American Journal of Bioscience and Clinical Integrity
https://biojournals.us/index.php/AJBCI
ISSN: 2997-7347

Modern Clinical Diagnosis of Vitamin D Deficiency in Women Undergoing Menopause

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Received: 2024, 15, Dec
Accepted: 2024, 21, Jan
Published: 2025, 10, Feb

Annotation: Research objective: To assess the effect of cholecalciferol on the severity of climacteric manifestations and the dynamics of cytokine status in women receiving phytoestrogen therapy.

Materials and methods. 303 women aged 46 to 56 years were examined. Of these, 229 women had symptoms of climacteric syndrome (CS). In the first stage of the study, clinical symptoms, 25 (OH) D levels, and cytokine profiles were assessed in women with CS (n = 229). Control data were the results of examination of women of similar age, but without symptoms of CS (control group, n = 73). In the second stage, the dynamics of clinical and immunological indicators in two groups of women with CS were studied. The first group (comparison group, n = 57) consisted of patients who received therapy with a phytoestrogen preparation for 6 months. The second group (main, n = 57) included women who, in addition to a similar 6-month course of phytoestrogens, were prescribed cholecalciferol using saturation schemes determined by the initial level of 25 (OH) D in the blood serum. During the course of treatment, the severity of clinical manifestations of CS was assessed, as well as the level of 25 (OH) D, interleukins IL-1β, IL-6, IL-8 and tumor necrosis factor α. After a 6-month

course of therapy, 55 women in the comparison group and 50 patients in the main group were re-examined.

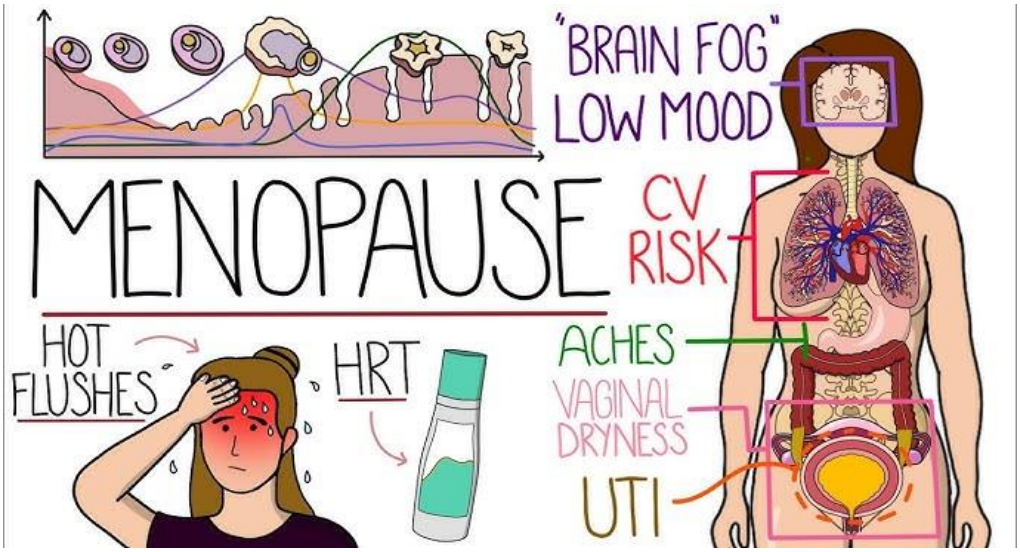
Results. Climacteric syndrome is characterized by increased serum IL-6 ($p = 0.042$) and IL-8 ($p = 0.036$) concentrations and is more often observed in women with vitamin D deficiency (81.1% vs. 68.5%; $p = 0.018$). The inclusion of cholecalciferol in the treatment regimen led to a significant decrease in anxiety and panic attacks, headache, somatic symptoms, the overall severity of climacteric syndrome according to the Green scale, as well as a significant decrease in IL-6 levels after 6 months of complex therapy. When analyzing the level of IL-8, a significant decrease was found only when phytoestrogens were taken in combination with cholecalciferol. The combination of phytoestrogens with cholecalciferol also provided a significant increase in serum 25(OH)D: from 17.77 [13.58; 24.76] ng/ml to 35.47 [31.49; 43.59] ng/mL ($p < 0.001$).

