SPECIFIC FEATURES OF HORMONAL PANEL OF REPRODUCTIVE AGE WOMEN WITH THE ENDOMETRIUM HYPERPLASTIC PROCESSES

V. Goncharenko
"Feofania" clinical hospital

Summary. *The article presents the results of the hormonally relationship study in women of reproductive age with endometrium hyperplastic processes. The overproduction of gonadotropin-releasing hormone with increased levels of basal secretion and a decrease in the amplitude of the ovulatory secretion, low progesterone typical for women with hyperplastic endometrium processes is shown. Giperestrogenemiya due to the high level estrone and estradiol throughout the menstrual cycle is demonstrated.*

The conducted research allow to recommend the determination of hormonal profile and morphometrically indicators to develop an individual treatment tactics, and also as a criterion for monitoring the effectiveness of therapy.

Key words: *endometrial hyperplasia, endometrial polyposis.*

Endometrium hyperplastic processes (hereinafter - EHP (V.H.) remain one of the most topical problems of contemporary gynecology due to the increasing rate of endometrium cancer [4,5,6]. The frequency of the EHP cases among women of the late reproductive age stands for 20-35%. Menstrual and reproductive functions' disorders accompany the EHP, along with preneoplastic (precancerous) states. The topicality of the given problem is explained by the following aspects: the EHP clinical manifestation peculiarities, reproductive potential decrease, limited possibilities of endometrium hyperplasia (hereinafter – EH (V.H.) conservative treatment of women with the concurrent extragenital diseases as well as the EH carcinomatous degeneration risk [1,2].

The problem of EHP genesis among women of reproductive age is urgent both from the point of view of the given processes recurring preventive treatment and the possibility of the reproductive function renewal and preservation [7]. Notwithstanding the fact that the problem of endometrium pathological states early detection, glandular hyperplasia and poliposis, in particular, has been enough discussed in literature within the recent years, some issues of development are still not enough studied [3,8].

It is well-known that one of the important constituents of pathogenesis proliferative processes is the excessive volume of estrogens and insufficiency of progesterone in blood, but still there is no clear point of view on the role of folliculo-stimulating (hereinafter - FSH (V.H.) and intestinal cell-stimulating hormones (hereinafter - LH (V.H.) and estrone (E1) correlation related to the given pathology [5,10]. The study of endocrine correlation's role in EHP genesis is of great importance as it gives the possibility to define the therapeutic-diagnostic

algorithm and the given pathology preventive measures' methods based on pathogenetic principles.

Aim of the study

The aim of the study is to define the role of hormonal homeostasis correlation violation in the EHP pathogenesis among women of reproductive age.

Material and methods of the study

139 women with the EHP detected (the age varies from 18 to 45 years old), the patients of the Centre for general gynecology, gynaecological endocrinology and reproductive medicine of "Feofania" clinical hospital, as well as the patients of the City maternity home #3, have been examined. The patients have been examined on the basis of the Order of the Ministry of Health # 676 from 31.12.2004. Having the diagnosis clarified, all the patients have been divided into groups. Group #1 consisted of 81 (58,2%) women with the simple EH without atypism (hereinafter - SEHWA (V.H.); group #2 was composed of women with endometrium poliposis (hereinafter - EP (V.H.), and stood for 58 women (41,7%).

The age range of women of reproductive age with EHP has varied from 22 to 45 years old, with the average age of $38,6 \pm 3,2$ years old. The control group has been composed of 30 women of reproductive age who have had the annual clinical examination, with the average age of $36,6 \pm 4,1$ years old.

The examination of hormone level in blood has been conducted on the 5-7 day of menstrual cycle (follicular phase of menstrual cycle - FPMC) in order to assess the hormone homeostasis of women with EHP and subjects from the control group: folliculo-stimulating hormone (hereinafter – FSH (V.H.)), intestinal cell-stimulating hormone (hereinafter – LH (V.H.)), mammotropic hormone (hereinafter - MTH (V.H.), estrone (E1), estradiol (E2), testosterone (T). with the aim of the LH and FSH secretion dynamics' more precise updating, the examinations have been conducted within the ovulatory phase of menstrual cycle (hereinafter – OPMC (V.H.)) – 13-14 days) and lutein phase of menstrual cycle (hereinafter - LPMC (V.H.) – 21-22 days); progesterone (P) rate has been defined within the lutein phase (days 21-22). Blood serum examination has been conducted by means of immune chemical method with electrochemiluminescence detection (ECLIA) in order to define the hormones content (rate).

Results of the study and their discussion (analysis?)

