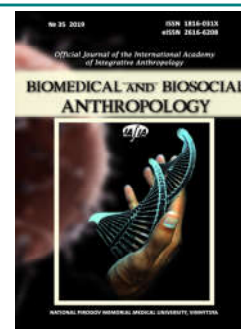




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Peculiarities of hormonal homeostasis in perimenopausal and postmenopausal women with menopausal disorders

Vaskiv O.V., Grigorenko A.P., Horbatiuk O.G., Shatkovska A.S., Binkovska A.N.

National Pirogov Memorial Medical University, Vinnytsya, Ukraine

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CORRESPONDING AUTHOR

e-mail: gynecology_fpo@vnmu.edu.ua
Vaskiv O.V.

According to WHO, now on the planet 46 % of women are over the age of 45 years, among women in Ukraine - this is almost half (13.2 million). Of these, 46-68 % suffer from climacteric syndrome. An increase in the duration of a healthy life and prolongation of the age of working capacity acquire not only medical, but also socio-economic significance, both in Ukraine and in other European countries. Therefore, the aim of the study was a comprehensive (involving pituitary, ovarian, adrenal and thyroid hormones) hormonal examination of women of peri- and postmenopausal age with menopause syndrome to identify the most likely hormonal predictors of this pathology. For this purpose, 64 women of perimenopausal and postmenopausal age with menopause and 42 healthy women of the same age categories had a study of the concentration of pituitary (LH, FSH, prolactin), ovarian hormones (estradiol, progesterone, testosterone), thyroid hormones (TSH, triiodothyronine (T3), thyroxine (T4)) and adrenal glands (DHEA-s, cortisol) in blood plasma. Hormones were determined using a set of test systems from "Immunotech" (Czech Republic-France) using the radio-immune method. Comparisons of the quantitative data of the two related groups (before and after treatment) were made using Wilcoxon signed rank test. When differences were detected, pairwise group comparisons were performed using the Mann-Whitney test. In women of perimenopausal and postmenopausal age with menopause syndrome, compared with healthy women of the same age groups, a significant increase in gonadotropin levels (LH by 3.7 and 3.0 times, respectively; FSH by 1.6 and 1.9 times) and a decrease indicator of prolactin in 1.5 and 1.2 times; estradiol 1.2 and 2.2 times and testosterone 2.9 and 2.4 times. A significant decrease in progesterone by 1.9 times occurred only in the group of postmenopausal women with menopause syndrome. In women of perimenopausal and postmenopausal age of the main group, a significant decrease was found in comparison with the control of DHEA-s levels by 1.3 times and 2.2 times, respectively; cortisol 1.2 and 2.0 times; TSH is 2.6 times and 2.0 times, respectively, however, thyroxine tended to increase (the probability $p < 0.05$ was valid only for women of perimenopausal age). Thus, in postmenopausal women with menopausal syndrome, hormonal imbalance is more pronounced, indicating a deep atrophy of hormone-dependent tissue receptors and, as a result, a deepening of involutive processes.

Keywords: hormonal homeostasis, perimenopause, postmenopause, menopausal disorders.

Introduction

The problem of disorders in the hormone-dependent organs and systems of the body of the woman during the period of perimenopause and post-menopause is becoming more urgent, since it is primarily concerned with the quality of life of women during their professional maturity and the greatest activity in family and public life [6, 7, 15, 19].

An analysis of the age structure of the population in

recent years shows that Ukraine is in a state of deep demographic crisis caused by depopulation, an increase in the share of elderly people, and a decrease in the average life expectancy [7, 18, 19]. This has a negative impact on the development of productive forces, the level of well-being of people and the economic situation in the country [18, 19].

According to WHO, 46 % of women are now over the

age of 45 (peri and post-menopausal) on the planet already, among women of Ukraine it is 13.2 million, that is almost half [5, 18, 19], therefore the increase in life expectancy and prolongation age of working capacity is gaining not only medical but also socio-economic importance, both in Ukraine and in other European countries.

