Short Communication

Effects of vitamin D supplementation on salivary cortisol and psychological health among postmenopausal women: A pilot quasi-experimental study

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Abstract

Menopause is a significant life transition often accompanied by mood disturbances, many of which are linked to cortisol levels and hypothalamic–pituitary–adrenal (HPA) axis dysregulation. Vitamin D deficiency is highly prevalent in postmenopausal women and shares overlapping adverse outcomes with menopausal symptoms. This study aimed to investigate the effect of vitamin D supplementation on salivary cortisol levels and psychological symptoms in postmenopausal women. This pilot study employed a quasi-experimental design, recruiting 32 postmenopausal women via consecutive sampling from the study population in Kwala Bekala Village, Medan Johor District. Participants were consecutively added into two groups, receiving either 1000 IU or 2000 IU of vitamin D daily for one month. Salivary cortisol levels and Depression, Anxiety, and Stress Scale (DASS) scores were measured before and after the intervention. The findings revealed that serum 25(OH)D levels increased significantly in both groups, with higher post-supplementation levels in the 2000 IU group than in the 1000 IU group (28.94±5.86 ng/mL vs 24.13±5.28 ng/mL, p=0.021). Salivary cortisol decreased in both groups, with a greater reduction observed in the 2000 IU group (median Δ=9.55 ng/mL vs mean Δ=4.92±4.29 ng/mL, p=0.032). Psychological symptoms measured by DASS scores also improved significantly, with the 2000 IU group showing a larger reduction (mean Δ=11.31±6.65 vs median Δ=3.5, p=0.022). Vitamin D supplementation at both 1000 IU and 2000 IU effectively reduced salivary cortisol and improved psychological symptoms in postmenopausal women. Due to differences in baseline characteristics, caution is warranted when inferring clear dose superiority.

Keywords: Menopause, vitamin D, salivary cortisol, DASS, psychological symptoms

Introduction

Menopause, defined as 12 consecutive months of amenorrhea, represents a major transitional stage in a woman's life, typically occurring between 49 and 52 years of age worldwide [1]. While some women perceive menopause positively, others associate it with negative aspects of aging [2]. This transition is often accompanied by a constellation of symptoms, including hot flashes, sleep disturbances, mood disorders, sexual and genitourinary dysfunction, weight gain, and cognitive decline [3]. The severity and perception of these symptoms are further shaped by psychological factors, socioeconomic status, cultural background, environmental conditions, marital status, and lifestyle practices [4].

Psychological well-being during menopause is strongly influenced by stress regulation, particularly through cortisol. Cortisol, the primary effector hormone of the hypothalamic–

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pituitary–adrenal (HPA) axis, is widely recognized as a biomarker of stress. The HPA axis is activated by psychological and physiological stressors, and elevated cortisol levels during the perimenopausal period are linked to increased stress and sleep disturbances [5,6]. Dysregulation of cortisol secretion may impair nervous system stability, disrupt restorative REM sleep, and alter circadian rhythms, leading to persistent sleep difficulties [7,8]. Elevated cortisol levels are also associated with cardiovascular symptoms such as palpitations and psychological manifestations including anxiety and panic attacks. Furthermore, hormonal changes during menopause—particularly increased FSH and decreased estrogen—may modulate cortisol dynamics, thereby contributing to mood disorders and insomnia [9].

Vitamin D, a secosteroid hormone, plays a critical role in calcium and phosphorus homeostasis and bone mineralization [10]. Its deficiency has been associated with increased risk of osteoporosis, cardiovascular disease, diabetes, cancer, and cognitive decline. Menopause and vitamin D deficiency share overlapping adverse outcomes, including bone loss, mood disorders, and heightened risk of cardiovascular and neoplastic disease [10]. Importantly, recent European data indicate that up to 80% of postmenopausal women present with serum 25-hydroxyvitamin D [25(OH)D] levels below 30 ng/mL, underscoring the high prevalence of deficiency in this population [11]. Beyond musculoskeletal health, vitamin D supplementation has been investigated for its potential to alleviate menopausal symptoms and genitourinary discomfort. Moreover, growing evidence suggests that vitamin D administration may lower cortisol levels and improve stress-related outcomes [12]. A 2023 systematic review of 19 clinical trials across 13 countries confirmed that vitamin D supplementation significantly improves serum 25(OH)D concentrations, particularly among women with low baseline status, lighter skin, prolonged treatment duration, and greater sun exposure [13].

