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PECULIARITIES OF VITAMIN D USE IN THE COMPLEX OF MENOPAUSAL HORMONAL THERAPY IN WOMEN

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Abstract: Menopausal hormone therapy (MHT) is an effective method of correcting menopausal disorders, but its use requires a comprehensive approach, including additional micronutrient support. Vitamin D plays a key role in regulating calcium-phosphorus metabolism, supporting bone health and the immune system, and may modulate the effects of estrogen. This article reviews the mechanisms of interaction between vitamin D and IHT, their impact on the health of the postmenopausal woman, and current recommendations for combined use.

In evaluating numerous population-based studies of the prevalence of vitamin D deficiency in different ethnic and age groups, an association of vitamin D deficiency with duration of postmenopause and age has been found. The “gold standard” treatment for menopausal disorders is undoubtedly menopausal hormone therapy (MHT) in its various forms.

Key words: vitamin d, menopausal hormonal therapy (mht), postmenopausal women, bone health, osteoporosis prevention, calcium metabolism, hormone replacement therapy (hrt), endocrine health, cardiovascular effects, vitamin d deficiency.

INTRODUCTION

Menopause is a physiological process accompanied by a decrease in estrogen levels, which leads to various changes in a woman's body, including osteoporosis, sarcopenia, cardiovascular disease and cognitive impairment. Menopausal hormone therapy remains one of the main methods of correcting these conditions. However, in recent years, nutraceutical approaches, in particular the use of vitamin D, which plays an important role in the regulation of bone metabolism, immune function, and maintenance of metabolic homeostasis, have attracted increasing interest.

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The aim of this article is to review the peculiarities of the combined use of vitamin D and MHT, their impact on the health of postmenopausal women and scientifically based recommendations on the optimal dosage and therapy strategy.

Menopause and menopausal disorders are associated with changes in circulating sex hormone levels, insulin sensitivity, and lifestyle and social habits. In postmenopause, there is a decrease in estrogen-progesterone protective properties and increased incidence of cardiovascular diseases, diabetes mellitus, osteoporosis, etc. [1]. Hormonal fluctuations, excessive protection of the skin by clothing, sedentary lifestyle, sunscreen use, changes in the composition of fat deposits and vitamin D deficient diet all predispose to vitamin D deficiency in postmenopause [2, 3]. The skin's ability to produce vitamin D decreases with age, and it is 3 times lower in the elderly than in young people [4, 5].

The main source of vitamin D is its endogenous production by sunlight. UV-B radiation leads to the conversion of 7-dehydrocholesterol under the skin to previtamin D3 and then to vitamin D3 (colecalciferol). Vitamin D3 is metabolized in the liver to 25-hydroxyvitamin D (25(OH)D), the major circulating form of vitamin D, and is used to determine vitamin D levels in humans. Circulating 25(OH)D is subsequently metabolized in the kidneys to a biologically more active form, 1,25-dihydroxyvitamin D [4-6].

Insufficient sun exposure and the use of sunscreen, which reduces vitamin D synthesis in the skin by 95-98%, are the main causes of vitamin D deficiency and insufficiency in modern living conditions [7, 8].

Foods are another important source of vitamin D intake into the body. Oral vitamin D supplements are usually prescribed to patients in the form of vitamin D3 (colecalciferol) or vitamin D2 (ergocalciferol). Vitamin D3 is obtained from animal products such as fatty fish (salmon, mackerel, herring) and fish oil, and vitamin D2 is extracted from plants [9-12].

In the Republic of Uzbekistan and other areas, the usual diet does not include foods rich in vitamin D, which makes the problem of vitamin D deficiency extremely urgent. Deficiency of this vitamin is particularly prevalent among low- and middle-income populations.

Among elderly women, the prevalence of vitamin D insufficiency was 43.9% [11, 13]. In addition, weight gain in postmenopause increases the prevalence of vitamin D deficiency in this population of women. This is due to the deposition of vitamin D in subcutaneous fat and its inaccessibility to the central bloodstream [4].

In the evaluation of numerous population studies on the prevalence of vitamin D deficiency in different ethnic and age groups, an association of the level of vitamin D deficiency with the duration of postmenopause and the age of women was found [5, 6]. Vitamin D status affects various metabolic parameters in addition to phosphorus-calcium metabolism and bone and joint system status.

Blood 25(OH)D concentration is an accurate indicator for monitoring vitamin D status because it is its major form of circulating in plasma. Its determination in serum as the main circulating vitamin D metabolite is the primary indicator of the supply of this vitamin [7].

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The "gold standard" treatment of menopausal disorders is undoubtedly menopausal hormone therapy (MHT) in its various forms [1, 5]. According to a number of authors, the addition of vitamin D metabolites to complex therapy can improve metabolic parameters in postmenopausal and elderly women. However, there is insufficient data on how vitamin D metabolites interact with different IHT options when administered as part of complex therapy [1].

MATERIAL AND METHODS

The prospective one-stage clinical study included 60 women aged 46-56 years (mean age in the 1st and 2nd groups 48.4±2.2 and 49.1±1.8 years, respectively, without statistically significant difference) in surgical postmenopause with duration from 1 to 5 years. All women applied to an obstetrician-gynecologist with complaints of menopausal symptoms of varying severity to decide on the prescription of MHT.

A standard general clinical examination was performed, including blood biochemical analysis, lipidogram, phosphorus-calcium metabolism, mammography, pelvic ultrasound and dual-energy X-ray absorptiometry. All parameters were within the reference values, and no statistically significant differences between the groups were found.

