



Dishormone and its Correction in Premature Ovarian Failure

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Abstract: We prospectively studied the hormonal status of women diagnosed with POI, with the removal of one ovary and without surgery. The study of the hormonal background revealed the syndrome of ovarian insufficiency in women after surgical treatment. Our studies were carried out in the period from 1 month to 3 months, from 4 to 6 months. and 7 months. up to 12 months after the operation. We have studied the changes in the level of the main informative hormones FSH, E2, LH, AMH, since the rest of the hormones, such as cortisol, prolactin, progesterone and testosterone in both groups, have changed little, while the ovary is preserved, the level of hormones is somewhat maintained, thanks to the follicular apparatus in it. And in patients of the second group, ovulatory cycles and normalization of hormonal levels gradually approached their previous state after 9-12 months.

Keywords: premature ovarian failure, "early aging", "early menopause", amenorrhea, infertility, hypomenstrual syndrome.

Doing. In the 2016 clinical guidelines, the European Society for Human Reproduction and Embryology (ESHRE) defines premature ovarian failure (POF) as a clinical syndrome, the main manifestation of which is the cessation of ovarian function before the age of 40, characterized by menstrual dysfunction, an increase in the level of gonadotropins and a decrease in estradiol concentrations [1, 2, 3].

Despite the large number of studies conducted in this direction, the etiology of primary POI in most cases (over 50%) remains unknown [1,2,4]. Given the devastating effects of estrogen deficiency on the body, the limited ability to solve reproductive problems in women with POF, and in most cases the loss of the follicular apparatus occurs gradually, there is an active search for the possibility of early diagnosis and prediction of this syndrome. These are markers of ovarian reserve AMH and inhibin B, the levels of which begin to decrease long before the increase in FSH levels and cycle disorders [3,5,6,7,8]. Currently, active work is underway to predict POI and develop diagnostic criteria for its preclinical forms.

Purpose of the study. To study the hormonal landscape of premature ovarian failure and choose the optimal hormonal correction.

Materials and research methods. The hormonal status of women diagnosed with POI was prospectively studied and they were divided into 3 groups: group 1, the main group consisted of 54 women with the removal of one ovary after gynecological operations for ovarian cysts; group 2, the comparative group consisted of 55 patients with the presence of both ovaries, but signs of POI and the control group of 30 healthy patients.

Hormone levels were assessed by immunochemiluminescent analysis on a Maglum 2000 plus automatic analyzer from Shibe (China). Blood sampling to determine the content of FSH, LH, progesterone, estradiol and anti-Mullerian hormone was carried out in the morning, on an empty stomach from the cubital vein. The obtained blood was centrifuged, the serum was frozen and stored at a temperature of 22-24C in labeled Eppendorf tubes until analysis. The study of the hormonal

background revealed the syndrome of ovarian insufficiency in women after surgical treatment and in women without surgical interventions, the absence of a normal menstrual cycle.

Results and its discussion. The study of the hormonal background revealed the syndrome of ovarian insufficiency in women after surgical treatment. Our studies were carried out in the period from 1 month to 3 months, from 4 to 6 months. and 7 months. up to 12 months after the operation. The level of hormonal changes was studied carefully in women with preserved ovaries and with ovaries removed in the first group in order to determine the methods of rehabilitation and selection of appropriate therapy for this subgroup. We have studied the changes in the level of the main informative hormones FSH, E2, LH, AMH, since the rest of the hormones, such as cortisol, prolactin, progesterone and testosterone, have changed little in both groups.

Thus, the average level of FSH one month after surgery in the main group was 13.3 ± 0.96 mIU/ml, and in the comparison group it was 5.5 ± 0.5 mIU/ml ($p < 0.05$); the level of LH in the main group was 12.4 ± 1.1 mIU/ml, and in the comparison group it was 6.1 ± 0.84 mIU/ml ($p > 0.05$). Normally, the content of E2 in the follicular phase is 30-120 pg / ml. In the postoperative period, we noted a decrease in their secretion in the main group almost three times, and in the comparison group by 1.2 times. Thus, estradiol in the main group was found to be 36 ± 7.1 pg/ml in the main group, and 82.4 ± 17.2 pg/ml in the comparison group ($p < 0.01$). In the early postoperative period, the level of E2 in the main group, in whom the ovaries were preserved, was 43.0 ± 1.36 , and in the group with the removal of one ovary, it was slightly reduced - it was 36.7 ± 0.60 , but from the indicators of women in groups 2 significantly differ - 82.0 ± 1.36 . This is due to the trauma of the surgery and the removal of the uterus and one ovary.