Considering the convergence of menopause-related health risks and the widespread prevalence of vitamin D deficiency, the potential interrelationship between vitamin D, cortisol, and psychological well-being warrants further investigation. This study aims to evaluate the effect of vitamin D supplementation on salivary cortisol levels in postmenopausal women. We hypothesize that vitamin D administration will reduce salivary cortisol levels and improve stress-related outcomes in this population.

Methods

Study design and setting

This pilot used a quasi-experimental interventional study design, conducted at the Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Sumatera Utara, between April 15 and May 15, 2025. Ethical approval was obtained from the Ethics Commission of Universitas Sumatera Utara (No. 293/KEPK/USU/2025), and institutional clearance was secured prior to data collection. All participants were informed about the study objectives and procedures, and written informed consent was obtained before enrollment.

Sample size and Eligibility Criteria

The minimum sample size was calculated using a formula for proportion testing, and consecutive sampling was applied, enrolling eligible participants sequentially until the required number was achieved. Based on these calculations, 12 postmenopausal women were included in each group for analysis.

Inclusion criteria required participants to have experienced menopause, defined as at least 12 consecutive months of amenorrhea, and to have provided written informed consent. Exclusion criteria were: (1) use of hormonal therapy or vitamin D supplementation within the preceding 12 weeks; (2) active sexually transmitted or urinary tract infections; (3) abnormal uterine bleeding; and (4) serious medical conditions such as cardiovascular, hepatic, or renal disease. Participants who failed to adhere to the prescribed vitamin supplementation regimen were also excluded.

Variables Definition

The dependent variable in this study was salivary cortisol level, while the independent variable was vitamin D supplementation. Salivary cortisol, the principal steroid hormone synthesized in

the zona fasciculata of the adrenal cortex, was measured from morning saliva samples using ELISA and expressed in ng/mL as a continuous variable.

Serum vitamin D was assessed as 25-hydroxyvitamin D (25(OH)D) concentration in venous blood, expressed in ng/mL, and analyzed using standardized laboratory procedures. Demographic and clinical characteristics, including age and duration of menopause, were obtained through structured questionnaires, while body mass index (BMI) was measured by physical examination. Postmenopausal stress symptoms, encompassing depression, anxiety, and stress, were evaluated using the Depression Anxiety Stress Scale-42 (DASS-42).

Intervention

Eligible participants underwent a one-month supplementation period with commercial vitamin D3 (cholecalciferol, NOW® brand). Participants were assigned consecutively into two groups: one group received 1000 IU of cholecalciferol daily, and the other received 2000 IU daily, both taken once at night. Adherence and safety were monitored through weekly telephone calls, during which participants reported side effects. Any adverse events were evaluated by a physician and classified as mild, moderate, or severe.

Data collection

Baseline characteristics, including age, duration of menopause, and body mass index (BMI), were obtained through structured interviews and physical examination. Salivary cortisol was measured from morning saliva samples collected in sterile tubes and analyzed using DBC Diagnostics Biochem® cortisol ELISA reagents with an ELISA Prismatic analyzer. Serum vitamin D status was assessed from 10 mL of venous blood collected in EDTA tubes, transported in a cooler box, and analyzed as 25-hydroxyvitamin D [25(OH)D] using an Architect instrument. All collected data were entered into a database, verified for completeness, and prepared for statistical analysis.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 22 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize baseline characteristics and outcome measures. Data normality was assessed using the Shapiro–Wilk test. For group comparisons, the Independent *t*-test was applied to normally distributed variables, while the Mann–Whitney U test was used for non-normally distributed variables. A two-tailed p value of <0.05 was considered statistically significant, with a 95% confidence level.

