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The ovarian functional state of the women with tubal-peritoneal infertility

Summary: 100 women of the active reproductive age with tubal-peritoneal infertility and 30 women of the same age without fertile malfunction were examined. Assessment of ovarian

reserve was performed on the content of Follicle-Stimulating Hormone (FSH), Inhibin B, Anti Muller Hormone (AMH) in the blood serum, according to the data of echoscopy of ovaries and Doppler studies of stromal vessels. It was found, that, in patients with infertility of tubal-peritoneal genesis, ovarian reserve is diminished. Parameters of ovarian reserve reflect the functional state of women's ovaries and the most reliable marker of ovarian reserve is the level of AMH.

Keywords: Infertility, ovarian reserve, Inhibin B, Anti Muller Hormone.

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Infertility is one of the most important problems of modern medicine. The infertile marriages rate in Russia exceeds 15 %, that, according to the data of the World Health Organization, is a critical level [3]. The tubal-peritoneal factor occupies the first place in the structure of main reasons of infertility (40-72 %) [6, 7, 9].

The widespread use of methods of assisted reproductive technologies in the treatment of various forms of female and male infertility necessitates the search of reliable markers to estimate the functional state of the reproductive system. Diagnostics of the functional state of the ovaries before the beginning of therapy allows to choose treatment strategy, dose of preparations and to determine indications for IVF adequately (T.A. Nazarenko and others, 2008).

In clinical practice, the concept of ovarian reserve is widely used. Despite the considerable amount of research works, the significance of different parameters for determination of the functional state of ovaries still is not fixed [3]. The value of FSH, Inhibin B, AMH, ultrasound characteristics of ovaries for ovarian reserve estimation [4] are under discussion.

Research objective: To study the ovarian functional activity of the native women of the North with tubal-peritoneal infertility for determining treatment tactics, including methods of assisted reproductive technologies.

Materials and methods

100 native women of the North with tubal-peritoneal infertility (the main group) were completely examined. The levels of FSH, LH (Luteinizing Hormone) were determined on days 2 – 3 of the menstrual circle, the Progesterone level – on days 20-22 of the period, using competitive Enzyme-Linked Immuno-Sorbent Assay (ELISA) method by means of test systems, produced by "Hema-Medina" Co., Moscow. The levels of Inhibin B and AMH were determined on days 2 – 3 of the menstrual cycle by the ELISA method, using commercial sets of "DSL" Co., USA.

At ultrasound research we defined the shape and sizes of uterus, its structure, the average sizes of the M-echo. When researching ovaries, we measured their sizes, volume, estimated the state of the follicular apparatus and Doppler sonographic imaging.

Based on the results of the perspective analysis of the content of FSH, Inhibin B, AMH, Progesterone and three-time echographic monitoring during the menstrual circle, two subgroups were made up: 1 subgroup – 65 women with tubal-peritoneal infertility without ovarian malfunction, 2 subgroup - 35 women with ovarian dysfunction. The comparison group included 30 native women of the North without reproductive malfunction.

Results and discussion

The age of examined women of the both groups ranged from 22 to 39 years old and on the average, was 30,7±0,7 years in the main group, 29,7±5,2 ($p>0,05$) in the comparison group. The middle age of women of subgroups 1 and 2 was 29,9+0,5 and 31,6+0,9 years old accordingly.

All women of the main group complained of infertility. The duration of infertility in the subgroup 1 was 4,9±0,4 years, in the subgroup 2 – 7,09±0,6 years ($p <0,05$). Gynecologic diseases were observed in the main group, being there 3,6 times more often ($p <0,01$). Sexually transmitted infections were 2,6 times more often in the main group than in the comparison group ($p <0,05$). Chronic inflammatory diseases of the pelvic organs can disrupt the ovarian function, leading to enhanced follicular atresia, due to activation of anti-inflammatory cytokine cascade [8].

The content of FSH in the blood serum of women with tubal-peritoneal infertility on days 2-3 of menstrual cycle was higher than in the group of women without fertile dysfunction (10,3±0,4 IU/ML vs 7,6±0,3 IU/ML; $p <0,05$) (tab.). In the group of women with ovarian malfunction the value of FSH reached 11,7±1,0 IU/ML ($p <0,001$). According to some authors,

the FSH content, being higher than 10 IU/ML, indicates diminished ovarian reserve [2]. However, some experts consider, that a moderate increase of FSH at the relatively young age is not necessarily an indication of early ovarian ageing and this fact should be taken into account when advising these patients [10,11,12].

The content of LH in the blood serum of women of the comparison group at the early follicular phase was 5,9±0,4 IU/ML, that had no significant difference with its content in the blood serum of women of the 1st and 2nd subgroups (4,6±0,2 IU/ML, 4,4±0,4 IU/ML;> 0,05). These results coincide with the ones of other researchers [15]. In women without reproductive dysfunction, the Progesterone content was 51,0±5,1 nmol/l, that did not differ from that of women from the main group and the subgroup with normal ovarian function (p>0,05). In the blood serum of the women of the subgroup 2 the Progesterone content was 2,2 times lower, than in the comparison group (p <0,01). The basal level of Estradiol in the blood serum of women of examined groups and subgroups did not differ significantly.