Systemic irreversible changes that develop in the body of a woman during menopause due to progressive estrogen deficiency [7, 12, 13, 14, 17], dictate the need to find effective methods for their prediction, as well as the introduction of alternative methods of prevention and treatment of menopausal disorders [4, 7, 11, 18].

It is very difficult to predict the individual age of menopausal disorders, since ovarian failure is a complex multifactorial and lengthy process. During menopause, the background of age-related changes in the body is dominated by involutionary processes in the reproductive system [6, 17, 20].

The gradual involution of the ovarian parenchyma is accompanied by a decrease in the production of sex hormones (estradiol, progesterone and androgens) [1, 3, 16]. Due to the fact that hormonal regulation in the body occurs on the principle of feedback, due to the decreased level of estrogen in the pituitary gland, there is an increase in the production and release of gonadotropic hormones [2, 4, 7, 10].

The purpose of our study was a comprehensive (involving pituitary, ovarian, adrenal, and thyroid hormones) hormonal examination of women of peri- and postmenopausal age with climacteric syndrome to identify hormonal predictors of menopausal disorders.

Materials and methods

We monitored 64 perimenopausal and postmenopausal women with menopausal mid- and severe-course disorders (main group). The control group included 42 healthy women of the same age categories.

Women of the main age group were distributed as follows: in the perimenopausal age (46-50 years) were 21 (32.8 %) women and in the postmenopausal (51-65 years) - 43 (67.2%) women. The control group consisted of 21 perimenopausal women (46-50) and 21 postmenopausal women without menopause disorders (51-65 years). By the severity of menopausal disorders, women of the main group were distributed as follows: severe disease was reported in 17 (38.6 %) women, medium-severe in 27 (61.4 %) women. All severe forms of the disease occurred exclusively in postmenopausal women. Moreover, the duration of menopause in such women ranged from 1 to 2 years.

Selection of individuals for inclusion in the study was performed on the basis of detailed anamnesis, complaints and examination using standard clinical and laboratory methods of investigation.

Investigation of the concentration of pituitary-ovarian hormones (LH, FSH, prolactin, estradiol, progesterone, testosterone), thyroid (TSH, triiodothyronine (T3), thyroxine (T4)) and adrenal glands (DHEA-s, cortisol) in the blood

plasma was determined by radioimmunoassay using "Immunotech" (Czech-France) test systems kits. All studies were performed on the basis of the enzyme immunoassay laboratory of the Municipal Enterprise "Khmelnitsky City Perinatal Center". All patients received the prior consent of the study.

Comparisons of the quantitative data of the two related groups (before and after treatment) were made using the Wilcoxon nonparametric paired-sample criterion. When differences were detected, pairwise group comparisons were performed using the Mann-Whitney test. Differences were significant at $p < 0.05$ levels [8, 9].

Results

In perimenopausal women, an increase in the concentration of gonadotropic hormones was found to be characteristic of menopause, and in women with climacteric syndrome this increase was significantly greater than in healthy women of the same age (Fig. 1). Thus, the LH level was increased in 3.7 times as compared to the control (35.71 ± 3.57 mIU/ml and 9.640 ± 1.050 mIU/ml, respectively, $p < 0.05$), FSH - 1.59 times (13.68 ± 1.040 mIU/ml and 8.560 ± 1.080 mIU/ml, respectively, $p < 0.05$), the LH/FSH ratio increased 2.34-fold (2.610 ± 0.470 and 1.126 ± 0.130 , $p < 0.05$, respectively). At the same time, prolactin decreases in 1.5 times (respectively 154.0 ± 17.2 μ IU/ml and 233.8 ± 23.1 μ IU/ml, $p < 0.05$), estradiol - 1.2 times (respectively 104.5 ± 9.1 ng/l and 126.3 ± 10.7 ng/l, $p < 0.05$), testosterone - 2.9 times (respectively 0.187 ± 0.020 ng/ml and 0.539 ± 0.090 ng/ml, $p < 0.05$). Progesterone concentration was at the control group level (0.358 ± 0.040 ng/ml and 0.379 ± 0.030 ng/ml, respectively, $p > 0.05$).

