

Hormonal homeostasis in women of reproductive age with adenomyosis

V.O. Beniuk, V.V. Kurochka, K.I. Susak, Yu.G. Drupp, O.O. Bala
Bogomolets national medical university, Kyiv

The problem of adenomyosis is particularly relevant for patients of reproductive age, as it is accompanied by the significant disturbances of menstrual and generative functions. The article presents the results of studying the condition of the hypothalamic-pituitary-ovarian system in women of reproductive age with adenomyosis.

The objective: to study the state of the hypothalamic-pituitary-ovarian system in women of reproductive age with benign endometrial and myometrial pathology.

Materials and methods. The main group included 120 women of reproductive age with benign endometrial and myometrial pathology (adenomyosis, endometrial hyperplasia and combined pathology), and the control group included 40 healthy women without gynecological pathology. The functional state of the hypothalamic-pituitary-ovarian system was evaluated by the levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL), estradiol (E₂) and progesterone (P) in blood serum in different phases of the menstrual cycle.

Results. In women with adenomyosis, endometrial hyperplasia and combined pathology, there is hyperproduction of gonadotropic hormones with an increase of their secretion level compared to a group of healthy women: the average concentration of FSH, regardless of the phase of the menstrual cycle, increased by 1.9 times ($p < 0.05$), LH – 2.2 times, PRL – 2 times, which indicates the presence of hyperprolactinemia. Both in the I and II phases of the menstrual cycle, the occurrence of additional FSH and LH peaks from basal hormone secretion was determined in patients of the main group, which reached the level of hormone concentration in the ovulatory peak. In the patients of the main group, hyperestrogenemia during the entire menstrual cycle and hypoprogesteronemia were detected. The expression of hormonal shifts depended on gynecological pathology (adenomyosis, endometrial hyperplasia and combined pathology) and the functional state of the woman.

Conclusions. The indicators of gonadotropic and prolactin-stimulating activity of the pituitary gland in women with benign uterine pathology confirm the participation of FSH, LH and prolactin in the complex processes of regulation of the reproductive system.

Keywords: adenomyosis, endometrial hyperplasia, hypothalamic-pituitary-ovarian system.

Гормональний гомеостаз у жінок репродуктивного віку з аденоміозом

V.O. Beniuk, V.V. Kurochka, K.I. Susak, Yu.G. Drupp, O.O. Bala

Проблема аденоміозу має особливу актуальність для пацієнток репродуктивного віку, оскільки він супроводжується значними порушеннями менструальної та генеративної функцій. У статті представлені результати вивчення стану гіпоталамо-гіпофізарно-яєчникової системи у жінок репродуктивного віку за наявності аденоміозу.

Мета дослідження: вивчення стану гіпоталамо-гіпофізарно-яєчникової системи у жінок репродуктивного віку з доброякісною патологією ендометрія та міометрія.

Матеріали та методи. До основної групи увійшли 120 жінок репродуктивного віку з доброякісною патологією ендометрія (аденоміоз, гіперплазія ендометрія та поєднана патологія), до контрольної – 40 здорових жінок без гінекологічної патології. Функціональний стан гіпоталамо-гіпофізарно-яєчникової системи оцінювали за даними рівнів фолікулостимулювального гормону (ФСГ), лютеїнізуючого гормону (ЛГ), пролактину (Прл), естрадіолу (E₂) та прогестерону (П) у сироватці крові у різні фази менструального циклу.

Результати. У жінок з аденоміозом, гіперплазією ендометрія та поєднаною патологією відзначається гіперпродукція гонадотропних гормонів із підвищенням рівня їхньої секреції порівняно з групою здорових жінок: середня концентрація ФСГ незалежно від фази менструального циклу збільшена в 1,9 раза ($p < 0,05$), ЛГ – у 2,2 раза, Прл – у 2 рази, що свідчить про наявність гіперпролактинемії. Як у I, так і у II фазі менструального циклу у хворих основної групи фіксували виникнення додаткових піків ФСГ та ЛГ від базальної секреції гормону, які досягали величини вмісту гормонів в овуляторний пік. У пацієнток основної групи виявлена гіперестрогенемія протягом усього менструального циклу та гіпопрогестеронемія. Вираженість гормональних зсувів залежала від гінекологічної патології (аденоміоз, гіперплазія ендометрія та поєднана патологія) та функціонального стану жінки.

