

## Modern Clinical Diagnostic Methods for Menopausal Women Based on Vitamin D Levels

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**Annotation:** In the evaluation of numerous population studies on the prevalence of vitamin D deficiency in different ethnic and age groups, a relationship between its deficiency and the duration and age of postmenopause has been found. The “gold standard” for the treatment of menopausal disorders is, of course, menopausal hormone therapy (MHT) in various forms. According to a number of authors, the addition of vitamin D metabolites to complex therapy can improve some metabolic parameters and clinical outcomes in elderly and postmenopausal women. However, there is insufficient information on how vitamin D metabolites interact with different types of MHT when used as part of combination therapy.

**Objective:** To compare the severity of changes in serum vitamin D levels in women using different forms of HRT.

**Materials and methods:** The study included 60 women aged 45-55 years in surgical postmenopause, which lasted from 1 to 5 years. Before the start of the study, all patients had vitamin D deficiency (less than 20 ng / ml). Depending on the type of HRT prescribed, the patients were divided into 2 groups of 30 people. In group 1, monotherapy with transdermal estrogens was prescribed (17 $\beta$ -estradiol - gel for

external use). In group 2, combined estrogen-progestogen oral MHT (1 mg 17 $\beta$ -estradiol + 5 mg dydrogesterone) was prescribed. In addition to MHT, all patients received cholecalciferol (vitamin D) at a dose of 6000-8000 IU per day for 8 weeks.

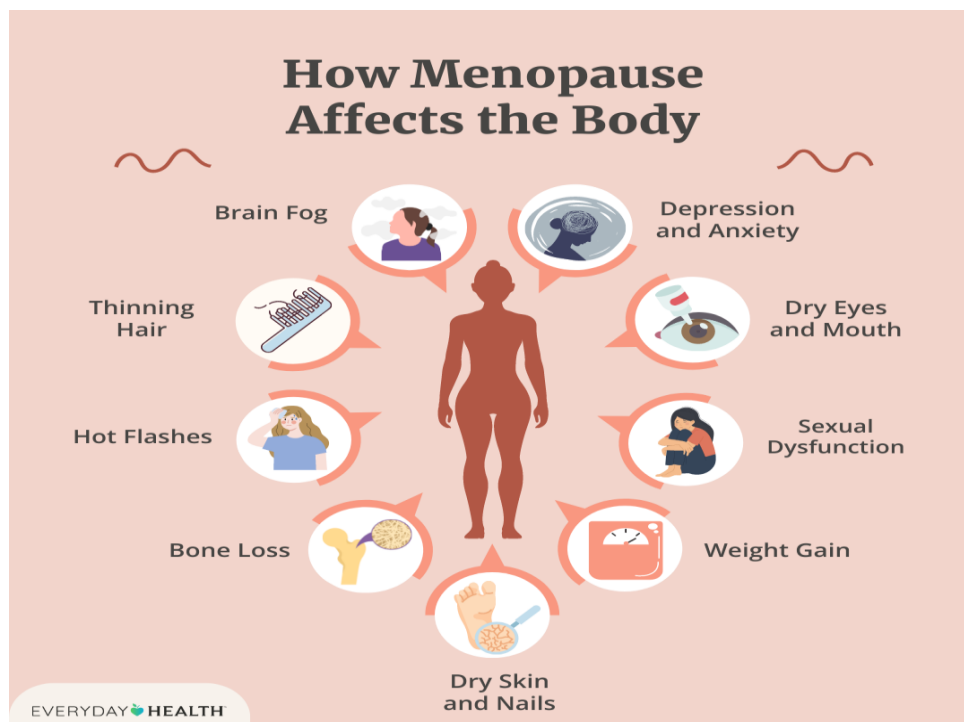
**Research results:** against the background of combined MHT, a significant increase in serum vitamin D levels was observed compared to the monotherapy group - with equal doses of drugs and the same initial level of vitamin deficiency.

**Conclusion:** Screening for vitamin D deficiency is recommended for all patients before starting HRT. If vitamin D levels are low, combined estrogen-progestogen forms of HRT should be preferred.