Postmenopausal women revealed the following (Fig. 2): LH level increased 3-fold compared to control (64.18 ± 3.31 mIU/ml and 21.13 ± 1.06 mIU/ml, respectively, $p < 0.05$), FSH in 1.9 times (respectively 42.21 ± 0.40 mIU/ml and 22.30 ± 1.09 mIU/ml, $p < 0.05$), the LH/FSH ratio

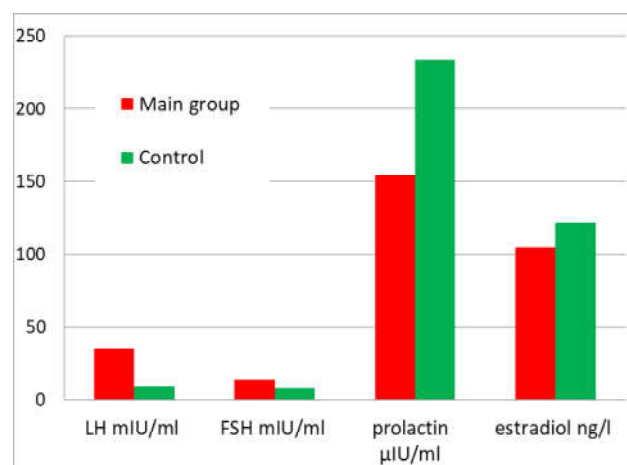


Fig. 1. Comparison of indicators of hormonal homeostasis of perimenopausal women with climacteric syndrome with healthy women of the same age.

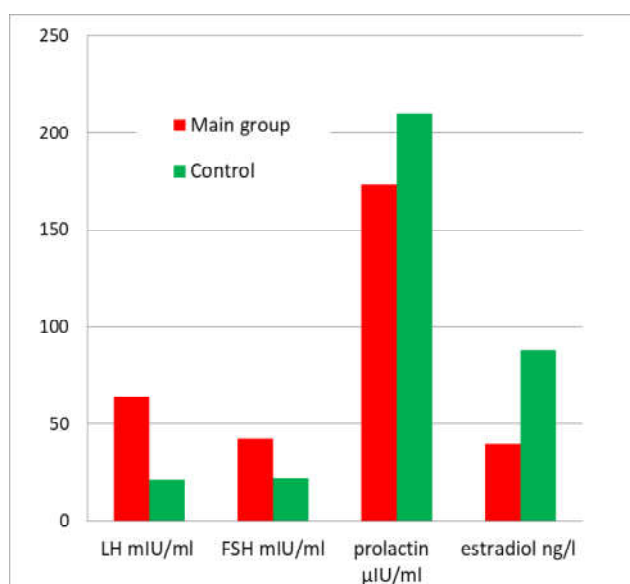


Fig. 2. Comparison of hormonal homeostasis indices of postmenopausal women with climacteric syndrome with healthy women of the same age.

Table 1. Thyroid function in women with climacteric syndrome in perimenopausal and postmenopausal age (M±m).

Hormones	Main group (n=21-43)	Control (n=21)	p
Perimenopausal age			
TSH (mIU/L)	0.840±0.130	1.420±0.340	<0.05
Triiodothyronine (T3) (nmol/L)	1.860±0.100	2.080±0.150	>0.05
Thyroxine (T4) (nmol/L)	107.9±1.7	87.38±1.82	<0.05
Postmenopausal age			
TSH (mIU/L)	0.540±0.100	1.090±0.110	<0.05
Triiodothyronine (T3) (nmol/L)	1.830±0.050	1.970±0.090	>0.05
Thyroxine (T4) (nmol/L)	90.18±2.04	85.00±3.92	>0.05

Table 2. Functional state of adrenal glands in women with climacteric syndrome in perimenopausal and postmenopausal age (M±m).

