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Features of the hormonal background of women with infertility on the background of endometriosis and methods of their correction

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Endometriosis-associated infertility is characterized by a number of specific features that must be considered when choosing treatment methods. In each case, treatment should be individual, taking into account all clinical factors, as well as the impact of the disease and the effect of treatment on the quality of woman's life. Objective - to analyze the concentration of the reproductive system hormones in women with endometriosis-associated infertility before and after sclerotherapy using pregravidary preparation with a complex vitamin medication with inositol and vitamin D3. The study included 70 women aged 21-40 years with endometriosis-associated infertility. The comparison group included 30 women with tuboperitoneal infertility factor. 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". The medicament FT 500 plus was prescribed in a dosage of 1 sachet - once a day from the 2nd or 3rd day of the cycle during 2 menstrual cycles (cycle in which sclerotherapy was performed and subsequent cycle) for 1 group. Vitamin D3 was prescribed in prophylactic doses of 2.000 IU to women who were not diagnosed with a deficiency of this vitamin and in medium therapeutic doses for hypovitaminosis during 2 menstrual cycles. The sclerotherapy procedure was performed in a sterile operating room on the 6th - 8th day of the menstrual cycle by transvaginal puncture of the cyst and aspiration of its contents under the control of transvaginal ultrasound, introduction into the cyst capsule 95 % ethanol solution. Women with endometriosis-associated infertility, who were prescribed pregravidary preparation with a complex vitamin medication with inositol and vitamin D3 and sclerotherapy had probably lower levels of AMH (by 12.90 %), progesterone (by 9.84 %) and probably higher levels of FSH (by 14.47 %), LH (by 21.14 %) estradiol (by 35.55 %) relative to the comparison group. At the same time, significantly lower indicators of FSH (by 21.98 %), LH (by 32.89 %) and estradiol (by 32.23 %) were found against their values before sclerotherapy. Performing of sclerotherapy with pregravidary preparation with a complex vitamin medication with inositol and vitamin D3 to women with endometriosis-associated infertility has a positive effect on the hormonal background.

Keywords: *infertility, endometriosis, hormones, sclerotherapy, inositol, vitamin D3, effect.*

Introduction

Genital endometriosis is one of the most common diseases in women of reproductive age, which attracts the attention of scientists and practitioners around the world. According to researches, every tenth woman of reproductive age suffers from endometriosis, which in turn is 176 million women (World Population Projection Tables by Country and Group, 2010). The main symptoms of endometriosis are infertility, menorrhagia, dysmenorrhea, dyspareunia,

chronic pelvic pain. In 20-25 % of women, this disease is asymptomatic [1].

Endometriosis-associated infertility is characterized by a number of specific features that must be considered when choosing treatment methods. In each case, treatment should be individual, taking into account all clinical factors, as well as the impact of the disease and the effect of treatment on the quality of woman's life [9, 22].

The classic surgical treatment of endometriosis is excision of the cyst capsule, at which, according to scientists, the lowest number of recurrences and the highest number of clinical pregnancies [6, 15, 16, 17]. However, it should be taken into account that in addition to the capsule, a significant part of healthy ovarian tissue with antral follicles is removed [10]. Therefore, the search for less traumatic and more effective treatments, which include puncture of endometriomas and sclerotherapy, continues [12].

To date, the choice of treatment tactics for women with endometriosis-associated infertility for assisted reproductive technology (ART) programs remains controversial. It is scientifically proven that in women with endometriosis-associated infertility, the balance between intracellular trace elements is disturbed; free radical oxidation processes are activated, which leads to oxidative stress, which in turn can negatively affect the effectiveness of ART. Reactive oxygen species usually play an important role in a number of reproductive tract functions, but their overproduction has a negative effect on estrogen levels, altering steroidogenesis, thereby preventing oocyte maturation and ovulation [5, 18]. Therefore, we consider it justified to use antioxidants during pregravidary preparation of patients with endometriosis-associated infertility before COS protocol.

The aim of our study was to analyze the concentration of the reproductive system hormones in women with endometriosis-associated infertility before and after sclerotherapy using pregravidary preparation with a complex vitamin medication with inositol and vitamin D3.

Materials and methods

The study included 70 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 study groups. 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 34 women of reproductive age with endometrioid cysts up to 6.5 cm in diameter, who underwent sclerotherapy and pregravidary preparation with a complex vitamin medication with inositol and vitamin D3; group 2 - 36 women who underwent sclerotherapy. The presence of cysts was confirmed by ultrasound and bimanual examination.

Determination of hormone indicators was performed in different phases of the cycle before and after

sclerotherapy and pregravidary treatment. 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".