**Keywords:** menopause, menopausal hormone therapy, vitamin D, cholecalciferol.

## INTRODUCTION

Menopause and climacteric disorders are associated with changes in circulating levels of sex hormones, insulin sensitivity, as well as lifestyle and social habits. In postmenopause, there is a decrease in the protective properties of estrogen-progesterone and an increase in the risk of cardiovascular diseases, diabetes, osteoporosis, etc. [1]. Hormonal fluctuations, excessive protection of the skin with clothing, a sedentary lifestyle, the use of sunscreens, changes in body fat composition and vitamin D deficiency predispose to vitamin D deficiency in postmenopause [2, 3]. The ability of the skin to produce vitamin D decreases with age, and in older people it is 3 times lower than in young people [4, 5].



The main source of vitamin D is endogenous production from sunlight. Ultraviolet B radiation causes the conversion of 7-dehydrocholesterol in the skin to previtamin D<sub>3</sub> and then to vitamin D<sub>3</sub> (cholecalciferol). Vitamin D<sub>3</sub> is metabolized in the liver to 25-hydroxyvitamin D (25(OH)D), the major circulating form of vitamin D, and is used to assess vitamin D status in humans. Circulating 25(OH)D is then metabolized in the kidneys to the more biologically active form, 1,25-dihydroxyvitamin D [4-6].

Insufficient exposure to sunlight and the use of sunscreens, which reduce 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 ].

Food is another important source of vitamin D. Oral vitamin D supplements are usually given to patients as vitamin D<sub>3</sub> (cholecalciferol) or vitamin D<sub>2</sub> (ergocalciferol). Vitamin D<sub>3</sub> is obtained from animal products such as oily fish (salmon, mackerel, herring) and fish oil, while vitamin D<sub>2</sub> is obtained from plants [9-12].

The prevalence of vitamin D deficiency among older women was 43.9% [11, 13]. In addition, postmenopausal weight gain 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 inability to reach the central circulation [4].

In evaluating the prevalence of vitamin D deficiency in various ethnic and age groups, numerous population-based studies have found a correlation between the degree of deficiency and the duration of postmenopause and the age of the women [5, 6]. Vitamin D status affects various metabolic parameters, in addition to phosphorus-calcium metabolism and the state of the musculoskeletal system.

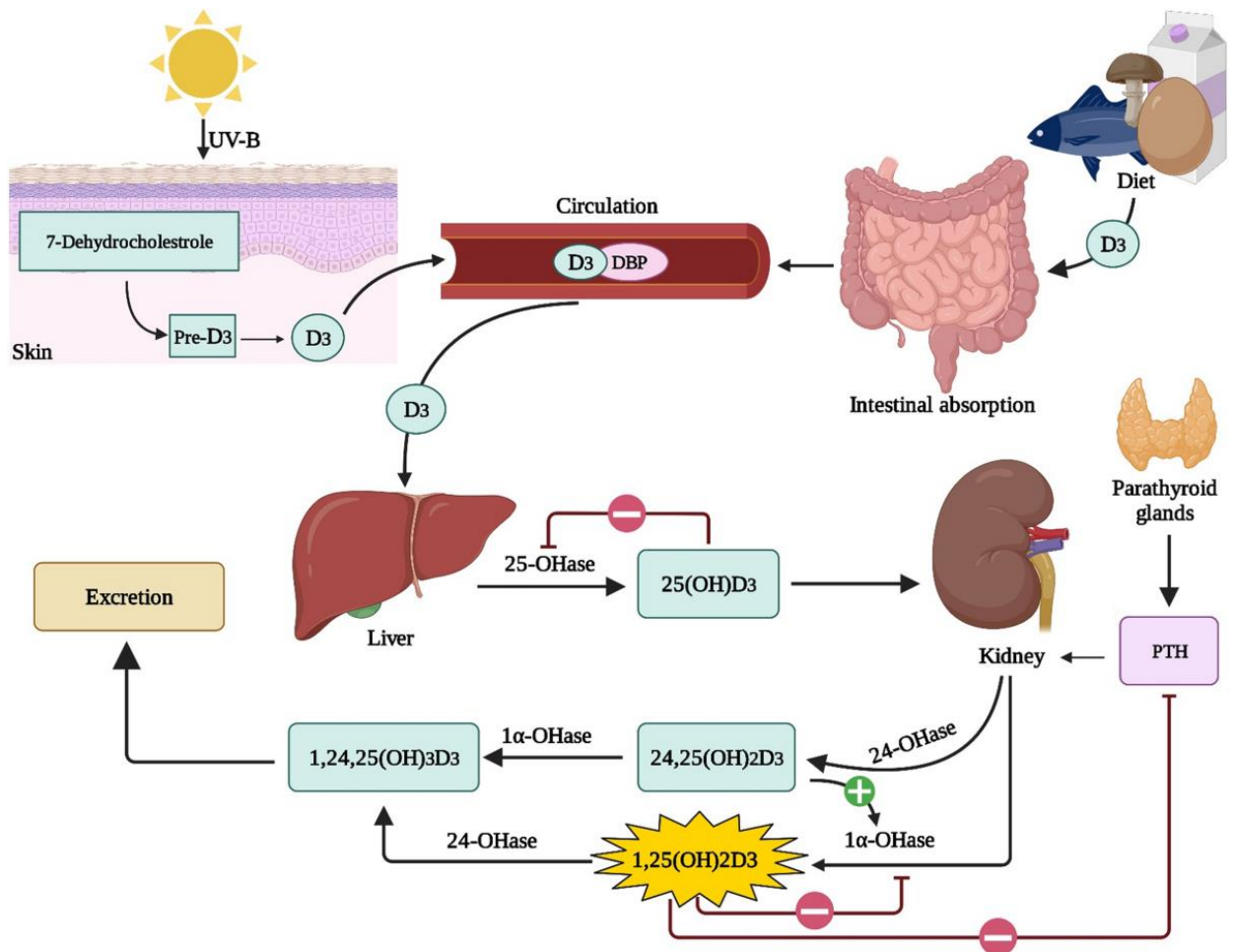
Blood 25(OH)D concentration is a reliable indicator for monitoring vitamin D status, as it is the major circulating form in plasma. Its detection in serum as the major circulating metabolite of vitamin D is a key indicator of vitamin D status [7].