The analysis of the data obtained has given all the grounds to state that the FSH rate of the subjects from the control group stood for 6,32 мME/ml within the FPMC, 10,29 мME/ml within the OPMC, and 4,71 мME/ml within the LPMC (See Chart 1)

The high average content of gonadotropic hormones within the menstrual cycle compared with the control group's results ($p<0,05$) has reliably been defined. The FSH level for the SEHWA group has been proved to be 1,6 times as much as

the corresponding index for the control group within the FPMC; the FSH level has been 1,2 times as much as the corresponding index for the control group within the OPMC; finally, it has been almost twice as much as the corresponding index for the control group within the LPMC. EP group has shown the similar FSH level fluctuations.

Chart 1

Hypophisial and sex hormones indexes for the women subjects of reproductive age depending on the menstrual cycle phase

	Phase of the cycle	**Group №1** SEHWA **n= 81**	**Group №2** **EP** **n= 58**	**Control group** **n= 30**
FSH (mME/m)	FPMC	10,04±1,05	9,64±0,35	6,32±0,35
	OPMC	13,56±1,16	12,98±1,11	10,29±1,65
	LPMC	8,16±1,16	7,08±0,43	4,71±0,33
LH (mME/ml)	FPMC	11,14±1,83	9,95±0,67	5,59±0,36
	OPMC	15,62±1,51	15,19±0,97	13,82±1,67
	LPMC	10,75±1,34	8,59±0,66	6,13±0,52
MTH (ng/ml)	FPMC	17,45±1,51	15,56±1,24	16,56±1,94
E2 (pg/ml)	FPMC	91,76±9,05	78,65±0,07	59,86±3,54
	LPMC	131,34±9,69	128,64±10,75	92,5±9,63
П (ng/ml)	FPMC	1,11±0,12	1,23±0,22	1,6±0,02
	LPMC	8,13±0,84	9,97±0,44	12,07±1,54
Estrone E1 (pg /ml)	FPMC	98,43±7,36	79,36±5,75	59,56±5,43
T (nmole/l)	FPMC	1,67±0,15	1,64±0,26	1,53±0,16

As for the LH content in blood dynamics' analysis, it has shown the following results: 5,59 мME/ml for the FPMC, 13,82 мME/ml for the OPMC and 6,13 мME/ml for the LPMC.

The LH level study for SEHWA and EP groups' women has given the evidence of its secretion disorder, that is, the cyclicity of its secretion has been preserved, but the LH basal secretion level index has been reliably higher than the one of the control ($p < 0,05$). LH high content has been detected within all the

phases of the menstrual cycle. Again reliably, LH index for the SEHWA group has been proved to be twice as much as the corresponding index for the control group within the FPMC; 1,2 times as much as the control group's index within the OPMC and 1,7 times as much as the corresponding index for the control group within the LPMC.

The LH/FSH correlation change within the FPMC deserves special attention in subjects' groups where this index has been more than 1 while the corresponding index has stood for less than 1. To our mind, this fact indicates the insufficiency of the LPMC. The patients' hormonal panel data analysis has proved the fact that the OPMC witnesses the LH and FSH ovulatory secretion's amplitude reduction; it is related to these hormones increased levels within the FPMC and may be explained by the chronic anovulation, which, in its turns, leads to the insufficiency of the LPMC. Thus, the SEHWA group has witnessed the LH level increase 1,4 times as much as the corresponding index for the FPMC, while the control group has witnessed the LH increase 2,5 times as much as the SEHWA group. The similar tendency has been noticed during the FSH fluctuation dynamics analysis; the amplitude of the given hormone increase has turned out to be lower compared with the control group's indexes.

Estradiol secretion level study among women of reproductive age has witnessed the increased content of estradiol both within the FPMC and LPMC compared with the corresponding index of the control group ($p < 0,05$). Not only the increase of the E2 average concentration has been noticed among SEHWA group women within the menstrual cycle, but the disorder of its secretion dynamics as well. Thus, the E2 level has been proved to be higher 1,5 times as much as the control group's index during the FPMC and higher 1,4 as much as the corresponding index ($p<0,05$) of the control group during the LPMC. The same tendency has been traced in the EP group where the estradiol level has turned out to be 1,4 higher as much as the control group's index.

Estrone (E1) secretion study has contributed the identification of the estrogens role in the EHP pathogenesis. The obtained data analysis has shown that the E1 level for women of reproductive age (control group) has stood for 59,58 pg /ml during the FPMC. As for SEWHA group women, the corresponding index has stood for 98,43 pg /ml which is 1,6 times as much as the index of the control group; as for the EP group, the estrone level has reliably been higher 1,3 times as much as the control group index ($p < 0,05$).

We have also studied the correlation between the estrone level and overweight (the body mass index (hereinafter - BMI (V.H.)) has been defined in accordance with the International Diabetes Federation criteria (2005)).