The medicament FT 500 plus for women of group 1 was prescribed in a dosage of 1 sachet - once a day from the 2nd or 3rd day of the cycle, after taking hormones blood test (AMH, FSH, LH) during 2 menstrual cycles (cycle in which sclerotherapy was performed and subsequent cycle). Vitamin D3 was prescribed in prophylactic doses of 2,000 IU to women who were not diagnosed with a deficiency of this vitamin and in medium therapeutic doses for hypovitaminosis during 2 menstrual cycles.

The sclerotherapy procedure was performed in a sterile operating room with/without general anesthesia on the 6th - 8th day of the menstrual cycle by transvaginal puncture of the cyst and aspiration of its contents under the control of transvaginal ultrasound, introduction into the cyst capsule (without violating its integrity) sclerosing solution. 95 % ethanol solution was used as a sclerosant, installed in a volume of 50 % - 100 % of the cyst size under ultrasound control with its subsequent aspiration.

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. With the wrong distribution of values, they were represented as Me (Q25; Q75) (medians and Q25 and Q75 quartiles).

Results

Analysis of the hormones level of the reproductive system in women with endometriosis-associated infertility indicated a probably lower level of anti-müllerian hormone (AMH) to the same extent in women before and after sclerotherapy in relation to the comparison group. It was found that performing of sclerotherapy to women with endometriosis-associated infertility led to a probable decrease of the concentration of follicle-stimulating hormone (FSH) by 20.31 % compared to the data before sclerotherapy of endometriomas but remained statistically significantly higher than the comparison group (by 20.75 %).

There was also a decrease of the concentration of luteinizing hormone (LH) in patients after sclerotherapy by 16.96 % compared to the data before sclerotherapy of endometriomas, but the studied indicator was statistically significantly higher than the data of the comparison group (by 39.02 %). The level of estradiol in blood serum of women with endometriosis-associated infertility after sclerotherapy was probably lower by 26.63 % relative to the results before surgery, but remained significantly higher than the data of the comparison group (by 41.11 %). Similar

Table 1. Concentration of the reproductive system hormones in women with endometriosis-associated infertility before and after sclerotherapy without pregravidary preparation (Me (Q25; Q75)).

Indicators	Comparison group (n=30)	Before sclerotherapy (n=36)	After sclerotherapy (n=36)
AMH	1.75 (1.56; 1.92)	1.50* (1.30; 1.73)	1.50* (1.30; 1.73)
FSH	7.95 (6.93; 8.50)	11.55* (10.90; 12.43)	9.60* (8.78; 10.60) p<0.05
LH	6,15 (5.45; 6.80)	10.00* (9.30; 10.70)	8.55* (7.98; 9.23) p<0.05
Estradiol at 2 - 3 d.m.c.	36.85 (33.70; 40.08)	65.85* (60.40; 73.90)	52.00* (48.63; 55.53) p<0.05
Progesterone at 19 - 21 d.m.c.	13.95 (12.63; 15.58)	9,70* (8,18; 11,43)	11.15* (9.63; 12.23) p<0.05
Prolactin	10.95 (10.40; 12.28)	10.40 (9.60; 11.40)	10.30 (9.50; 11.08)

Note: * - statistically significant control results; p - statistically significant results between groups before and after sclerotherapy.

Table 2. Concentration of the reproductive system hormones in women with endometriosis-associated infertility before and after sclerotherapy, whose pregravidary preparation was carried out with a complex vitamin medication with inositol and vitamin D3 (Me (Q25; Q75)).

Indicators	Comparison group (n=30)	Before sclerotherapy (n=34)	After sclerotherapy (n=34)
AMH	1.75 (1.56; 1.92)	1.55* (1.40; 1.78)	1.50* (1.30; 1.80)
FSH	7.95 (6.93; 8.50)	11.10* (10.50; 12.40)	9.10* (8.30; 9.88) p<0.05
LH	6.15 (5.45; 6.80)	9.90* (8.65; 11.00)	7.45* (6.93; 8.65) p<0.05
Estradiol at 2 - 3 d.m.c.	36.85 (33.70; 40.08)	66.05* (61.50; 74.10)	49.95* (43.73; 55.38) p<0.05
Progesterone at 19 - 21 d.m.c.	13.95 (12.63; 15.58)	10.45* (8.95; 12.48)	12.70* (11.13; 13.50) p<0.05
Prolactin	10.95 (10.40; 12.28)	11,00 (9.53; 12.18)	10.80 (10.00; 12.00)

changes were recorded for progesterone levels at 19-21 d.m.c. in blood serum of women with endometriosis-associated infertility after sclerotherapy, in particular, its increase by 14.94 % relative to the data before sclerotherapy, but by 25.11 % lower data against the comparison group. Note that sclerotherapy did not affect the level of prolactin (Table 1).

