis is a chronic, hormone-dependent disease characterized by the presence of endometriotic heterotopias and the development of pelvic inflammation. According to various studies, infertility occurs in 30–50% of women with endometriosis, due to decreased ovarian reserve, ovulation disorders, changes in oocyte quality, and damage to ovarian tissue during surgery.

Ovarian reserve reflects the quantity and quality of the follicular apparatus and is assessed using anti-Müllerian hormone (AMH) levels and antral follicle count (AFC). In patients with endometrioid cysts (endometriomas), AMH levels decline more rapidly than in healthy women of the same age.

The aim of this article is to analyze modern strategies for preserving ovarian reserve and reproductive potential in women with endometriosis.

1. The impact of endometriosis on ovarian reserve

1.1 Inflammatory mechanisms

Chronic inflammation leads to elevated cytokine levels, oxidative stress, and follicle damage. Microcirculation and oocyte maturation are disrupted.

1.2. Endometriomas

Endometrioid cysts put pressure on the surrounding ovarian tissue, causing ischemia, cortical thinning, and loss of primordial follicles.

1.3. Surgical treatment

Endometrioma removal is one of the most common causes of a sharp decrease in AMH due to accidental removal of healthy ovarian tissue and damage to the vascular network.

2. Principles of preserving reproductive potential

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2.1. Early diagnosis

Use of high-resolution transvaginal ultrasound

MRI of the pelvis

Evaluation of fertility markers (AMH, AFC)

Early diagnosis allows to avoid late surgical treatment and choose gentle tactics.

3. Medicinal methods of preserving ovarian reserve

3.1 Hormonal therapy

COCs - suppression of ovulation, reduction of the inflammatory response

Progestins (dienogest) are effective in suppressing the growth of endometriotic lesions .

GnRH agonists/antagonists are used in short courses, mainly in preoperative preparation

Hormonal therapy helps reduce disease activity and slows the loss of ovarian reserve.

3.2. Antioxidant therapy

Coenzyme Q10

Myo- inositol

Omega-3

The positive effect on oocyte quality in patients with endometriosis is discussed.

4. Surgical approaches and organ-preserving techniques

4.1. Indications for surgery

Endometrioma >4 cm

Severe pain syndrome

Suspected complication (rupture/bleeding)

Dysfunction of adjacent organs

The high incidence of this last complication indicates that today we face a socially significant problem that requires us to urgently seek solutions. Undoubtedly, modern specialists have a wide range of both conservative and surgical treatments for endometriosis, but their use, like the disease itself, leads to a decrease in ovarian reserve.

This paradoxical situation demonstrates that patients with this pathology should not only be warned about the consequences of their disease, they also need a thorough assessment of their ovarian reserve and information on all possible ways to preserve it.

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Literary data and extensive practical experience indicate that ovarian endometriosis is the most common form of pathology among reproductively active women. Such patients are at high risk for developing premature ovarian failure (POF) due to the inevitable need for surgery and the potential for recurrence. Another important feature of an endometrioid lesion is its morphological structure. Recent studies indicate that the wall of an endometrioid cyst contains a large number of follicles. Moreover, their multiplicity is directly related to the patient's age: the younger the patient, the more follicles [5].

It is obvious that in the presence of such a correlation, any impact on the tissue will lead to depletion of the ovarian reserve, in connection with which the attending physician must conduct a qualitative assessment of its parameters before the operation (1)

Achieving this goal is complicated by the fact that currently we have markers that only allow us to indirectly assess the condition of the follicular apparatus. These include a hormonal profile assessment, which includes determining the levels of anti-Müllerian hormone (AMH), follicle-stimulating hormone (FSH), inhibin B, and estradiol on days 2-3 of the menstrual cycle. Of the instrumental diagnostic methods, transvaginal an ultrasound examination of the pelvic organs, which will include determination of ovarian volume, counting the number of antral follicles and assessment of intraovarian blood flow.

