

FEATURES OF THE WOMEN HORMONAL BACKGROUND WITH ENDOMETRIOSIS-ASSOCIATED INFERTILITY

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Abstract

Introduction. According to experts, endometriosis affects 10-15% of women of reproductive age; the percentage of endometriosis-associated infertility in this category of women is 30-50%. Given that endometriosis affects women of young reproductive age, the question arises about conservative and surgical ways to restore reproductive function.

Objective of the research: to analyze retrospectively the level of serum hormones of patients with endometriosis-associated infertility, depending on the type of treatment of endometrioid cysts.

Materials and methods. The study included 114 women aged 21- 40 years with endometriosis-associated infertility, who were treated at the “Professor S. Khmil Clinic Medical Center”. The comparison group included 30 women with tuboperitoneal infertility factor. Patients with endometriosis-associated infertility were divided into 2 groups. Group 1 consisted of 54 women of reproductive age with unoperated endometrioid cysts up to 4 cm in diameter, group 2 - 60 women with a medical history of surgical treatment of endometrioid cysts. Each of the groups was divided into 2 subgroups. 1a - monolateral endometrioid cysts; 1b - bilateral endometrioid cysts; 2a - without recurrent cysts in the previously operated ovary; 2b - with mono- or bilateral cysts in the previously operated ovary.

Determination of the concentration of the reproductive system hormones was performed in an accredited laboratory of the “Professor S. Khmil Clinic Medical Center” with

the help of “Diagnostic Systems Laboratories, Inc.” test system (USA) using the analyzer “StatFax”.

Results and Discussion. It was found that the concentration of AMH was probably lower in the blood serum of women who underwent cystectomy, but did not differ statistically significantly between groups 2a and 2b. The concentration of FSH in the experimental groups was probably higher than in the comparison group, but its level in different experimental groups probably did not differ when analyzing the rank variations of Kruskal-Wallis. Changes in LH concentration had similar dynamics to FSH, in particular, the level of LH in the experimental groups was probably higher against the data of the comparison group. It should be noted that the concentration of LH in 2b group was probably higher in relation to 1a (by 26.25%), 1b (by 22.42%) and 2a (by 20.24%) groups. Progesterone level was statistically significantly lower in groups 1a, 1b and 2b relative to the comparison group. Analysis of prolactin level did not show statistical difference both in the analysis of rank variations of Kruskal-Wallis, and when compared with the data of the comparison group.

Conclusions. Women with endometriosis-associated infertility have hormonal disorders characterized by increased levels of follicle stimulating and luteinizing hormones, estradiol, decreased levels of progesterone and anti-müllerian hormone, with AMH probably lower in women after cystectomy, according to data of unoperated patients.

Key words: endometriosis; infertility; treatment; hormones

Introduction. Genital endometriosis is a widespread, polyetiological disease characterized by benign, focal tissue growth (the structure of which is characterized by the presence of epithelial and stromal elements inherent in the endometrium) in the myometrium or other organs of the genital system and beyond. Typical symptoms of the disease are dysmenorrhea and menstrual cycle disorders (occurs in 70% and 15% of patients, respectively), pelvic pain (40% of women), 33% of women suffer from dyspareunia, 35% have endometriosis-associated infertility [1]. The prevalence of endometriosis is increasing sharply, so this disease remains one of the most pressing problems in modern gynecology. According to experts, endometriosis affects 10-15% of women of reproductive age; the percentage of endometriosis-associated infertility in this category of women is 30-50% [2, 3]. The main mechanisms that explain infertility at endometriosis are impaired folliculogenesis, impaired sperm transport, inferiority of the secretory phase, impaired fertilization, reduced probability of implantation, changes in the properties of peritoneal fluid, the development of the adhesion process [4]. The impact of endometriosis on reproductive health is estimated by

the fertility rate, which is calculated as the ratio of the number of live births to the number of women of reproductive age, and in this category is 0.02-0.10, while in healthy women this ratio is 0.15-0.20 [5].

Given that endometriosis affects women of young reproductive age, the question arises about conservative and surgical ways to restore reproductive function [6, 7]. On the one hand, surgical treatment of endometriosis has a positive effect not only on its clinical manifestations, such as reducing pain, improving quality of life, but also on the further realization of reproductive function [8]. On the other hand, according to the National Consensus on the management of patients with endometriosis [9], conservative treatment is currently a priority and only in case of its ineffectiveness in agreement with the patient surgical treatment is resorted.

The aim of this study was to analyze retrospectively the level of serum hormones of patients with endometriosis-associated infertility, depending on the type of treatment of endometrioid cysts.