Hormones	Main group (n=21-43)	Control (n=21)	p
Perimenopausal age			
DHEA-s (nmol/L)	5.450±0.260	6.920±0.240	<0.05
Cortisol (nmol/L)	378.8±7.0	440.0±12.3	<0.05
Postmenopausal age			
DHEA-s (nmol/L)	1.860±0.110	4.060±0.330	<0.05
Cortisol (nmol/L)	189.2±10.7	385.6±11.7	<0.05

increased in 1.4 times (1.520 ± 0.220 and 0.950 ± 0.130 , $p < 0.05$, respectively). The level of prolactin decreased in 1.2 times (respectively 173.3 ± 8.5 μ IU/ml and 210.1 ± 32.1 μ IU/ml, $p < 0.05$), estradiol - 2.2 times (respectively 39.93 ± 2.71 ng/ml and 87.93 ± 14.10 ng/ml, $p < 0.05$), progesterone - 1.9 times (respectively 0.147 ± 0.030 ng/ml and 0.280 ± 0.040 ng/ml, $p < 0.05$), testosterone - 2.4 times (respectively 0.158 ± 0.120 ng/ml and 0.377 ± 0.200 ng/ml,

$p < 0.05$).

The functional status of the thyroid gland (TSH, triiodothyronine (T3) and thyroxine (T4)) and adrenal glands (DHEA-c, cortisol - involved in the functioning of the reproductive system) in women of perimenopausal and postmenopausal age are presented in Table 1 and 2.

Discussion

In the available literature, there is no comparison of hormonal changes in the age range, and between groups of women with and without climacteric syndrome, and are not involved in the study of thyroid and adrenal hormones [11, 14, 17, 20].

If we compare hormone indices in women of the main group of perimenopausal age and control, we should note a significant increase in LH and FSH levels, LH/FSH ratio, and a significant decrease in estradiol, prolactin, and total testosterone [1, 3]. No significant increase in progesterone was observed. These indicators are correlated with the data of many researchers [4, 5, 6, 7].

Postmenopausal women, due to the atrophy of the receptor apparatus of hormone-dependent organs, exacerbate the involutive processes, which is certainly consistent with the literature [1, 2, 3, 15]. However, we have found that ovarian and pituitary hormone depletion in women with climacteric syndrome is much deeper than in healthy postmenopausal women. In perimenopausal and postmenopausal periods, levels of gonadotropins increase and prolactin, estradiol, progesterone and testosterone levels decrease [2, 4], but in women with climacteric syndrome these changes are more pronounced.

Analysis of hormonal parameters of thyroid function in women with climacteric syndrome of perimenopausal and postmenopausal age showed that TSH levels were significantly lower than controls, however, thyroxine tended to increase ($p < 0.05$ was valid only for women of perimenopausal age).

Analysis of the functional state of the adrenal glands in women with climacteric syndrome perimenopausal age showed that the level of DHEA-c in women of perimenopausal age was lower than the control 1.3 times ($p < 0.05$), and the level of cortisol was 1.2 times lower ($p < 0.05$). Postmenopausal women also experienced a 2.2-fold decrease in DHEA-s compared to controls, and a 2.0-fold decrease in cortisol ($p < 0.05$).

Thus, perimenopausal and postmenopausal women with climacteric syndrome have increased levels of gonadotropins and decreased levels of prolactin, estradiol, progesterone, and testosterone compared with healthy women of the same age groups. Moreover, in postmenopausal women, these changes are significantly more pronounced than in the perimenopause, indicating a deep atrophy of receptors of hormone-dependent tissues and, as a consequence, the deepening of involutional processes.

A comparative study of the density of the receptor

apparatus in estrogen-dependent organs in peri and postmenopausal women with and without climacteric syndrome is promising.

Conclusions

1. In perimenopausal and postmenopausal women with climacteric syndrome, there are increased ($p < 0.05$) levels of gonadotropins - LH in 3.7 and 3.0 times, respectively, and FSH in 1.6 and 1.9 times; and decreased ($p < 0.05$) prolactin levels by 1.5 and 1.2 times, estradiol by 1.2 and 2.2 times, and testosterone by 2.9 and 2.4 times, respectively, compared with healthy women of similar age groups. A significant decrease in progesterone 1.9 times occurred only in the group of postmenopausal women with climacteric syndrome.