The “gold standard” for the treatment of menopausal disorders is undoubtedly hormone therapy (HRT) in various forms of menopause [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 information on how vitamin D metabolites interact with different types of HRT when prescribed as part of combination therapy [1].

Objective: To compare the severity of changes in serum vitamin D levels in women using different forms of HRT.

### **Materials and methods**

A prospective single-stage clinical study was conducted on 60 women aged 45-55 years (mean age in groups 1 and 2,  $48.4 \pm 2.2$  and  $49.1 \pm 1.8$  years, respectively, without statistically significant differences) in surgical postmenopause lasting from 1 to 5 years. The study was approved by the local ethics committee of the Federal State Budgetary Educational Institution of Higher Education Dagestan State Medical University of the Ministry of Health of the Russian Federation. Patients signed voluntary informed consent to participate in the study. All women consulted an obstetrician-gynecologist with complaints of climacteric symptoms of varying severity to decide on the appointment of HRT.



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

Before the study, all patients had vitamin D deficiency (less than 20 ng/ml) and underwent total or subtotal hysterectomy with adjuncts due to combined uterine and ovarian pathology (uterine fibroids and benign ovarian tumors, adenomyosis and benign ovarian tumors).

Depending on the type of HRT recommended, patients were divided into 2 groups of 30 people. In group 1, women after hysterectomy were prescribed monotherapy with transdermal estrogens (17 $\beta$ -estradiol - gel for external use). In group 2, combined estrogen-progestogen oral MHT (1 mg 17 $\beta$ -estradiol + 5 mg dydrogesterone) was recommended in a long-term regimen.

In addition to MHT, all patients were recommended to take oral cholecalciferol (vitamin D). Correction of vitamin D deficiency was performed at a dose of 6000-8000 IU per day for 8 weeks.

The data obtained during the study were subjected to statistical processing. Statistical analysis was performed using IBM SPSS Statistics version 24 for Windows. The Kolmogorov-Smirnov test was used to assess the normality of the data distribution. Numerical indicators are expressed in absolute and percentage terms. Quantitative variables are presented as means and standard deviations.

Student's t-test for normally distributed data and Mann-Whitney U-test for non-normally distributed data were used for comparisons between two groups. The criterion for statistical significance was  $p < 0.05$ .