Materials and methods. The study included 114 women aged 21- 40 years with endometriosis-associated infertility, who were treated at the “Professor S. Khmil Clinic Medical Center”. The comparison group included 30 women with tuboperitoneal infertility factor, diagnosed by laparoscopy or echosalpingography. Patients with stage III – IV endometriosis, polycystic ovary syndrome, uterine fibroids (submucosal, symptomatic subserosal or intramural with a diameter of more than 2 cm) were not included in the retrospective analysis group. External genital endometriosis was verified during laparoscopy and confirmed by histopathological examination (endometrioid cyst of the ovary or endometrioid cysts of the ovaries).

Patients with endometriosis-associated infertility were divided into 2 groups. Group 1 consisted of 54 women of reproductive age with unoperated endometrioid cysts up to 4 cm in diameter, group 2 - 60 women with a medical history of surgical treatment of endometrioid cysts. Each of the groups was divided into 2 subgroups. 1a (n = 26) - monolateral endometrioid cysts; 1b (n = 28) - bilateral endometrioid cysts; 2a (n = 23) - without recurrent cysts in the previously operated ovary; 2b (n = 37) - with mono- or bilateral cysts in the previously operated ovary. The presence of cysts was confirmed by ultrasound and bimanual examination.

Determination of the concentration of the reproductive system hormones was performed in an accredited laboratory of the “Professor S. Khmil Clinic Medical Center” with

the help of “Diagnostic Systems Laboratories, Inc.” test system (USA) using the analyzer “StatFax”.

Statistical analysis of the study results was performed using computer software “Microsoft Office Excel” and “Statistica 7.0”. The choice of the analysis method of the obtained data was based on the number of groups included in the survey, the correctness of the distribution of values in them, as well as the equality of variances. Quantitative values, due to their non-parametric distribution, are presented in the form of median, Q25 and Q75 quartiles, and compared using the Mann–Whitney test. Comparative analysis of quantitative indicators in three or more groups was performed using the Kruskal–Wallis test, which was considered statistically significant at $p < 0.05$. Further pairwise comparison of groups was performed using the Mann–Whitney U-test, taking into account the Bonferroni correction when assessing the level of statistical significance.

Results and discussion. It was found that the concentration of AMH was probably lower in the blood serum of women who underwent cystectomy, but did not differ statistically significantly between groups 2a and 2b. The concentration of FSH in the experimental groups was probably higher than in the comparison group, but its level in different experimental groups probably did not differ when analyzing the rank variations of Kruskal-Wallis. Changes in LH concentration had similar dynamics to FSH, in particular, the level of LH in the experimental groups was probably higher against the data of the comparison group. It should be noted that the concentration of LH in 2b group was probably higher in relation to 1a (by 26.25%), 1b (by 22.42%) and 2a (by 20.24%) groups. The concentration of estradiol in the experimental groups was probably higher than in the comparison group, but its level in different experimental groups probably did not differ when analyzing the rank variations of Kruskal-Wallis. It should be noted that a pairwise comparison of estradiol concentrations revealed a significantly lower level of estradiol in women with endometriosis-associated infertility with unoperated monolateral cysts, in relation to 1b (by 26.50%) and 2b (by 20.68%) groups. Progesterone level was statistically significantly lower in groups 1a, 1b and 2b relative to the comparison group. Notably that a pairwise comparison of the progesterone concentration showed a significantly higher level in women with endometriosis-associated infertility with unoperated monolateral cysts, in relation to 1b (by 28.74%) and 2a (by 60.45%) groups. Analysis of prolactin level did not show statistical difference both in the analysis of rank variations of Kruskal-Wallis, and when compared with the data of the comparison group (table 1).

Table 1 - Concentration of the reproductive system hormones of women with endometriosis-associated infertility (Me (Q25; Q75))

	Comparison group (n=30)	1a (n=26) Unoperated monolateral	1b (n=28) Unoperated bilateral	2a (n=23) Operated without recurrences	2b (n=37) Operated with recurrences	Kruskal-Wallis criterion
AMH	1.75 (1.56; 1.92)	1.76 (1.30; 1.90)	1.60 (1.33; 1.90)	0.72# (0.60; 1.00)	0.95# (0.55; 1.15)	H=5.39; p>0.05
FSH	7.95 (6.93; 8.50)	10.15# (8.94; 10.90)	10.20# (9.50; 11.00)	10.60# (9.95; 11.20)	10.60# (9.10; 11.80)	H=1.06; p>0.05
LH	6.15 (5.45; 6.80)	8.00# (6.81; 9.38)	8.25# (6.95; 9.15)	8.40# (7.73; 9.30)	10.10# (7.80; 11.80)	H=5.50; p>0.05
Estradiol	36.85 (33.70; 40.08)	49.80# (40.70; 58.63)	63.00# (50.38; 77.93)	55.30# (44.60; 61.80)	60.10# (49.79; 70.23)	H=3.26; p>0.05
Progesterone	13.95 (12.63; 15.58)	10.75 (7.83; 14.15)	8.35# (5.43; 10.50)	6.70# (4.10; 12.20)	9.80# (6.10; 11.90)	H=3.46; p>0.05
Prolactin	10.95 (10.40; 12.28)	11.10 (9.55; 14.70)	12.65 (10.25; 14.70)	10.30 (7.95; 14.70)	12.20 (9.50; 14.90)	H=0.56; p>0.05

Note 1. * - statistically significant results within the experimental groups.

