

Research Article

# The modern approach to the correction of menopausal disorders in women with physiological menopause and after ovariectomy

Nataliya Henyk, Lyudmyla Hinchytska, Igor Levytskyi, Olga Neiko, Ruslana Gotsaniuk\*

## Abstract

The problem of menopause attracts attention for many decades of not only gynecologists, but urologists, cardiologists, psychiatrists and other doctors. This is related to systemic complications of estrogen deficiency.

The **objective** of our work is to establish clinical and hormonal changes in women of menopausal age with physiological menopause and after ovariectomy and also assess the effectiveness of the offered treatment. During the examination and treatment the women were divided as follows: I – main group – 48 women with physiological menopause: Ia (n=27) – within three months received a complex of non-hormonal treatment, Ib (n=21) – hormone replacement therapy (HRT); II group – 34 women after total ovariectomy: IIa (16) with therapeutic purpose received a complex of non-hormonal treatment for three months, IIb (18) – HRT. The offered complex of non-hormonal treatment included Cimicifuga, Menopace, Noophen. This treatment was used in women with early menopause who have contraindications to HRT or refused to take hormones. The degree of severity of menopausal syndrome was judged according to the menopausal index of Kuperman. In the study of hormonal status the determination of a set of hormones by immunochemical method was performed. During study we obtained results that indicate the inverse dynamics of menopausal disorders in both study groups. For the prevention and treatment of individual selection of treatment of climax manifestations it is appropriate the dynamic definition of hormonal mirrors of the patients.

## Keywords

menopause; clinical manifestations; treatment

*Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine*

**Corresponding author:** [ruslana54321@i.ua](mailto:ruslana54321@i.ua)

## Problem statement and analysis of the recent research

The problem of menopause for many decades attracts attention not only of gynecologists but also of urologists, cardiologists, psychiatrists and other doctors. This is due to systemic complications of estrogen deficiency [1,3,4]. For a long time the hypothesis of the beginning of menopause due to changes in primary hypothalamic centers with their reduced sensitivity to estrogens and inadequate increase of pituitary gonadotropins has dominated (follicular-stimulating (FSH) and luteinizing (LH) hormones). Now the hypothesis of a primary deficiency of inhibin products by aging ovaries dominates. Its decline causes increase of FSH and then of LH [1-4,12]. That is, the levels of FSH and inhibin are inversely proportional ratios, that leads to anovulatory cycles and in future to complete follicular atresia [2-4].

Already during the premenopause, ovaries are less responsive to pituitary gonadotropins and reduce the secretion of estrogens and progestogens (the degree of estradiol levels reduction in blood reaches 90.0%). At the same time the level of androgen such as androstenedione reduces by half, but testos-

terone concentration decreases slightly. As a result, against the backdrop of estrogens' deficiency various clinical manifestations in the form of disease states develop in menopause. Often they are of pronounced character that serves as the basis for their allocation into a separate nosological form – climacteric syndrome (CS), which is manifested by neurovegetative (NVS), psycho-emotional (PES) and metabolic-endocrine (EMS) symptomatic complexes [4,5]. A woman spends in menopause almost a third of life, so the goal of treatment is not only leveling of the symptoms of menopausal syndrome, but also the prevention of atherosclerosis, urogenital disorders, osteoporosis.

Most pathogenetically reasonable method of treatment, which is aimed at the key mechanisms of menopausal complications, is hormone replacement therapy (HRT), which is widely used around the world [1,5,6,7]. If there are any contraindications to the use of hormone replacement therapy (cancer of the uterus and breasts, uterine bleedings of unexplained genesis, acute thrombophlebitis, thromboembolic disorders associated with estrogens intake, renal and liver failure, porphyria, meningioma and others [1,3,9]) as an alternative they use phytoestrogens – the non-steroidal plant

molecules possessing estrogen, anti-inflammatory, antioxidant and anti-cancer activity [2,8,10].

The objective of the work. To determine the clinical and hormonal changes in women of menopausal age with physiological menopause before and after ovariectomy. To evaluate the effectiveness of the offered treatment.