Results

Characteristics of the included patients

A total of 32 postmenopausal women were enrolled and assigned equally into two groups: 16 participants received 1000 IU of cholecalciferol daily, and 16 received 2000 IU. The median age in the 1000 IU group was 58 years (range 55–66), while the 2000 IU group had a mean age of 60.69±4.22 years, with no significant difference between them (p=0.240). The mean BMI was 22.32±1.28 kg/m² in the 1000 IU group and 23.78 kg/m² (range 18.61–24.98) in the 2000 IU group, also showing no significant difference (p=0.200). The median duration of menopause was 7 years (range 3–15) in the 1000 IU group compared to 8 years (range 5–15) in the 2000 IU group (p=0.263). However, baseline salivary cortisol was significantly higher in the 2000 IU group (median 11.45 ng/mL, range 2.5–14.6) compared to the 1000 IU group (median 4.65 ng/mL, range 0.8–13.3) (p=0.019). Similarly, baseline serum 25(OH)D levels were higher in the 2000 IU group (21.75±5.25 ng/mL) than in the 1000 IU group (17.69±5.91 ng/mL) (p=0.049). Baseline psychological distress, measured by the DASS score, was also significantly greater in the 2000 IU group (24.5±13.71) than in the 1000 IU group (13.25±10.34) (p=0.014). The summary of these baseline characteristics is presented in **Table 1**.

After supplementation, the mean serum 25(OH)D level increased to 24.13±5.28 ng/mL in the 1000 IU group and 28.94±5.86 ng/mL in the 2000 IU group, with a significant difference between groups (p=0.021) (**Table 2**). However, the change in vitamin D levels (Δ) was not significantly different, with a mean increase of 6.44±4.93 ng/mL in the 1000 IU group and 7.19±5.74 ng/mL in the 2000 IU group (p=0.694). Post-intervention salivary cortisol levels

decreased to 1.0 ng/mL (range 0.2–3.2) in the 1000 IU group and 1.91±1.03 ng/mL in the 2000 IU group, without a significant difference (p=0.138). Nonetheless, the reduction in salivary cortisol was significantly greater in the 2000 IU group (median decrease of 9.55 ng/mL, range 1.3–11.6) compared to the 1000 IU group (mean decrease of 4.92±4.29 ng/mL) (p=0.032).

Table 1. Baseline characteristics of the participants

Characteristics	Cholecalciferol		p-value
	1000 IU (n=16)	2000 mg (n=16)	
Age, median (min-max) (years)	58 (55–66)	60.69±4.22	0.240
Body mass index (BMI), mean±SD (kg/cm²)	22.32±1.28	23.78 (18.61–24.98)	0.200
Menopause duration, median (min-max), (years)	7 (3–15)	8 (5–15)	0.263
Salivary cortisol, median (min-max) (ng/mL)	4.65 (0.8–13.3)	11.45 (2.5–14.6)	0.019
25(OH)D, mean±SD (ng/mL)	17.69±5.91	21.75±5.25	0.049
Depression, anxiety, and stress scale (DASS)	13.25±10.34	24.5±13.71	0.014

Regarding psychological outcomes, the mean DASS score after supplementation was 7.31±4.74 in the 1000 IU group and 13.19±7.48 in the 2000 IU group, showing a significant difference (p=0.013). The reduction in DASS scores was also significantly greater in the 2000 IU group (mean decrease of 11.31±6.65) than in the 1000 IU group (median decrease of 3.5, range 0–19) (p=0.022) (**Table 2**).

Table 2. Comparisons between the 25(OH)D, salivary cortisol, and depression, anxiety, and stress scale (DASS) score before and after supplementation

Variables	Cholecalciferol		p-value
	1000 IU (n=16)	2000 IU (n=16)	
25(OH)D, mean±SD (ng/mL)			
After the supplementation	24.13±5.28	28.94±5.86	0.021
Δ Vitamin D	6.44±4.93	7.19±5.74	0.694
Salivary, mean±SD (ng/mL)			
After the supplementation	1 (0.2–3.2)	1.91±1.03	0.138
Δ Saliva Cortisol	4.92±4.29	9.55 (1.3–11.6)	0.032
DASS score			
After the supplementation	7.31±4.74	13.19±7.48	0.013
Δ DASS score	3.5 (0–19)	11.31±6.65	0.022

Discussion

The present study examined the effects of vitamin D supplementation on salivary cortisol and psychological symptoms in postmenopausal women. Both 1000 IU and 2000 IU daily doses effectively increased serum 25(OH)D concentrations, reduced salivary cortisol, and improved DASS scores after one month of supplementation. These findings support the potential role of vitamin D in modulating stress-related physiological and psychological outcomes in postmenopausal women.