Conclusion: The results obtained indicate that there is a favorable clinical and immunological effect of vitamin D intake in women with climacteric syndrome.

Keywords: vitamin D, cytokines, climacteric syndrome, modern diagnostics.

INTRODUCTION

Climacteric syndrome (CS) is a pathological condition that occurs in most women during the period of physiological decline in ovarian function. The most common early symptoms of menopause include vasomotor symptoms, including hot flashes and night sweats, and emotional disturbances (depressive states, sleep disturbances, etc.), which are observed in approximately 75% of perimenopausal women and can last for 10 years or more [1-5].



It is currently believed that immune dysregulation, particularly changes in cytokine balance, may play an important role in the pathogenesis of early menopause [6, 7]. Vitamin D metabolism disorders may also be involved in the pathogenesis of KS. Thus, a link between 25(OH)D deficiency and vasomotor symptoms has been identified [8].

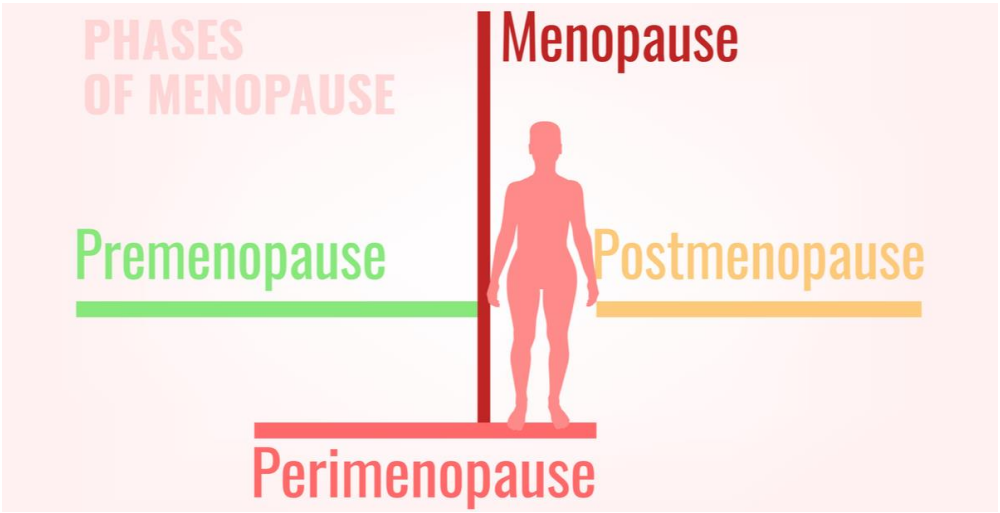
To date, one of the least studied areas in the treatment of early menopause is the use of vitamin D (VD), which is often prescribed for late menopause [9, 10]. Data on the effects of VD drugs on early symptoms of CS are limited and conflicting [11, 12].

The aim of the study was to evaluate the effect of cholecalciferol on the severity of climacteric symptoms and the dynamics of the cytokine status in women with climacteric syndrome receiving phytoestrogen therapy.

MATERIALS AND METHODS

A total of 303 women aged 47 to 56 years with a postmenopausal period of up to 5 years were examined. The selection of women for the study was carried out by random sampling. The presence of CS was confirmed based on the results of a survey and clinical examination, including a questionnaire on the Green scale.

Inclusion criteria for the study: female gender, postmenopause lasting up to 5 years, written voluntary consent to participate. Exclusion criteria: taking hormonal drugs and immunosuppressants; autoimmune, endocrine diseases, as well as the presence of chronic inflammatory, oncological, hematological and mental diseases, metabolic diseases, chronic kidney and liver diseases.



The first phase of the study assessed clinical signs and symptoms of VD and cytokine profiles in women with CS (n = 229). Control data were the results of a study of women of similar age but without symptoms of CS (control group, n = 73).

In the second phase, the dynamics of clinical and immunological indicators were studied in two groups of women with CS, randomly selected and not differing in age, clinical and laboratory parameters. The first group (comparison group, n = 57) consisted of patients who received therapy with a phytoestrogen preparation for 6 months. The second group (main, n = 57) included women who, in addition to a similar 6-month course of phytoestrogens, were prescribed cholecalciferol using saturation schemes determined by the initial level of 25 (OH) D in the blood serum [12].