When re-measured several months after the operation, a sharp change in the hormonal background of 37.7 ± 1.36 was revealed in women with the removal of one ovary, and in the comparison group these figures were 77.8 ± 1.36 . This is explained by the fact that with the preserved ovary, the level of hormones is somewhat maintained, thanks to the follicular apparatus in it. And in patients of the second group, ovulatory cycles and normalization of hormonal levels gradually approached their previous state after 9-12 months.

The levels of pituitary hormones (FSH and LH) increased in the early postoperative period, so FSH was 13.3 ± 0.96 mIU/ml in the main group, 5.5 ± 0.5 mIU/ml in the control group, and the concentration of LH was 12.4 ± 1.1 mIU/ml and 6.1 ± 0.84 mIU/ml, respectively, by groups. During the observation, the level of FSH in women of the 1st group with one ovary preserved was 9.3 ± 0.10 , and in women of the 2nd group this figure is 9.6 ± 0.10 , which means that this hormone is approaching the norm. After 12 months, the level above this hormone differs dramatically depending on the presence of an ovary. Since in women with one ovary preserved, this FSH level is 15.5 ± 0.10 , and in the second group, the FSH values approach the norm - 11.3 ± 0.10 , but lag behind the control group - 14.1 ± 0.34 . Estradiol in women after the removal of one ovary decreased by 2.9 times, and in women of the second group only by 1.2 times - 36 ± 7.1 pg/ml and 82.4 ± 17.2 pg/ml, respectively.

The average level of FSH one month after surgery in the main group was 13.3 ± 0.96 mIU/ml, and in the comparison group it was 5.5 ± 0.5 mIU/ml ($p < 0.05$); the level of LH in the main group was 12.4 ± 1.1 mIU/ml, and in the comparison group it was 6.1 ± 0.84 mIU/ml ($p > 0.05$). Normally, the content of E2 in the follicular phase is 30-120 pg / ml. In the postoperative period, we noted a decrease in their secretion in the main group almost three times, and in the comparison group by 1.2 times. Estradiol in the main group was found to be 36 ± 7.1 pg/ml in the main group, and 82.4 ± 17.2 pg/ml in the comparison group ($p < 0.01$). In the early postoperative period, the level of E2 in the main group, in whom the ovaries were preserved, was 43.0 ± 1.36 , and in the group with the removal of the ovary, it was slightly reduced - it was 36.7 ± 0.60 , but the indicators of women in group 2 were significantly differ - 82.0 ± 1.36 . This is due to the trauma of the surgery and the removal of one ovary.

Re-measurement a few months after the operation revealed a sharp change in the hormonal background 37.7 ± 1.36 in women with ovary removal, and with a preserved ovary 77.8 ± 1.36 approaches the indicators of patients of the second group - 92.0 ± 1.36 . This is due to the fact that

with a preserved ovary, the level of hormones is somewhat maintained, thanks to the follicular apparatus in it. And in patients of the second group, ovulatory cycles and normalization of hormonal levels gradually approached their previous state after 9-12 months.