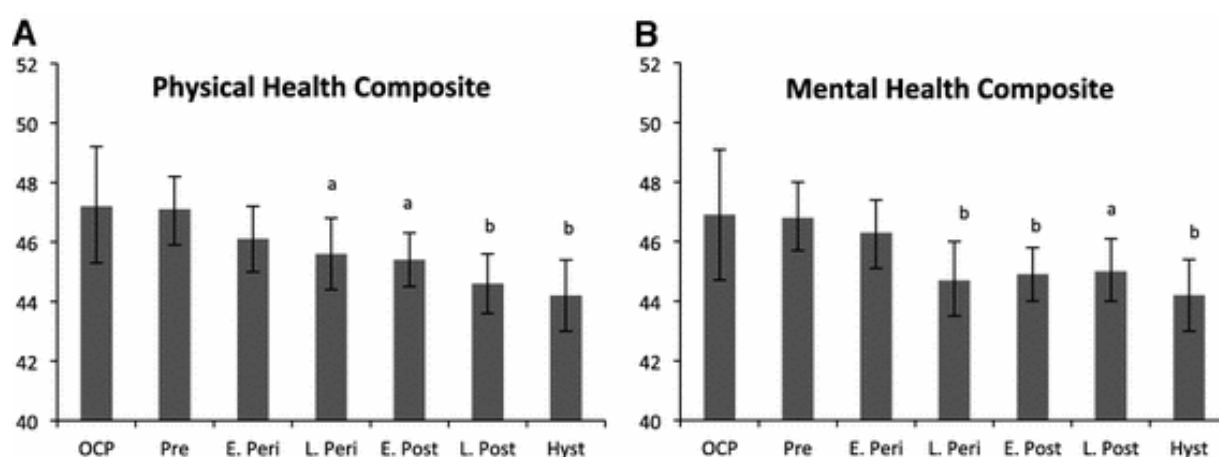
## Results and discussion

In our study, combination HRT resulted in a more rapid increase in serum vitamin D levels

compared with estrogen monotherapy. The doses of the drugs were comparable with a statistically insignificant difference in baseline vitamin D levels in both groups.

It was found that women living in the mountains, when prescribed the same doses of drugs, are prone to a rapid increase in vitamin D levels, as in the case of its deficiency. The inclusion of a progestogen component in the MHT regimen increases the absorption of vitamin D. Thus, with equal initial values and equal replenishment doses, its level increases faster in group 2. This is consistent with limited data from foreign studies and we confirmed it in a small sample of patients [3]. Due to the small sample size, additional studies are needed to confirm the reliability of the identified characteristics and develop new recommendations for treating physicians on the possibility of quickly correcting its level in case of vitamin D deficiency in order to reduce morbidity and improve the quality of life of patients.

The prevalence of vitamin D deficiency is 25 to 50% [3]. The importance of vitamin D supplementation is undeniable. It improves calcium and phosphate absorption, thereby promoting musculoskeletal health. Dietary intake is inversely associated with early menopause, but no studies have confirmed a similar risk for plasma 25-hydroxyvitamin D [25(OH)D] concentrations [8]. According to the literature, a decrease in its level is associated with the development of postmenopausal osteoporosis, but not with the severity or progression of climacteric symptoms. Several studies have not found a clinically significant relationship 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 regulating the development and differentiation of the stratified vaginal epithelium, as well as the maturation of vaginal cells [11].

## Conclusion

In postmenopausal women, impaired vitamin D metabolism has a significant impact on their health. Determination of vitamin D levels is recommended for all patients aged 45-55 years, since they are at high risk of developing its deficiency before prescribing MHT. The inclusion of a progestogen component in the HRT regimen increases the absorption of vitamin D, and with equal initial values and equal replenishment doses, its level increases more quickly. In this regard, in the presence of a pronounced deficiency of vitamin D, it is recommended to give preference to combined estrogen-gestagen forms of HRT to replenish it more quickly. It is necessary to continue studies in large samples in different geographical populations to identify differences in vitamin D absorption in order to clarify the mechanisms of action of vitamin D in this group of patients and to determine a complex therapy regimen for individual correction.

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