Висновки. Показники гонадотропної та пролактинстимулювальної активності гіпофіза у жінок із доброякісною патологією матки підтверджують участь ФСГ, ЛГ та пролактину у складних процесах регуляції репродуктивної системи.

Ключові слова: аденоміоз, гіперплазія ендометрія, гіпоталамо-гіпофізарно-яєчникова система.

Despite the centuries-long history of studying various aspects of the endometriosis problem, the disease does not lose its medical and social significance in the 21st century, which is associated with a progressive clinical

course and the formation of a persistent pain syndrome and, as a result, a decrease in the quality of life of patients [1–3].

Endometriosis is a hormone-dependent pathological process, the essence of which is the benign growth of tissue

similar to the endometrium in terms of morphological and functional properties, which occurs against the background of hormonal and immune imbalance in the presence of a genetic predisposition [4, 5]. Internal endometriosis affects the body of the uterus, the cervical canal, the intramural part of the fallopian tubes and is diagnosed as a separate disease and is denoted by the term adenomyosis [6, 7].

Adenomyosis is especially relevant for patients of reproductive age, as it is accompanied by significant disturbances of menstrual and generative function [8, 9]. The frequency of genital endometriosis ranges from 12% to 50%. Adenomyosis makes up 53–80% of the structure of endometriosis [10–12].

Adenomyosis and endometrial hyperplasia are not isolated diseases and are accompanied by a violation of hormonal homeostasis. However, the formation of this pathology results from an imbalance in the activity of a woman's endocrine system. The features of the hormonal status in adenomyosis, endometrial hyperplasia, and combined endometrial and myometrial pathology presented in the literature are pretty contradictory [13–15].

Modern principles of treatment of adenomyosis are based on the concept of it as a hormone-dependent pathological process. Hormonal therapy takes a leading place in the conservative treatment of patients and requires a careful diagnosis of the condition of the hypothalamic-pituitary-ovarian system [16, 17]. In addition, the choice of treatment tactics requires an individual and differentiated approach depending on the age of the patient, the severity of clinical symptoms, the prevalence of the pathological process, the duration of the disease, interest in the continuation of reproductive function, the presence of extragenital pathology [18–20].

The objective: is to study the state of the hypothalamic-pituitary-ovarian system in women of reproductive age in case of adenomyosis.

MATERIALS AND METHODS

The functional state of the hypothalamic-pituitary-ovarian system was assessed based on the data on the levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL), estradiol (E2), and progesterone (P) in the follicular phase, periovulatory period, and luteal phase of the menstrual cycle in 120 women of reproductive age with benign endometrial and myometrial pathology (adenomyosis, endometrial hyperplasia, and combined pathology). The evaluation of the activity of the thyroid gland was determined by the level of thyroid-stimulating hormone (TSH) and the free fraction of thyroxine (T4). Changes in the level of hormones depending on the clinical form were analyzed in comparison with the indicators of 40 gynecologically healthy women in the observation control group [21].

RESULTS AND DISCUSSION

The obtained results of the hormonal examination of women of the leading group with benign uterine pathology indicate significant changes in the gonadotropic function of the pituitary gland and steroidogenesis of the gonads. The level of FSH in patients with benign pathology of the endometrium and myometrium varied cyclically during the menstrual cycle, as in healthy women, but significantly

exceeded the indicators of the control group ($p < 0.05$) [22]. The average concentration of FSH in women with adenomyosis (A) exceeded the intermediate hormone level of healthy women by 1.4 times, with endometrial hyperplasia (EH) – by 2.0 times, with the combined pathology of A+EH – by 2.2 times and amounted to A – $(8.26 \pm 1.05 \mu\text{g/l})$, with EH – $12.97 \pm 1.48 \mu\text{g/l}$, with A+EH – $(13.14 \pm 1.05 \mu\text{g/l})$.