The severity of clinical manifestations of CS and laboratory parameters were assessed during the treatment dynamics. After a 6-month course of therapy, 55 women in the comparison group and 50 patients in the main group were re-examined.

Quantitative characteristics of all clinical signs and laboratory parameters are presented as median and first and third quartiles (Q1; Q3). Percentages are given with standard error of the ratio. Comparisons of two independent samples were performed using the Mann-Whitney test and the Wilcoxon two-sample t-test. Multiple comparisons of independent samples were performed using the Kruskal-Wallis one-way rank analysis. The χ 2 criterion was used to compare the frequency of the feature within groups. Differences were considered statistically significant at $p < 0.05$.

RESULTS

No significant differences were found when comparing serum IL-1β and TNF-α levels in early postmenopausal women with and without CS. In addition, CS was found to be accompanied by a significant increase in serum concentrations of IL-6 (p = 0.042) and IL-8 (p = 0.036).

There was no significant difference in 25(OH)D levels between patients with CS and control participants, but nevertheless, an additional analysis was conducted to assess the frequency of detection of CS at different 25(OH)D levels (Table 2). All patients were divided into four groups: normal 25(OH)D content (n = 32; 10.6%), its deficiency (n = 95; 31.5%), moderate (n = 132; 43.7%) and severe (n = 43; 14.2%). The results of multiple comparisons of the results obtained in the four groups did not show significant differences (p = 0.085).

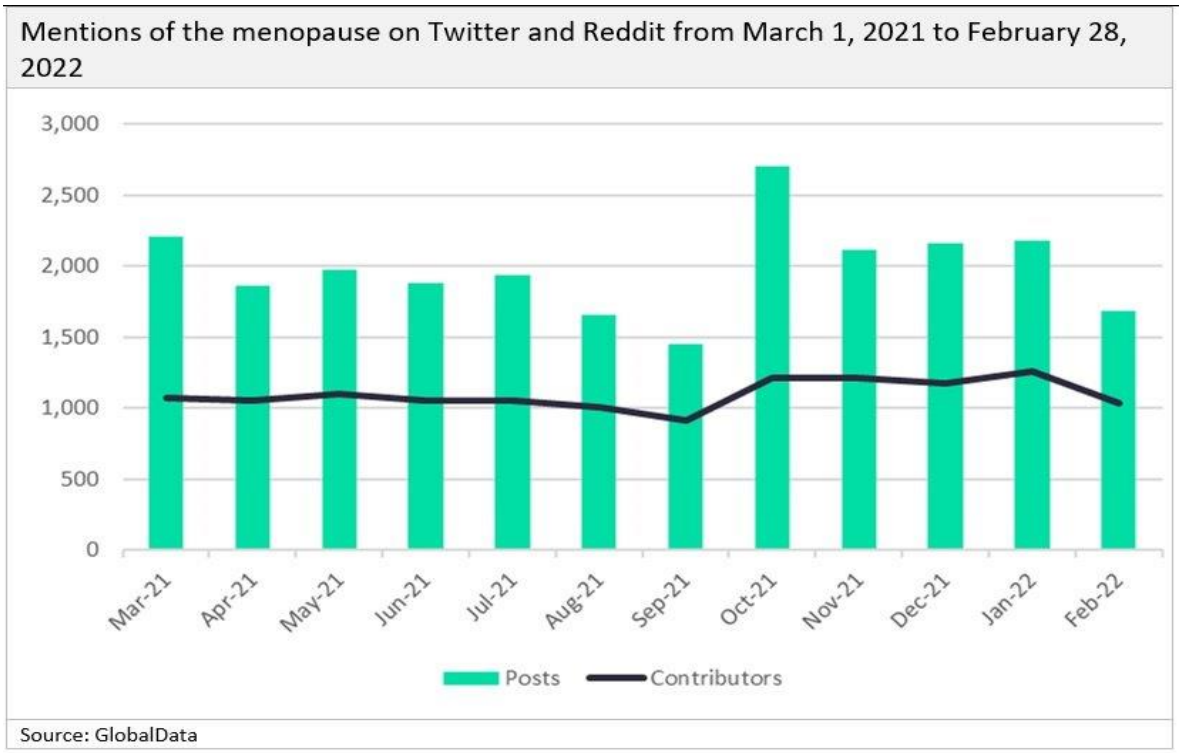
However, when comparing patients in two combined groups with 25(OH)D values of 20.0 ng/mL or more in one group and <20.0 ng/mL in the other (Figure 1), significant differences were found (p = 0.018).