2. Women with climacteric syndrome of perimenopausal and postmenopausal age showed a significant decrease in TSH compared to similar controls: 2.6 times and 2.0

times, respectively; however, thyroxine tended to increase ($p < 0.05$ was only valid for perimenopausal women).

3. Analysis of the functional state of the adrenal glands in women with climacteric syndrome of perimenopausal age showed a significant decrease in the level of DHEA-s 1.3 times and the level of cortisol 1.2 times relative to control ($p < 0.05$). In postmenopausal age, there was a 2.2-fold decrease in DHEA-s compared with controls ($p < 0.05$); cortisol - 2.0 times ($p < 0.05$).

4. In postmenopausal women with climacteric syndrome, hormonal imbalance is more pronounced, indicating profound atrophy of hormone-dependent tissue receptors and, as a consequence, deepening of involutive processes.

5. The deep imbalance of hormonal indices of the pituitary-ovarian axis and adrenal glands may be a predictor of menopausal disorders in women of peri- and postmenopausal age.

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ОСОБЛИВОСТІ ГОРМОНАЛЬНОГО ГОМЕОСТАЗУ У ЖІНОК ПЕРИМENOПАУЗАЛЬНОГО ТА ПОСТМЕНОПАУЗАЛЬНОГО ВІКУ З КЛІМАКТЕРИЧНИМИ ПОРУШЕННЯМИ

Васьків О.В., Григоренко А.П., Горбатюк О.Г., Шатковська А.С., Бінковська А.М.

За даними ВООЗ зараз на планеті 46 % жінок перебувають у віці старше 45 років, серед жінок України - це майже половина (13,2 мільйона). З них 46-68 % страждають на клімактеричний синдром. Збільшення тривалості здорового життя та пролонгування віку працездатності набувають не тільки медичного, а й соціально-економічного значення, як в Україні, так і в інших європейських країнах. Тому, метою дослідження було комплексне (з залученням гіпофізарних, яєчникових, наднирникових та тиреоїдних гормонів) гормональне обстеження жінок пери- та постменопаузального віку з клімактеричним синдромом для виявлення найбільш вірогідних гормональних предикторів даної патології. Для цього у 64 жінок перименопаузального та постменопаузального віку з клімактеричними порушеннями та у 42 здорових жінок цих же вікових категорій було виконано дослідження концентрації гіпофізарних (ЛГ, ФСГ, пролактину), яєчникових гормонів (естрадіолу, прогестерону, тестостерону), гормонів щитоподібної залози (ТТГ, трийодтиронину (Т3), тироксину (Т4)) та наднирників (ДГЕА-с, кортизолу) в плазмі крові. Гормони визначали за допомогою набору тест-систем фірми "Immunotect" (Чехія-Франція) радіоімунним методом. Порівняння кількісних даних двох пов'язаних груп (до та після лікування), здійснили за допомогою непараметричного критерію Вілкоксона для парних вибірок. При виявленні різниці виконували попарні порівняння груп за допомогою критерію Манна-Уїтні. У жінок перименопаузального та постменопаузального віку з клімактеричним синдромом порівняно зі здоровими жінками цих же вікових груп було виявлено достовірно підвищені рівні гонадотропінів (ЛГ у 3,7 та 3,0 рази, відповідно; ФСГ у 1,6 та 1,9 разів) та знижені показники пролактину у 1,5 та 1,2 рази; естрадіолу у 1,2 та 2,2 рази та тестостерону у 2,9 та 2,4 рази. Достовірне зниження прогестерону в 1,9 рази мало місце лише у групі жінок постменопаузального віку з клімактеричним синдромом. У жінок перименопаузального та постменопаузального віку основної групи встановлено достовірне зниження (порівняно з контролем) рівня ДГЕА-с - в 1,3 та 2,2 рази, відповідно; кортизолу у 1,2 та 2,0 рази; ТТГ у 2,6 та 2,0 рази. Разом із тим, тироксин має тенденцію до підвищення ($p < 0,05$ була дійсна лише для жінок перименопаузального віку). Таким чином, у жінок постменопаузального віку з клімактеричним синдромом гормональний дисбаланс є більш вираженим, що свідчить про глибоку атрофію рецепторів гормонозалежних тканин і, як наслідок, поглиблення інволютивних процесів.