The levels of pituitary hormones (FSH and LH) increased in the early postoperative period, so FSH was 13.3 ± 0.96 mIU/ml in the main group, 5.5 ± 0.5 mIU/ml in the control group, and the concentration of LH was 12.4 ± 1.1 mIU/ml and 6.1 ± 0.84 mIU/ml, respectively, by groups. During the observation, the level of FSH in women of the 1st group with one ovary preserved was 9.3 ± 0.10 , and in women of the 2nd group this figure is 9.6 ± 0.10 , which means that this hormone is approaching the norm. After 12 months, the level

Table 1. Indicators of the hormonal status of the examined women

Index	FSH mIU/ml	LH mIU/ml	E pg/ml	AMH pg/ml
1 gr. removal of one ovary 1-3 months, n=54	$6,50 \pm 0,09$	$7,30 \pm 0,11$	$43,0 \pm 1,26$	$1,50 \pm 0,05$
2gr. without surgery -1-3 months, n=55	$13,27 \pm 0,32$	$12,43 \pm 0,28^{***}$	$36,73 \pm 0,80^{***}$	$1,37 \pm 0,05^{***}$
1 gr. 4-6 months	$9,29 \pm 0,12$	$8,40 \pm 0,08$	$77,80 \pm 1,36$	$1,50 \pm 0,04$
1 group 4-6 months	$9,59 \pm 0,11^{***}$	$8,30 \pm 0,13^{***}$	$92,0 \pm 1,73^{***}$	$1,60 \pm 0,04^{***}$
2 gr. 7-12 months	$15,50 \pm 0,09$	$7,30 \pm 0,11$	$42,99 \pm 1,15$	$1,80 \pm 0,04$
1gr. 7-12 months	$17,31 \pm 0,22$	$12,40 \pm 0,19^{***}$	$36,70 \pm 0,58^{***}$	$1,40 \pm 0,04^{***}$
Control group	$14,11 \pm 0,34$	$11,21 \pm 0,28$	$69,96 \pm 1,71$	$2,12 \pm 0,05$

Note: * - differences relative to the data of the control group are significant (***) - $P < 0.001$

Based on the above examinations of hormonal changes in women with preserved ovaries and with their removal, the following conclusions can be drawn:

In the postoperative period, in women with the removal of one ovary, a persistent increase in the level of the FSH hormone was observed, this was clearly manifested in women of the 1st group, these indicators are similar to those of the menopausal period. In the early postoperative period, it did not change sharply from the parameters of the comparison group, but in further analyzes, an increase in the level of this hormone was observed. This is due to the fact that the preserved ovary covers hormonal deficiency for several months, but in the future, the process of exhaustion also increases and approaches menopause. A preserved ovary cannot fully cover the function of another ovary and hormonal fluctuations occur in the body. As can be seen from Table 4.2, the function of the preserved ovary will last to maintain hormonal homeostasis only for the early stages of the postoperative period, and further HRT is required.

Given the sharp decrease in estrogen levels and an increase in FSH in women with the removal of one ovary and preservation in the active reproductive period, which coincides with the indicators of the menopausal period, it requires an urgent timely appointment of HRT in order to prevent "early aging" of the body.

It can be assumed that a decrease in estrogen levels contributes to a further increase in the tone of small vessels and the progression of deterioration in blood supply and, thus, a vicious circle occurs. Surgical trauma, tissue edema cause a deterioration in blood supply to the ovaries and a decrease in steroidogenesis, while a low level of estradiol, in turn, contributes to an increase in tone in the microvascular bed. This fact requires urgent rehabilitation measures.

Conclusion. Based on the above surveys of hormonal changes in women with preserved ovaries and with their removal, the following conclusions can be drawn:

In the postoperative period, women showed a persistent increase in the level of the FSH hormone, this was clearly manifested in women of the 1st group with the removal of one ovary, these indicators are similar to those of the menopausal period. However, in women of the second group, the presence of two ovaries also showed an increase in FSH. In the early postoperative period, it did not change sharply from the parameters of the comparison group, but in further analyzes, an increase in the level of this hormone was observed. This is due to the fact that the preserved ovary covers hormonal deficiency for several months, but in the future, the process of exhaustion increases and approaches menopause. A preserved ovary cannot fully cover the function of another ovary and hormonal fluctuations occur in the body. The function of the preserved ovary will last to maintain hormonal homeostasis only for the early stages of the postoperative period, and further HRT is required. Given the sharp decrease in estrogen levels and an increase in FSH in women with one ovary and preservation in the active reproductive period, which coincides with the indicators of the menopausal period, it requires an urgent timely appointment of HRT in order to prevent "early aging" of the body.

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