After studying the characteristics of the cytokine profile and 25 (OH) D values during CS, two groups of patients were identified for observation during the dynamics of treatment (Table 3). A comparative analysis of the severity of CS symptoms in women during therapy showed that the isolated intake of phytoestrogens was accompanied by a significant decrease in the severity of 14 CS symptoms, the total score in psychosocial clusters, somatic and vasomotor symptoms, and the Green scale as a whole (p <0.050 to p<0.050). When using a complex of phytoestrogens and cholecalciferol, 15 symptoms of CS, including pain in muscles and joints, the total score in psychosocial clusters, somatic and vasomotor symptoms, and the Green scale as a whole (p <0.05 to p<0.01), were significantly reduced. Furthermore, the inclusion of cholecalciferol in the regimen resulted in a significant and significant reduction in anxiety and panic attacks, headaches, somatic symptoms, and overall severity of CS after 6 months of complex therapy.

Note: Statistically significant differences in the comparison of indicators after treatment between the main group and the comparison group: (*) - p = 0.045; (**) - p = 0.015; (***) - p = 0.017.

It should be noted that in the case of phytoestrogens alone, serum VD concentrations remained unchanged during treatment, from 18.16 [12.70; 24.23] ng/ml before therapy to 17.71 [13.73; 24.01] ng/ml after treatment (p > 0.05). The combination of phytoestrogens with cholecalciferol provided a significant increase in serum 25(OH)D: from 17.77 [13.58; 24.76] ng/ml to 35.47

[31.49; 43.59] ng/ml (p < 0.001).



Analysis of the content of the anti-inflammatory cytokine IL-6 (Fig. 3) showed that the isolated consumption of phytoestrogens was accompanied by a decrease in its content from 0.7 [0.0]; 1.2] to 0.5 [0.0; 1.1] pg/ml (p = 0.037). The combination of phytoestrogens with the drug VD also contributed to a significant decrease in the content of IL-6 - from 0.9 [0.0; 1.4] to 0.4 [0.0; 0.8] pg/ml (p < 0.001). The values achieved as a result of therapy did not differ from those in the control group (p> 0.05).

When analyzing the level of IL-8, after 6 months of therapy, a significant decrease was detected in the serum of women taking only phytoestrogens in combination with cholecalciferol (Fig. 4). In the comparison group, the concentration of the cytokine before and after treatment was 5.5 [3.4; 9.0] pg/ml and 6.8 [4.2; 10.2] pg/ml, respectively (p > 0.05). In the main group, the level of IL-8 before treatment was 5.5 [3.9; 8.7] pg/ml and after 6 months of therapy - 4.5 [2.7; 6.0] pg/ml (p < 0.001). After 6 months of phytoestrogen therapy, the average concentration of IL-8 in the comparison group significantly exceeded similar indicators in the control (p <0.05) and main groups (p <0.01). Serum levels of interleukin 8 (IL-8) in women with climacteric syndrome in the dynamics of therapy and in the control group.