Note 2. # - statistically significant control results.

Note 3. AMH: p<0.05 for the Kruskal-Wallis coefficient, p<0.017 (according to Bonferroni correction) for a pairwise comparison of groups 1a-2a, 1a-2b, 1b-2a, 1b-2b

Note 4. LH: p<0,05 for the Kruskal-Wallis coefficient; p<0,017 (according to Bonferroni correction) for a pairwise comparison of groups 1a-2b, 1b-2b, 2a-2b.

Note 5. Estradiol: p<0,05 for the Kruskal-Wallis coefficient, p<0,017 (according to Bonferroni correction) for a pairwise comparison of groups 1a-1b, 1a-2b.

Note 6. Progesterone: p<0,05 for the Kruskal-Wallis coefficient, p<0,017 (according to Bonferroni correction) for a pairwise comparison of groups 1a-2a, 1a-1b.

Comparison of changes in hormone levels of patients with endometriosis-associated infertility depending on the location of cysts indicates the highest values of estradiol and the lowest - progesterone in unoperated women with endometriosis-associated infertility with bilateral cysts (Fig. 1).

In order to compare the hormonal background of unoperated and operated in the medical history women with endometriosis-associated infertility, an analysis of rank variations of Kruskal-Wallis was performed between the combined groups with unoperated

mono- and bilateral cysts (1a + 1b) and group 2a. It was found that AMH in the blood of women with endometriosis-associated infertility in group 2a was probably lower compared to groups with unoperated mono- and bilateral cysts (by 57.65%), (Table 2).

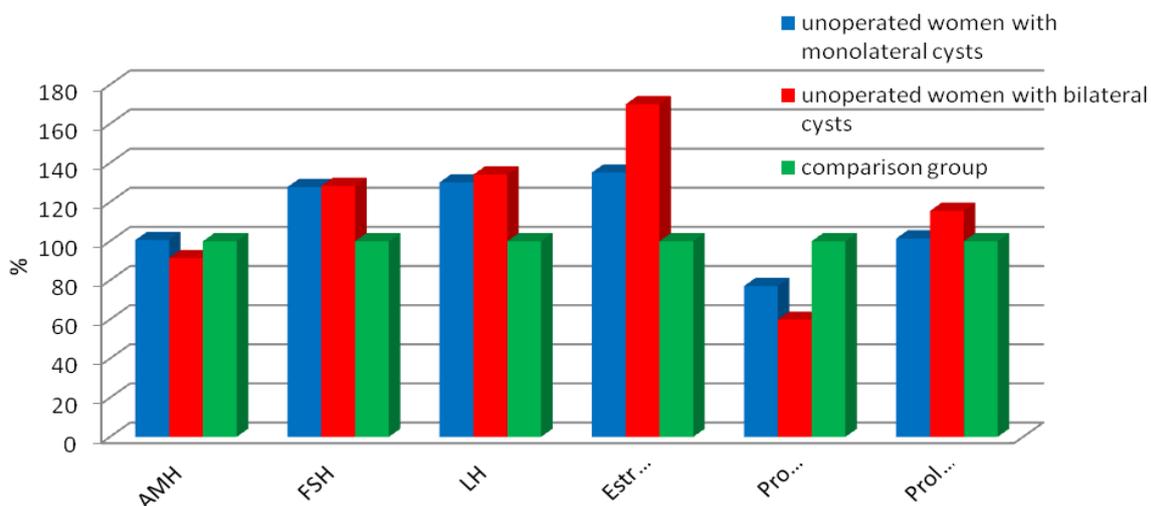


Fig. 1. Comparison of changes in hormone levels of patients with endometriosis-associated infertility depending on the location of cysts

Table 2 - Concentration of the reproductive system hormones of women with endometriosis-associated infertility (Me (Q25; Q75))

	1a + 1b (n =54) Unoperated	2a (n = 23) Operated without recurrences	Kruskal-Wallis criterion
AMH	1.70 (1.30; 1.90)	0.72 (0.60; 1.00)	H=5.06; p=0.02*
FSH	10.15 (9.20; 10.90)	10.60 (9.95; 11.20)	H=0.08; p>0.05
LH	8.05 (6.85; 9.30)	8.40 (7.73; 9.30)	H=1.22; p>0.05
Estradiol	55.90 (47.83; 68.70)	55.30 (44.60; 61.80)	H=2.38; p>0.05
Progesterone	10.05 (6.53; 12.05)	6.70 (4.10; 12.20)	H=0.27; p>0.05
Prolactin	11.70 (9.88; 14.83)	10.30 (7.95; 14.70)	H=0.22; p>0.05

Note. * - statistically significant results.