The analysis of data obtained has shown that pre-obesity had been detected among 31 patient of the SEHWA group (38, 3%), among 17 patients of EP group

(29,3%) and 7 subjects of the control group (23,5%) (See Chart 2). As for the I grade obesity, it had been detected among 14 patients of the SEHWA group (17,2%), 9 patients of the EP group (15, 5%) and 2 subjects of the control group (6, 6%). II grad obesity had been detected among 6 patients of the SEHWA group

Chart 2

Distribution of EHP patients and control group subjects on the basis of BMI

BMI	Group №1 SEHWA n= 81	Group №2 EP n= 58	Control group n= 30
	31,2±1,6 кг/м²	**28,9± 1,7 кг/м²**	**25,1±1,2т± кг/м²**
18,5 >	-	1 (1,7%)	1 (3,3%)
18,5-24,9 norm	28 (34,5%)	25 (43,1%)	19 (63,3%)
25-30 preobesity	30 (37,3%)	17 (29,3%)	7 (23,5%)
30-35 I grade obesity	14 (17,2%)	9 (15,5%)	3 (9,9%)
35-40 II grade obesity	6 (7,4%)	4 (6,8%)	-
>40 III grade obesity	3 (3,7%)	2 (3,4%)	-

(7,4%), among 4 patients of the EP group (6,8%). No II grade obesity had been detected among the subjects of the control group. Finally, III grade obesity had been detected among 3 patients of the SEHWA (3, 7%) and 2 patients of the EP (3, 4%) groups. Again, no III grade obesity had been detected among the control group subjects.

Thus, 38, 3% of the SEHWA group patients and 25,8% of the EP group patients had been diagnosed obesity, which indicates the correlation of the overweight, estrone high level and significant risk of the EHP development.

The study of the progesterone (P) level in blood of women of reproductive age, the subjects of the control group, has shown that the P content stands for 1,6 ng/ml during the FPMC, but 12,07 ng/ml during the LPMC. Thus, the P level within the LPMC had stood for 8, 13 ng/ml in the SEHWA group, while the corresponding index for the control group had stood for 12,07 ng/ml, which is 1,5 times less than the control group's index and indicates the progesterone insufficiency. it should be noted that the P level content in blood of EP women is 1,3 times as lower as the corresponding index for the control group which gives grounds to presuppose the preservation of ovulation among certain percent of women with the given pathology ($p < 0,05$).

MTH and T content in blood analysis has not shown any reliable from the point of view of statistics differences among women of reproductive age between the patients' groups and the control group's subjects ($p > 0,05$). Within the study, out of 139 women with EHP 9 (6,4%) have shown the increased mammotropic

hormone which led to the additional diagnostic studies; these additional diagnostic studies have shown that 2 women (1,3%) have been diagnosed the pituitary adenoma, 7 patients (5,1%) – hyperprolactinemia of nonneoplastic genesis. Patients with the hyperprolactinemia have been prescribed the individual treatment course.

Conclusions

The analysis of the conducted studies' data has shown that the EHP women of reproductive age are likely to have the hyper production of gonadotropic hormones with the increased level of basal secretion (the increase stands for 1,3-2 times) along with the decrease of the ovulatory secretion amplitude and low content of progesterone in blood (1,4 – 1,6 times) compared with the control group. Hyperestrogenemia is determined by the high content of E1 and E2 within the entire menstrual cycle.

6,1% of EHP women are diagnosed hyperprolactinemia which needs the individual approach towards examination and treatment of such patients.

Obesity has been detected among 38,3% of SEHWA and 25,8% of EP patients, which indicates the correlation between the overweight and EHP development risks, determines the necessity of complex treatment measures (involving the approximal specialists – endocrinologist, nutritionist and psychotherapist) prescribed to such patients.

The studies conducted give all the grounds to recommend the hormone panel and morphometric indexes' identification for the development of the individual treatment tactics as well as the criterion for the therapy effectiveness monitoring.

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Резюме. *У статті представлені результати вивчення гормональних взаємовідносин у жінок репродуктивного віку з гіперпластичними процесами ендометрія. Продемонстровано характерну для жінок з гіперпластичними процесами ендометрія гіперпродукцію гонадотропних гормонів з підвищеним рівнем базальної секреції і зменшенням амплітуди овуляторної секреції, низьким рівнем прогестерону. Гіперестрогенемія обумовлена високим рівнем естрону і естрадіолу протягом всього менструального циклу.*

Проведені дослідження дозволяють рекомендувати визначення гормонального профілю та морфометричеких показників для вироблення індивідуальної лікувальної тактики, а також в якості критерію моніторингу ефективності терапії.

Ключові слова: *гіперпластичні процеси ендометрія, проста гіперплазія ендометрія, поліпоз ендометрія.*