DISCUSSION

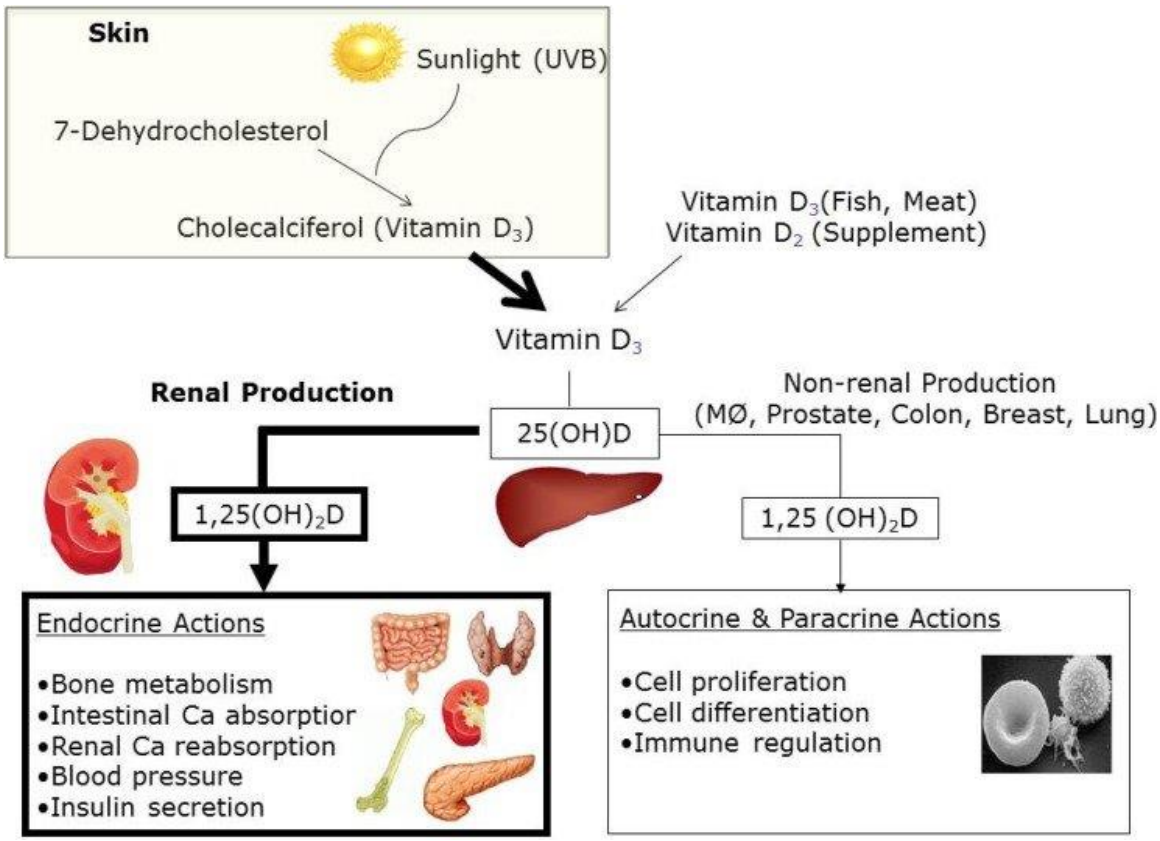
Early postmenopausal women with CS symptoms showed increased production of the pro-inflammatory cytokines IL-6 and IL-8 (p < 0.05). Patients with 25(OH)D levels less than 20.0 ng/mL were also shown to have a significantly higher incidence of CS, consistent with VD deficiency (p < 0.05).

We found that the association between CS and VD deficiency, as well as the decrease in 25(OH)D during CS in the majority of women examined (89.4%), served as the basis for standard correction of this vitamin deficiency. The combination of phytoestrogens and cholecalciferol provided a significant reduction in the severity of clinical manifestations of CS and normalization of IL-8 levels due to a decrease in cytokine production during treatment (p <0.001).

Our findings regarding the high incidence of VD deficiency and deficiency in postmenopausal women are consistent with the results of a study by H. Vázquez-Lorente et al. [14] . VD deficiency may be one of the factors in the development of clinical symptoms of CS [15] and normalization

of 25 (OH) D levels may help reduce the intensity of symptoms of the syndrome [12] .

Currently, there is no doubt about the important role of VD in the functioning of various organs and systems of the human body. Among the wide range of skeletal and extraskeletal effects of the vitamin, its immunotropic effect occupies a special place. VD has the ability to act through receptors corresponding to the activity of monocytes/macrophages, T- and B-lymphocytes and other cells of the immune system, to regulate their proliferation and maturation, and to control their physiological functions, including the secretion of various cytokines. At the same time, VD deficiency leads to a decrease in the effectiveness of the immune response, excessive activation of immunocompetent cells and increased production of pro-inflammatory cytokines, which is associated with an increased risk of autoimmune and allergic diseases, susceptibility to various infections and the development of oncological diseases [13].



In connection with the above, one of the possible mechanisms by which VD influences the clinical manifestations of CS may be its indirect effect on the pathogenesis of CS through its regulatory effects on cells of the immune system, including its properties of inhibiting excessive synthesis of proinflammatory cytokines.