Vitamin D deficiency is recognized as a widespread public health issue across diverse populations. Recent global estimates highlight a high prevalence of deficiency among patients with knee osteoarthritis, exceeding 50 % in pooled analyses, underscoring the urgent need for improved screening and supplementation strategies [14]. This broadens the relevance of our findings, as addressing hypovitaminosis D could enhance not only musculoskeletal health but also stress resilience and psychological well-being. Incorporating supplementation in postmenopausal populations may therefore address overlapping risks, including osteoporosis, mood disturbances, and metabolic changes. In addition, a meta-analysis among diabetic patients demonstrated that lower serum vitamin D levels were significantly associated with increased cardiovascular disease risk (p-total<0.001) [15]. This reinforces the concept that vitamin D deficiency affects multiple interrelated health domains and further supports supplementation as a preventive measure in at-risk groups.

In the present study, reductions in salivary cortisol were observed in both supplementation groups, with the 2000 IU dose producing a significantly larger decrease in continuous measures. These findings are consistent with previous evidence that vitamin D may influence hypothalamic–pituitary–adrenal (HPA) axis activity. One proposed mechanism involves the

downregulation of 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1), which converts cortisone to cortisol in adipose and liver tissues. Suppression of this pathway may reduce local cortisol regeneration, contributing to the observed decreases in salivary cortisol, a reliable biomarker of physiological stress [8,16]. Cortisol itself is a well-established marker of psychological distress [12,17].

Psychological symptoms also improved after supplementation, supporting the role of vitamin D in mood regulation. The presence of vitamin D receptors (VDRs) in brain regions involved in emotional processing provides biological plausibility for these effects [17]. On continuous measures, the 2000 IU group showed greater reductions in DASS scores, whereas categorical analyses suggested a trend toward higher normalization in the 1000 IU group. Taken together, these results indicate that while vitamin D supplementation benefits psychological well-being, clear dose superiority cannot be established. Previous reports suggest that factors such as short intervention duration and dose-dependent regulatory effects may contribute to these inconsistent findings [18-24].

The main limitation of this study is the small sample size (n=32), which reduces statistical power and limits the generalizability of the results. Further, the one-month intervention period was relatively short, and longer follow-up may be needed to determine sustained effects of supplementation. Another limitation is the absence of control for potential confounders such as sunlight exposure, dietary intake, physical activity, and psychosocial stressors, all of which can influence vitamin D status and stress responses in postmenopausal women.

Conclusion

Vitamin D supplementation at both 1000 IU and 2000 IU daily effectively increased serum 25(OH)D, lowered salivary cortisol, and improved psychological symptoms in postmenopausal women. Although the 2000 IU dose was associated with greater reductions in continuous measures, the evidence does not establish clear dose superiority. Given the high prevalence of vitamin D deficiency and its association with psychological health in postmenopausal women, supplementation represents a simple and low-cost intervention with broad potential benefits. Further studies with larger samples, longer follow-up, and careful control of confounders are needed to validate these findings and determine the optimal dosing strategy.

Ethics approval

This study received ethical approval from the Ethics Commission of Universitas Sumatera Utara No. 293/KEPK/USU/2025. The authors received hospital approval before performing the data collection. Prior to data collection, all patients were informed about the study objectives and provided written informed consent.

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Competing interests

All the authors declare that there are no conflicts of interest.

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of artificial intelligence use

ChatGPT (OpenAI, San Francisco, CA, USA) was used to improve the clarity, grammar, and flow of the manuscript text. The authors reviewed and take full responsibility for all content.

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