Comparison of changes in hormone levels of operated patients with endometriosis-associated infertility depending on the absence / presence of recurrence indicates the highest

values of LH and estradiol in group 2b and the lowest - AMH and progesterone in group 2a (Fig. 2).

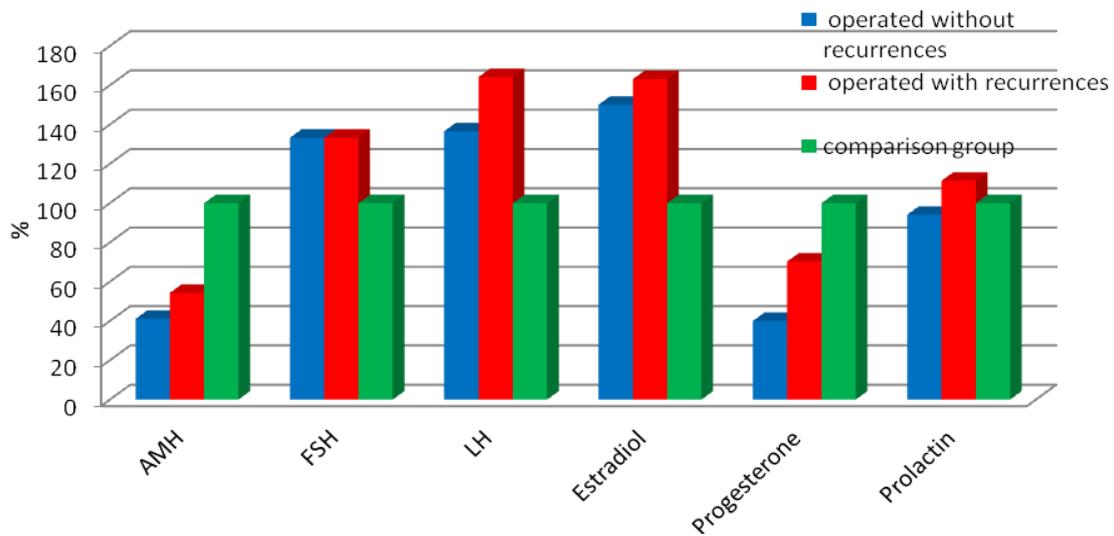


Fig. 2. Comparison of changes in hormone levels of patients with endometriosis-associated infertility who were operated in medical history depending on the absence / presence of recurrence.

The obtained results indicate the maximum hormonal imbalance in women with recurrent cystectomy. According to the literature, surgery of the internal genitals can disrupt ovarian function both due to loss of ovarian tissue and due to impaired local blood flow [10], which is reflected in the results of our study. Among the indicators of the hormonal background, the level of AMH is the most important, which according to the results of our study was probably lower in patients who underwent cystectomy (groups 2a and 2b). The obtained data were reflected in a number of studies that found that surgical removal of cysts was associated with a decrease of AMH levels, especially in patients with bilateral cysts and cysts with a diameter of 5 cm or more [11-13]. Among a large number of studies, only Ercan CM and colleagues did not show a decrease of AMH concentration after surgery in women with endometriosis [14].

Women with endometriosis-associated infertility have probably a high concentration of estradiol. According to a number of researchers, in granulosa cells in women with endometriosis-associated infertility, there is an increased activity of the enzyme aromatase, which in turn leads to increased secretion of estradiol. Increased indicator of serum estradiol contributes to the pathological proliferation of the endometrium and the emergence of new foci of endometriosis [15-19]. Increased levels of FSH and LH indicate a reduced

reproductive potential [20]. Decreased progesterone levels may be due to the fact that women with endometriosis develop resistance to all the biochemical effects of progesterone, which may be the result of changes in isoforms of progesterone receptors [21].

Conclusions. Women with endometriosis-associated infertility have hormonal disorders characterized by increased levels of follicle stimulating and luteinizing hormones, estradiol, decreased levels of progesterone and anti-müllerian hormone, with AMH probably lower in women after cystectomy, according to data of unoperated patients.

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