To date, there are isolated studies, the conclusions of which confirm the role of changes in the cytokine balance in the development of CS. An increase in the level of some pro-inflammatory cytokines, in particular, TNF-α and IL-8, has been detected in CS [11]. A significant correlation between increased circulating IL-8 concentrations and the presence and severity of hot flashes was shown by A. Malutan et al. [19]. A connection between systemic inflammation and depression as one of the manifestations of CS in peri- and postmenopause has been shown [7, 20]. A significant increase in the level of IL-6 and TNF-α in the serum of perimenopausal women was also found against the background of depression [6].

CONCLUSION

Our results indicate that vitamin D supplementation has a positive clinical and immunological effect in women with CS, and its use is recommended in the treatment and prevention of such patients.

List of used literature:

1. Avis NE Vasomotor symptoms during the menopausal transition: differences between women. Obstetrics. Gynecology. Clin. North Am. 2018;45(4):629–40. DOI: 10.1016/j.ogc.2018.07.005
2. Nappi RE, Kroll R, Siddiqui E, Stoykova B, et al. A global cross-sectional survey of women with menopause-related vasomotor symptoms: prevalence and quality of life burden. Menopause. 2021;28(8):875–82. DOI: 10.1097/GME.000000000000001793
3. Ozdemir K., Sahin S., Guler DS, Unsal A. et al. Depression, anxiety, and fear of death in postmenopausal women. Menopause. 2020;27(9):1030–6. DOI: 10.1097/GME.00000000000001578
4. Yadav V., Jain A., Dabar D., Goel AD et al. A meta-analysis on the prevalence of depression in perimenopausal and postmenopausal women in India. Asian J. Psychiatr. 2021;57:102581. DOI: 10.1016/j.ajp.2021.102581
5. Monteleone P., Mascagni G., Giannini A., Genazzani AR, et al. Menopausal symptoms - global prevalence, physiology and consequences. Nat. Rev. Endocrinol. 2018;14(4):199–215. DOI: 10.1038/nrendo.2017.180
6. Guo L., Ren L., Zhang C. Relationship between depression and inflammatory factors and brain-derived neurotrophic factor in patients with perimenopausal syndrome. Exp. There. Med. 2018;15(5):4436–40. DOI: 10.3892/etm.2018.5985
7. Pasquali MA, Harlow BL, Soares CN, Otto MW, et al. A longitudinal study of neurotrophic, oxidative, and inflammatory markers in first-onset depression in middle-aged women. Eur. Arch. Clin Psychiatry. Neurolog. 2018;268(8):771–81. DOI: 10.1007/s00406-017-0812-z
8. Arslanca T., Korkmaz H., Arslanca SB, Pehlivanoglu B. et al. The relationship between vitamin D and vasomotor symptoms in the postmenopausal period. Clin. Labor. 2020;66(7). DOI: 10.7754/Clin.Lab.2019.191116
9. Liu C., Kuang X., Li K., Guo X., et al. Effects of combined calcium and vitamin D supplementation on osteoporosis in postmenopausal women: a systematic review and meta-analysis of randomized controlled trials. Food Func. 2020;11(12):10817–27. DOI: 10.1039/d0fo00787k
10. Riazi H., Ghazanfarpour M., Taebi M., Abdolahian S. The effect of vitamin D on vaginal health in menopausal women: a systematic review. J. Menopause Med. 2019;25(3):109–16. DOI: 10.6118/jmm.19194
11. LeBlanc ES, Hedlin H, Qin F, Desai M, et al. Calcium and vitamin D supplementation do not affect menopausal symptoms: Results from the Women's Health Initiative Trial. Maturitas. 2015;81(3):377–83. DOI: 10.1016/j.maturitas.2015.04.007
12. Polisseni AF, Andrade ATL, Ribeiro LC, Castro IQ, et al. Effects of a continuous combination regimen of low-dose hormone therapy (estradiol and norethindrone acetate) and tibolone on quality of life in symptomatic postmenopausal women: a double-blind, randomized study. Maturitas. 2013;74(2):172–8. DOI: 10.1016/j.maturitas.2012.11.001
13. Pigarova EA, Rojinskaya L.Ya., Belaya JE, Dzeranova LK, et al. Russian Endocrinology on the diagnosis, treatment and prevention of vitamin D deficiency in adults