## 1. Materials and methods

Study was begun collecting complaints from time to review and after treatment, and then performed the gynecological examination by the conventional scheme. During examination and treatment, women were divided as follows: I – the main group – 48 women with physiological menopause: Ia (n=27) – within three months received a complex of non-hormonal treatment, Ib (n=21) – HRT; II group – 34 women after total ovariectomy: IIa (16) with therapeutic purposes received a complex of non-hormonal treatment for three months, IIb (18) – HRT.

The offered complex of non-hormonal treatment included Cimicifuga, Menopace, Noophen. This treatment was used in women with early menopause who had contraindications to HRT or refused to take hormones because of possible side effects [11]. Cimicifugaracemosa or bugbane clustering (Black cohosh) belongs to a class of phytohormones. Chemical components are a number of triterpenoids, derivatives of cinnamic acid and esters of inosine and fuknin acids. It has estrogen effect, as evidenced by lower level of luteinizing hormone [8], but Cimicifuga unlike phytoestrogens (isoflavones, ligands, kumestans) does not bind to estrogen receptors  $\alpha$  and  $\beta$  [10,13]. Several biological properties of Cimicifuga allow us to consider it as phyto-selective modulators of estrogen receptors. While the effect of phytoestrogens is several hundred times lower than 17- $\beta$  estradiol [8]. Noofen is used as anti-hypoxant and as anti-anamnestic means. It has tranquilizer properties, reduces the severity of cognitive disorders, manifestations of anxiety and fear, normalizes sleep, improves physical and mental performance, anticonvulsant property. Menopace is anti-menopause complex of twenty-two vitamins, minerals and bioactive substances that weaken the symptoms of menopause.

The degree of menopausal syndrome severity was judged by the menopausal Kuperman index modified by E. Uvarova [1,6]. Each symptom was assessed by the level of severity from 0 to 3 points, after which the total amount of points determined the level of severity of menopausal syndrome. In the study of hormonal status, the determination of several hormones by immunochemical method of electrochemiluminescent detection (ECLICA) using test kits Roche Diagnostics (Switzerland) and analyzer “Cobas 6000” was performed.

## 2. Results

General clinical study was conducted under the standard scheme, which provides clarification of the complaints at

the moment of examination, anamnesis and also objective therapeutic and gynecological examination.

It is known that Cimicifuga effectively reduces hot flashes (at the level of mesolimbic system), has hypotensive action, normalizes psycho-emotional background. Cimicifuga dopaminergic effect via dopamine (D2) receptors and its serotonergic activity reduces the frequency and intensity of hot flashes, causes anti-depressant effect and has a pronounced positive effect on sleep, reduction of dryness in vagina, positive effect on trophism of urinary bladder and muscular-articular symptoms [13]. Cimicifuga also leads to the increase of the activity of bone specific alkaline phosphatase, indicating the activity of osteoblasts and hence to bone-protective effect [8,10]. The positive impact of the offered complex of treatment is confirmed by the assessment of clinical manifestations and post-ovariectomy syndrome (POS) and physiological menopause according to menopausal index uniting all above-studied symptom-complexes (Table 1).

After our treatment the percentage of women with climacteric disorders of moderate level of severity decreased in Ia group from 70.4% to 11.1%, in IIa – from 75.0% to 31.3%, while using HRT in Ib – from 61.9% to 19%, and in IIb – from 72.2% to 27.8%. Somewhat higher rates during physiological menopause after the use of hormonal treatment (19.0%) as opposed to the Ia group (11.1%) are due to the fact that before the treatment this group included women with severe menopause. We can see a high therapeutic effect of combination of medicines such as Klimactoplan, Menopace and Noophen to arresting of menopausal symptoms of mild and moderate levels of severity, both in physiological and surgical menopause within a relatively short time. Taking into account the importance of relationship between central and peripheral unit of pituitary-ovarian system, we performed a study of the concentration of estradiol and follicle-stimulating hormone in the blood serum of women from the studied groups. Data collected during the study are represented in Table 2.