Ключові слова: гормональний гомеостаз, перименопауза, постменопауза, клімактеричні порушення.

ОСОБЕННОСТИ ГОРМОНАЛЬНОГО ГОМЕОСТАЗА У ЖЕНЩИН ПЕРИМENOПАУЗАЛЬНОГО И ПОСТМЕНОПАУЗАЛЬНОГО ВОЗРАСТА С КЛИМАКТЕРИЧЕСКИМИ НАРУШЕНИЯМИ

Васьків О.В., Григоренко А.П., Горбатюк О.Г., Шатковская А.С., Бинковская А.М.

По данным ВОЗ сейчас на планете 46 % женщин находятся в возрасте старше 45 лет, среди женщин Украины - это почти половина (13,2 миллиона). Из них 46-68 % страдают от климактерического синдрома. Увеличение продолжительности здоровой жизни и пролонгации возраста работоспособности приобретают не только медицинское, но и социально-экономическое значение, как в Украине, так и в других европейских странах. Поэтому, целью исследования было комплексное (с вовлечением гипофизарных, яичниковых, надпочечниковых и тиреоидных гормонов) гормональное обследование женщин пери- и постменопаузального возраста с климактерическим синдромом для выявления наиболее вероятных гормональных предикторов данной патологии. Для этого у 64 женщин перименопаузального и постменопаузального возраста с климактерическими нарушениями и у 42 здоровых женщин этих же возрастных категорий было выполнено исследование концентрации гипофизарных (ЛГ, ФСГ, пролактин), яичниковых гормонов (эстрадиола, прогестерона, тестостерона), гормонов щитовидной железы (ТТГ, трийодтиронина (Т3), тироксина (Т4)) и надпочечников (ДГЭА-с, кортизола) в плазме крови. Гормоны определяли с помощью набора тест-систем фирмы "Immunotect" (Чехия-Франция) радиоиммунным методом. Сравнение количественных данных двух связанных групп (до и после лечения), осуществили с помощью непараметрического критерия Вилкоксона для парных выборок. При выявлении разницы выполняли попарные сравнения групп с помощью критерия Манна-Уитни. У женщин перименопаузального и постменопаузального возраста с климактерическим синдромом по сравнению со здоровыми женщинами этих же возрастных групп было выявлено достоверное повышение уровней гонадотропинов (ЛГ в 3,7 и 3,0 раза, соответственно; ФСГ в 1,6 и 1,9 раз) и снижение показателей пролактина в 1,5 и 1,2 раза; эстрадиола в 1,2 и 2,2 раза и тестостерона в 2,9 и 2,4 раза. Достоверное снижение прогестерона в 1,9 раза имело место только в группе женщин постменопаузального возраста с климактерическим синдромом. У женщин перименопаузального и постменопаузального возраста основной группы установлено достоверное снижение, по сравнению с контролем, уровня ДГЭА-с в 1,3 раза и 2,2 раза, соответственно; кортизола в 1,2 и 2,0 раза; ТТГ в 2,6 раза и 2,0 раза, соответственно. Вместе с тем, тироксин имел тенденцию к повышению ($p < 0,05$ была действительна только для женщин перименопаузального возраста). Таким образом, у женщин постменопаузального возраста с климактерическим синдромом гормональный дисбаланс является более выраженным, что свидетельствует о глубокой атрофии рецепторов гормонозависимых тканей и, как следствие, углублении инволютивных процессов.

Ключевые слова: гормональный гомеостаз, перименопауза, постменопауза, климактерические нарушения.