LH indicators were characterized by a marked violation of the rhythm and level of cyclic and basal secretion. The average level of basal LH secretion in women with benign uterine pathology exceeded the indicators of healthy women by 2.2 times: in patients with A – 1.7 times higher than in controls, with EH and A+EH by 2.5 times and 2.3 times, respectively. An increase in the content of LH was observed in both phases of the menstrual cycle, but the most pronounced was noted in the I phase, the level of lutropin exceeded the level of LH in healthy women by five times and amounted to $12.30 \pm 0.48 \mu\text{g/l}$. In addition to the ovulatory peak in LH secretion in patients with benign uterine pathology, additional lutropin peaks were observed in both the I and II phases of the menstrual cycle, which exceeded the ovulatory indicators of the hormone content. LH concentration increased in all clinical groups of women with benign uterine pathology in the I and II phases of the menstrual cycle. It was most pronounced in women with EH and A+EH.

In the patients of the leading group, hyperprolactinemia was observed with an increase in the average level of PRL ($560.22 \pm 30.46 \mu\text{IU/ml}$) by 1.9 times the indicator of the control group. In the dynamics of the menstrual cycle, the level of PRL was the highest in the I phase and was 2.8 times higher than that of the control group. Apparent violations of the prolactin-secreting function of the pituitary gland in patients with benign uterine pathology cause shifts in the regulation of ovarian function, which explains the high percentage of infertility in this category of women [23]. No statistically significant differences in PRL secretion depending on the clinical group of patients were found. Violations of PRL production in the case of A, EH and A+EH are associated with a violation of hormonal-receptor relationships in the uterus affected by the pathology.

When evaluating the functional state of the ovaries in women of reproductive age with benign endometrial and myometrial pathology, a significant increase in the level of estradiol (E2) was observed both in the I and II phases of the menstrual cycle compared to the control group ($p < 0.05$). The average content of E2 in patients of the leading study group was 1.9 times higher than the level of healthy women and amounted to $1.10 \pm 0.02 \text{ nmol/l}$. During the menstrual cycle, not only a significant increase in the average concentration of E2 but also a violation of the dynamics of the hormone level was established. In the first phase of the menstrual cycle, in the case of A, the level of E2 was three times higher than that of the control group and amounted to $0.88 \pm 0.05 \text{ nmol/l}$. At the peak of ovulation in patients with A, as in healthy women, the content of E2 increased, but the hormonal height compared to the content of E2 in the I phase of the menstrual cycle was less pronounced and increased only 1.3 times than in the control group - by 3.2 times. The average level of E2 during ovulation in patients with A was $1.14 \pm 0.08 \text{ nmol/l}$, which is 1.2 times higher than the level of this hormone in healthy women. In the luteal phase of the menstrual cycle, the content of

E2 decreased, but hyperestrogenemia remained: the level of estradiol was 1.7 times higher than the level of the hormone in the control group and amounted to 0.76 ± 0.07 nmol/l.

In EH and A+ EH, more pronounced hyperestrogenemia was observed than in adenomyosis. The highest average indicators of the level of E2 in both phases of the menstrual cycle were in women with combined pathology of the uterus and amounted to 0.99 ± 0.06 nmol/l in the I phase, in the ovulatory period – 1.58 ± 0.02 nmol/l, in II phase – 1.17 ± 0.07 nmol/l. The total average concentration of E2 with A+ EH was 2.2 times higher than the control indicators.

We found that the average progesterone content in women with benign endometrial and myometrial pathology (7.5 ± 0.57 nmol/l) is 1.6 times lower than in the group of healthy women. But in the dynamics of the menstrual cycle, the secretion of P had the following features: in the I phase – the level of P in patients with A did not reliably differ from the indicators of the control group, and therefore the expected hypoprogesteronemia was not observed, on the contrary, the average content of the hormone (2.15 ± 0.16 nmol/l) exceeded the average benchmark by 1.2 times.