It should be noted that these research methods are actively used in clinical practice; however, their effectiveness remains a matter of debate. One of the first hormones proposed for assessing ovarian reserve was FSH. However, after numerous studies, scientists have been unable to formulate the absolute values of its concentration that can definitively conclude that ovarian reserve has decreased. Some studies consider 10 IU/L critical, others 15 IU/L, and still others 20-25 IU/L. The situation is further complicated by the fact that in some cases, FSH levels can fluctuate between high and low values in different menstrual cycles. It should be noted that this symptom should be treated with caution, but it should be remembered that it is not a marker of ovarian function [1]. Another indirect indicator of ovarian reserve is AMH. It is secreted by granulosa cells of ovarian follicles and is responsible for the transition of dormant primordial follicles into the active growth phase. This implies that the number of primordial follicles is indirectly reflected by the number of growing follicles. Consequently, a factor secreted predominantly by growing follicles will reflect the size of the primordial follicle pool. Therefore, AMH, which is secreted by growing follicles prior to selection, can be tested in serum and is a promising marker for determining ovarian reserve [1].

Another advantage of AMH is that its concentration level depends little on the phase of the cycle and apparently reflects the number of follicles in the basal growth phase [1, 3].

This makes this hormone a unique marker of ovarian aging and ovarian reserve. When conducting further hormonal testing, it is important to remember that inhibin B plays a leading role in regulating FSH levels at the beginning of the menstrual cycle. This specific protein is structurally similar to transforming growth factor. It is produced by ovarian granulosa cells and plays a key role in regulating folliculogenesis . High plasma protein concentrations ensure basal FSH levels at the beginning of the menstrual cycle. Accordingly, a decrease in inhibin B levels will indicate a decrease in the population of small antral follicles and will cause a sharper

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increase in FSH concentration, which ultimately leads to rapid growth of the dominant follicle and early ovulation. Similar mechanisms are likely to operate with reduced ovarian reserve [1, 7].

The data presented suggest that plasma sex hormone levels, while controversial, are informative. Combining this test with ultrasound assessment of ovarian volume, antral follicle counting, and Doppler mapping allows us to obtain a more comprehensive understanding of surgical outcomes. In cases of high risk of decreased ovarian reserve, we should inform the patient about existing oocyte preservation options, such as cryopreservation . This method is justified and a good choice for women with endometriosis. Its advantage is that it is the least invasive compared to other fertility preservation methods and does not affect future ovarian reserve. However, one should be prepared for the fact that, given a decreased oocyte count, multiple oocyte collection cycles may be required, which does not correlate with an increased risk of disease recurrence [3, 4].

Despite a number of advantages, some scientists oppose oocyte cryopreservation in patients with endometriosis. Their opinion is based on the fact that the effectiveness of in vitro fertilization (IVF) in these women is reduced due to the significant risk of impaired embryo implantation in the uterine cavity. The validity of this position is beyond doubt; however, we were unable to find any studies with a high level of evidence in the literature. Meanwhile, reproductive specialists express a completely opposite view. They argue that if healthy oocytes are fertilized, the rate and quality of embryo implantation will not be affected [7].

It should be noted that this method is experimental, as only 60 babies have been born using it so far. The cortical tissue cryopreservation technique requires the determination of follicle density markers, among which AMH levels play a key role. A decrease in plasma hormone concentrations will indicate a reduced number of antral follicles, which will lead to an insufficient ovarian response and an increased need for high doses of gonadtropins during subsequent controlled ovarian stimulation .

Thus, the use of fertility preservation technologies can now be widely adopted as a standard of care for women at high risk of premature ovarian failure. Personalized counseling for ovarian tissue preservation is beneficial for all patients with endometriosis, taking into account age, the degree of ovarian involvement, current ovarian reserve, previous and upcoming surgeries for endometriosis, as well as current success rates and potential risks associated with modern technologies. When counseling patients with endometriosis, the benefits of early conception should be emphasized, as they will increase success rates and may reduce the rate of disease progression. However, early conception advice may not be practical for many women. In such cases, they should be offered ovarian-sparing surgery and the latest cryopreservation techniques , which are already widely used in cancer patients: cryopreservation of oocytes, embryos, or ovarian tissue at a younger age. Freezing embryos or unfertilized oocytes is the most optimal method for preserving fertility in women with endometriosis. It does not affect ovarian reserve and offers a realistic chance of future pregnancy when a sufficient number of oocytes or embryos are preserved.

Therefore, in women of reproductive age with endometriosis who have not yet completed family planning, the potential risk of low ovarian reserve, premature ovarian failure, and future infertility should be carefully assessed to ensure adequate counseling regarding the need for

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fertility preservation. These recommendations are based on existing literature and experience. Continued data collection, coupled with growing experience with ovarian reserve preservation technologies, allows for refinement of current indications for fertility preservation in the context of endometriosis, taking into account both economic aspects and known success rates.