For a better understanding of the functional state of the ovaries the measurement of Inhibin B and AMH was important. Women of the senior reproductive age or young patients with diminished ovarian reserve had not enough antral and growing follicles and, accordingly, had low concentration of Inhibin B. As Inhibin B regulates the hypophysis secretion of FSH, determining the content of Inhibin B allows to estimate the ovarian function more precisely, than FSH measuring [5]. At the same time, some experts consider that Inhibin B is not very informative as compared with FSH, because it has direct correlation dependence with the latter. Trying to assess the prognostic value of Inhibin B, we analysed its content in the compared groups. In the group of women without fertile disorder the content of Inhibin B did not differ from the one of women with tubal-peritoneal infertility (64,5±6,7 pg/ml and 59,6±6,2 pg/ml accordingly; p>0,05), that confirms the opinion of other authors about little informative value of Inhibin B as an early marker of the diminished ovarian reserve. However, the decline of Inhibin B was detected in the subgroup of women with ovarian dysfunction (47,8±4,4 pg/ml; p <0,01) as compared with the group of women with normal ovarian function and the comparison group (66,0±3,0 pg/ml, 64,5±6,7 pg/ml accordingly). Therefore, we think that the measurement of its content in the blood serum can be used in the algorithm of examination of women with infertility of tubal-peritoneal origin.

AMH is of the greatest interest in the estimation of ovarian reserve and reproductive potential of women. AMH is one of the most significant regulators of female reproductive function, that reflects the growth of follicles from the primordial pool stage to the stage of large antral follicles [2]. When analyzing the AMH content in the blood serum, lower indicators

(1,9±0,1 ng/ml) were obtained in the group of women with tubal-peritoneal infertility as compared with the group of women without fertile malfunction (2,5±0,3 ng/ml; p <0,05). The lowest content of AMH was observed in the group of women with ovarian dysfunction (1,3±0,2 ng/ml; p <0,01), indicating the decrease of the primordial follicles pool amount. Thus, it confirms the opinion of other experts about the importance of determining the level of AMH as the best marker showing the diminution of ovarian reserve.

The hemodynamics state in the stroma of ovaries was studied three times: in the early follicular phase, in the preovular period and in the period of the maximum growth and activity of the corpus luteum . In the preovular period the Resistance Index (RI) of the gynecologically healthy women was 0,47±0,05 s.u. in the right ovary, 0,48±0,05 s.u. - in the left ovary, 0,42±0,050 s.u., 0, 43±0,06 s.u. - in the period of the maximum growth and activity of the corpus luteum respectively, and was lower (p <0,05) as compared with RI of infertile women during the same periods of the menstrual cycle, that characterizes the best hemodynamics in the ovarian stroma. Animals studies confirmed that increase of the blood supply to the ovaries is the determining factor in selection of the dominant follicle [13]. According to some authors, the decrease of the ovarian blood supply, detected by Colour Doppler Mapping, serves as an earlier marker of diminished ovarian reserve, than increase of the FSH level. Poor ovarian blood supply can, in its turn, lead to the resistance of the ovary to stimulation and to ovarian failure [1].

In women with ovarian dysfunction the average number of antral follicles in the early follicular phase was 5,7±1,5 in the right ovary and 4,8±1,7 in the left ovary, and was less than the ones in women with normal ovarian function and without reproductive disorders (p <0,05). It was found, that the availability of less than 5 antral follicles in an ovary is an unfavorable prognostic sign of the ovarian reserve. According to a number of authors, the reduction of the number of antral follicles is the best indicator of the ovarian extinction, after determining the AMH content in the blood serum[16].

Pregnancy rate in the examined groups

We carried out the comparative analysis of pregnancy rate among women of the main group. In the subgroup of women without ovarian dysfunction 21 (32,3 %) women got pregnant, including: 11 (52,3 %) patients - after the course of combined therapy (antibacterial, anti-inflammatory and physiotherapy), 8 (38,1 %) women - after laparoscopic surgery, 2 (9,5 %) women - after IVF and Embryo Transfer (ET). In the IVF program 5 women from this group took part.

In the subgroup of women with ovarian dysfunction 4 (11,4 %) patients achieved pregnancy, including: 2 women - after the course of combined treatment, 1 patient – after laparoscopic surgery and 1 woman – after IVF with ovum donation. In the IVF program 4 women participated.

Thus, in the group of women without ovarian dysfunction the pregnancy rate was 2,8 times higher.

Conclusions

In women with infertility of tubal-peritoneal origin, the state of ovarian reserve is worsening; the time for realisation of reproductive plans is shortening. The basic principles of treatment of tubal-peritoneal infertility lie in the integrated approach, taking into account the functional state of the ovaries.

Parameters of ovarian reserve (the content of FSH, Inhibin B, AMH, number of antral follicles) reflect the functional state of the ovaries.

The most reliable marker of the ovarian reserve state is the AMH level.

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Table

Parameters of ovarian reserve

Groups	The levels of hormones			Number of antral follicles	
	FSH (IU/ML)	AMH (IU/ML)	Ingibin B	Right ovary	left ovary
Main (n=100)	10,3±0,4 p<0,05	1,9±0,1 p<0,05	59,6±6,2	5,07± 1,5	4,9± 1,7
Subgroup: 1 (n=65)	8,9±0,2	2,2±0,1	66,0±3,0	5,1± 1,5	5,1± 1,6
2 (n=35)	11,7±1,0 pcp-2<0,01	1,3±0,2 pcp-2<0,01 p1-2<0,01	47,8±4,4 pcp-2<0,01 p1-2<0,05	5,02±1,6 pcp-2<0,05	4,6±1,8 pcp-2<0,05 p1-2<0,05
Comparison (n=30)	7,6±0,3	2,5±0,3	64,5±6,7	5,7± 1,2	5,6± 1,1

p – the differences between the main group and a comparison group; p cp-2 - between the comparison group and a subgroup 1 p 1-2- between the subgroups 1 and 2.