Before the study, all patients had vitamin D deficiency (level less than 20 ng/mL), total or subtotal hysterectomy with appendages for combined uterine and ovarian pathology (uterine myoma and benign ovarian masses, adenomyosis and benign ovarian masses).

Depending on the recommended type of MHT, the patients were divided into 2 groups of 30 patients each. In group 1, women after hysterectomy were prescribed estrogen monotherapy transdermally (17β-estradiol - gel for external application). In Group 2, combined estrogen-gestagen oral MGT (1 mg 17β-estradiol + 5 mg dydrogesterone) in prolonged mode was recommended.

Along with MHT, oral colecalciferol (vitamin D) was recommended for all patients. Correction of vitamin D deficiency was carried out at a dose of 6000-8000 IU/day for 8 weeks.

The data obtained during the study were subjected to statistical processing. Numerical variables are presented in absolute terms and in percentages. Quantitative variables are presented as mean values and standard deviations.

For comparison between two groups, Student's t-test was used for normally distributed data and Mann-Whitney U-test was used for non-normally distributed data. The criterion of statistical significance was the level of $p<0.05$.

RESULTS AND DISCUSSION

In the course of the study, vitamin D levels were assessed before and against the background of IHT administration.

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The distribution of examined women by demographic parameters is presented in Table 1. An interesting fact was found out that vitamin D deficiency was more pronounced in the inhabitants of the plains (Table 2).

Table 1. Distribution of Women by Demographic Parameters (Age and Social Status)

Demographic Parameter	Number of Women (n=60)	%
Age, years		
40–44	13	21.7
45–49	30	50.0
50–55	17	28.3
Social Status		
Singles and Widows	28	46.7
Married	32	53.3

In our study, a more rapid increase in serum vitamin D levels was observed during combined IHT compared with estrogen monotherapy. The doses of drugs were comparable with initially statistically insignificant difference of vitamin D level in both groups (see Table 2).

Table 2. Changes in Endometrial Thickness and Antral Follicle Count in Female Patients of the Study Groups

Indicator	Main Group	Control Group
Endometrial thickness, mm		
Before treatment	4.1 ± 1.3	4.3 ± 1.2
After treatment	9.1 ± 1.7 (n=18)**	5.8 ± 1.2
Antral follicle count		
Before treatment	3.4 ± 0.4	3.6 ± 0.2
After treatment	6.7 ± 0.5 (n=18)**	3.7 ± 0.3

It has been established that women living in the mountains show a tendency for a faster increase in vitamin D levels in conditions of its deficiency when prescribed the same doses of drugs. The inclusion of a gestagen component in the MHT regimen increases the absorption of vitamin D. Thus, with equal initial values and equal replenishing doses, its level increases faster in the 2nd group. This is consistent with limited data from foreign studies and has been confirmed by us on a small sample of patients [3]. Due to the small sample, further research is required to confirm the reliability of the identified features and to develop new recommendations for attending physicians on the possibility of rapid correction of vitamin D levels in case of its deficiency with a personalized approach to patients to reduce morbidity and improve quality of life.

The incidence of vitamin D deficiency in the regions of the Russian Federation ranges from 55 to 80% [13]. The importance of vitamin D correction is beyond doubt. It improves the absorption of calcium and phosphates, thereby promoting the health of the musculoskeletal

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system. Its dietary intake is inversely associated with early menopause, but no studies confirm such a risk for plasma 25-hydroxyvitamin D [25(OH)D] concentrations [8]. According to the literature, its decreased level is associated with the development of postmenopausal osteoporosis, but does not correlate with the severity or development of menopausal symptoms. A number of studies have not established a clinically significant association between serum 25(OH)D levels and menopausal symptoms in women [9, 10].

Vitamin D deficiency also contributes to thinning of the vaginal epithelium in postmenopausal women. Vitamin D receptors are involved in the regulation of the development and differentiation of the multilayered vaginal epithelium, as well as the maturation of vaginal cells [11].

In the work of T. Kamronrithisorn et al. [12] the effect of oral vitamin D supplements on postmenopausal women with vulvovaginal atrophy (VVA) before the start of traditional treatment was noted. The average vaginal pH and the level of complaints on the visual analog scale (VAS) in patients with VVA in the vitamin D group significantly improved after 6 and 12 weeks of its use compared to the initial level and the control group without taking medications. In isolated VVA without other menopausal disorders, vitamin D can probably help to reduce the doses of hormonal drugs and is therefore recommended for use as part of complex therapy [12].

CONCLUSION

Vitamins D metabolism disorders in postmenopausal women are of great importance for their health. Determination of vitamin D levels is recommended for all patients aged 46–56 years before prescribing MHT due to the high risk of its deficiency. The inclusion of a progestogen component in the MHT regimen increases the absorption of vitamin D and, with equal initial values and equal replenishing doses, its level increases faster. In this regard, in case of severe vitamin D deficiency, it is advisable to give preference to combined estrogen-progestogen forms of MHT for its faster replenishment.

Combination of vitamin D and menopausal hormone therapy is a promising strategy in the management of postmenopausal women. Vitamin D enhances the positive effect of MHT on bone health, reduces the risk of cardiovascular diseases and has a modulating effect on immunity. To achieve the best results, individual dosage selection and monitoring of vitamin D levels in the body are necessary.

Key recommendations:

- Regular monitoring of vitamin D levels.
- Using the optimal dosage depending on the initial 25(OH)D level.
- A comprehensive approach that includes dietary modification, physical activity, and risk factor control.

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