Women with endometriosis-associated infertility, who were prescribed pregravidary preparation with a complex vitamin medication with inositol and vitamin D3 and

Fig. 1. Comparison of the relative level of the reproductive system hormones in women with endometriosis-associated infertility after sclerotherapy in relation to their values before sclerotherapy of the endometrioma.

sclerotherapy had probably lower levels of AMH (by 12.90 %), progesterone (by 9.84 %) and probably higher levels of FSH (by 14.47 %), LH (by 21.14 %) estradiol (by 35.55 %) relative to the comparison group. At the same time, significantly lower indicators of FSH (by 21.98 %), LH (by 32.89 %) and estradiol (by 32.23 %) were found against their values before sclerotherapy (Table 2).

In order to compare the obtained results, we analyzed the effect of pregravidary preparation on the concentration of reproductive hormones in women with endometriosis-associated infertility after sclerotherapy, so the value of hormones before this surgical manipulation, we considered 100 %. It was found that the use of a complex vitamin medication with inositol, as well as vitamin D3 caused a decrease of LH level (by 10.25 %), as well as an increase of progesterone level (by 6.58 %) (Fig. 1.)

Discussion

The obtained data indicate a positive effect of sclerotherapy on the hormonal background of women with endometriosis-associated infertility. According to the literature, sclerotherapy of endometriomas is recommended for women with recurrent endometrioid cysts [14] to preserve the ovarian reserve, avoiding the next surgical excision [13]. It was found that the recurrence rate after sclerotherapy ranges from 12.9 % to 20 %, which is almost no different from indicators after laparoscopic cystectomy [2, 8].

The researchers found that the number of antral follicles increased in patients who underwent sclerotherapy for recurrent endometriomas [7, 19]. The level of AMH in blood serum was an indirect marker of ovarian reserve. In our study, there were no mean changes of AMH level in blood serum before and after sclerotherapy, which is comparable to other studies [4]. Sclerotherapy can improve ovarian blood supply and follicle growth [7], which in turn may

increase the probability of future fertility in women, who are undergoing sclerotherapy. The question of the effect of sclerotherapy on the reproductive hormones level remains debatable. Thus, in a study of Wang Xiaotao and co-authors decreased levels of E2, FSH and LH are established [21]. In a study of Saeed Alborzi and co-authors, the effect of sclerotherapy was associated with ovarian activity; in particular, a decrease of FSH level, as well as an increase of the number of AMH level and antral follicles [3]. On the other hand, a study of Aflatoonian A. et al. [2] did not show a significant difference between the studied hormones (FSH, LH) before and after sclerotherapy. The difference of the results may be due to different sizes of cysts in women included in the study (our study included women with endometrioid cysts up to 6.5 cm in diameter), presence of cystectomy in medical history, localization (unilateral or bilateral endometrioma), recurrence of endometrioid cysts.

The use of pregravidary preparation with a complex vitamin medication with inositol and vitamin D₃ had a slight effect. Inositol is a component of phospholipids and is a part of the content of cytoplasmic membranes as a phosphoinositide. Inositol binds Ca²⁺ channels and stimulates the intracellular release of Ca²⁺. Increased intracellular Ca²⁺ level plays an important role in oocyte maturation, fertilization, and embryonic development. A

sufficient concentration of inositol in the follicular fluid reduces the level of free radicals and damage of membrane protein and increases the number of good quality oocytes [11]. 1.25-dihydroxyvitamin-D₃ (vitamin D), except calcium-phosphate homeostasis, has a pronounced immunomodulatory effect (affects the local immune environment in an autocrine / paracrine way), affects the processes of cell proliferation and differentiation. Studies have shown that vitamin D intake reduces the concentration of anti-inflammatory cytokines: IL-6, interferon- γ , IL-2, and TNF- α [11]. The combination of vitamin D₃ multivitamin complex with inositol normalizes ovarian activity, improves metabolic and hormonal profile, in particular, reduces increased level of luteinizing hormone and oxidative stress [20].

Conclusions

Performing of sclerotherapy with pregravidary preparation with a complex vitamin medication with inositol and vitamin D₃ to women with endometriosis-associated infertility has a positive effect on the hormonal background, in particular, probably lower indicators of FSH (by 21.98 %), LH (by 32.89 %) and estradiol (by 32.23 %) against their values before sclerotherapy.

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