As it is seen from the above-given data represented in the table, in women after the treatment the concentration of estradiol in blood serum increased from  $19.03 \pm 3.29$  to  $22.12 \pm 3.35$  in the main group and from  $12.08 \pm 1.94$  to  $15.27 \pm 2.39$  in the comparison group. Indexes of FSH after three months of the performed therapy decreased at almost 18% in both groups.

## 3. Conclusions

During the study we have obtained the results that indicate the reversal dynamics of menopausal disorders in both study groups. The use of our proposed complex: Klimactoplan, Menopace and Noophen have significant advantages of the influence (minimum of side effects) on the body over HRT.

## References

- [1] Vykhlyaeva EM. Climacteric syndrome. Guide in endocrine gynecology. MIA. 2006; 603-650.

**Table 1.** Dynamics of modified menopausal index according to the severity of the clinical course on women of studied groups

MMI	Groups															
	Ia(n=27)				Ib (n=21)				IIa(n=16)				IIb (n=18)			
	before treatment		after treatment		before treatment		after treatment		before treatment		after treatment		before treatment		after treatment	
	abs	%	ab	%	abs	%	abs	%	abs	%	ab	%	abs	%	abs	%
mild	8	29.6	24	88.9	5	23.8	17	81	4	25	11	68.7	1	5.6	13	72.2
medium	19	70.4	3	11.1	13	61.9	4	19	12	75	5	31.3	13	72.2	5	27.8
severe	0	0	0	0	3	14.3	0	0	0	0	0	0	4	22.2	0	0

**Table 2.** Indicators of hormonal status in women of studied groups before and after the performed treatment

Indexes	Main group Ia (n=27)				Comparison group IIa (n=16)			
	before treatment		after treatment		before treatment		after treatment	
estradiol, pg/ml	19.03±3.29		22.12±3.35		12.08±1.94		15.27±2.39	
FSH, MO/l	91.82±27.63		75.77±22.82		112.74±28.72		92.14±26.21	

- [2] Diukova GM, Smetnyk VP, Nazarova NA. The state of psycho-vegetative and sexual activity in women during perimenopause. Guide in menopause. Guidance for doctors. MIA. 2001; 361-380.
- [3] Koziuk GV. Climacterium (menopause) and hormone replacement therapy. Meditsynskiye novosti. 2004; 7:48-54.
- [4] Kulakov VI, Savelyeva GM, Manukhina IB. Gynecology. National Guidance. Goetar-media. 2009;1088.
- [5] Manukhin IB, Taktarov VG, Shmeleva SV. Women's health in menopause. Monograph. Lyterra. 2010; 244.
- [6] Smetnyk VP. Medicine of menopause. M. 2009; 847.
- [7] Lomranz J, Becker D, Eyal N, Pines A, Mester R. Attitudes towards hormone replacement therapy among middle-aged women and men. Eur. J. Obstet. Gynecol. Reprod. Biol. 2000; 93:199-203.
- [8] Stute P, Nisslein T, Gotte et al. Effects of black cohosh on estrogen biosynthesis in normal breast tissue in vitro. Maturitas. 2007; 57:382-392.
- [9] Freedman RR. Pathophysiology and treatment of menopausal hot flashes. Semin, reprod. med. 2005; 23(2):117-125.
- [10] Rice S, Amon A. Whitehead etanolic extracts of black cohosh (*Acetaearacemosa*) inhibit growth and oestradiol synthesis from oestransulphate in breast cancer cell. Maturitas. 2007; 56:359-367.
- [11] Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women. Principal Results From the Women's Health Initiative Randomized Controlled Trial. JAMA. 2002; 288:321-333.
- [12] Shen W, Stearns V. Treatment strategies for hot flushes. Expert.Opin.Phar-macother. 2009; 10 (7):1133-1144.
- [13] Wuttke W, Seidova-Wuttke D, Gorkow C. The Cimi-cifuga preparation BNO 1055 vs conjugated estrogens in a double-blind placebo-controlled study: effects on menopause symptoms and bone-markers. Maturitas.2003;44(1):67-77.

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