During the menstrual cycle, the production of P in the primary research group preserved the patterns of the rhythm of hormone secretion characteristic of healthy women – the content of P increased in the ovulatory peak and was significantly greater in the luteal phase. But the degree of increase in P in benign uterine pathology did not correspond to the increase in P in healthy women and was much lower. The average content of P during ovulation in patients of the leading group was 2.7 times lower than the indicator of the control group and in the luteal phase – by 1.5 times, which amounted to 3.42 ± 0.16 nmol/l and 17.17 ± 0.41 nmol/l, respectively.

We analyzed the function of the thyroid gland in women of the principal and control groups. Indicators of thyroid-stimulating hormone and thyroxine in patients with adenomyosis, endometrial hyperplasia, and combined pathology of the uterus were within the normal range. There were no statistically significant differences in the clinical forms of the central and control groups of women established.

CONCLUSIONS

The results of our study showed that women with adenomyosis, endometrial hyperplasia, and combined pathology have hyperproduction of gonadotropic hormones with an increase in the level of their basal and cyclic secretion compared to a group of healthy women: the average concentration of FSH, regardless of the phase of the menstrual cycle, is increased by 1.9 times; intermediate LH level – 2.2 times; hyperprolactinemia was observed – the moderate PRL content increased by two times. In addition, both in the I and in the II phase of the menstrual cycle in patients of all clinical groups, the occurrence of additional peaks of FSH and LH from the basal secretion of the hormone, which in terms of the level reached the value of the hormone content in the ovulatory peak, was noted.

All clinical groups of examined women showed hyperestrogenemia throughout the menstrual cycle and relative or absolute hypoprogesteronemia. The expression of hormonal shifts depended on the clinical group of patients and functional status.

Thus, indicators of gonadotropic and prolactin-stimulating activity of the pituitary gland in women of reproductive age with benign uterine pathology confirm the participation of FSH, LH, and prolactin in the complex processes of regulation of the reproductive system [24–26].

Information about the authors

Beniuk Vasyl O. – MD, PhD, DSc, Professor, Head, Department of Obstetrics and Gynecology No. 3, Bogomolets National Medical University, Kyiv; tel.: (044) 405-60-33

ORCID: 0000-0002-5984-3307

Kurochka Valentyna V. – MD, PhD, Assistant of Professor, Department of Obstetrics and Gynecology No. 3, Bogomolets National Medical University, Kyiv. *E-mail:* kurochkavv78@gmail.com

ORCID: 0000-0001-6800-310X

Susak Kamila I. – MD, Postgraduate Student, Department of Obstetrics and Gynecology No. 3, Bogomolets National Medical University, Kyiv

Drupp Yurii G. – MD, PhD, Associate Professor, Department of Obstetrics and Gynecology No. 3, Bogomolets National Medical University, Kyiv. *E-mail:* urag2602@gmail.com

ORCID: 0000-0001-6179-9141

Bala Oksana O. – MD, PhD, Assistant of Professor, Department of Obstetrics and Gynecology No. 3, Bogomolets National Medical University, Kyiv. *E-mail:* oksana_bala@ukr.net

Відомості про авторів

Бенюк Василь Олександрович – д-р мед. наук, проф., завідувач, кафедра акушерства і гінекології № 3, Національний медичний університет імені О.О. Богомольця, м. Київ; тел.: (044) 405-60-33

ORCID: 0000-0002-5984-3307

Курочка Валентина Валеріївна – канд. мед. наук, асистентка, кафедра акушерства і гінекології № 3, Національний медичний університет імені О.О. Богомольця, м. Київ. *E-mail:* kurochkavv78@gmail.com

ORCID: 0000-0001-6800-310X

Сусяк Каміла Імглізівна – аспірантка, кафедра акушерства і гінекології № 3, Національний медичний університет імені О.О. Богомольця, м. Київ

Друпп Юрій Григорович – канд. мед. наук, доцент, кафедра акушерства і гінекології № 3, Національний медичний університет імені О.О. Богомольця, м. Київ. *E-mail:* urag2602@gmail.com

ORCID: 0000-0001-6179-9141

Бала Оксана Олегівна – канд. мед. наук, асистентка, кафедра акушерства і гінекології № 3, Національний медичний університет імені О.О. Богомольця, м. Київ. *E-mail:* oksana_bala@ukr.net

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