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Sexual function and depressive symptoms in young women with low vitamin D status: a pilot study

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ABSTRACT

Objective: Although vitamin D deficiency is associated with an increased risk of numerous disorders, no previous study has investigated its association with sexual dysfunction. The aim of this study was to investigate female sexual functioning and depressive symptoms in young women with low vitamin D status.

Study design: The study included 14 women with vitamin D deficiency, 14 women with vitamin D insufficiency, as well as 14 matched healthy women. All participants of the study completed questionnaires evaluating female sexual functioning (Female Sexual Function Index – FSFI) and the presence and severity of depressive symptoms (Beck Depression Inventory-Second Edition – BDI-II).

Results: The total FSFI score was lower while the overall BDI-II score higher in women with vitamin D deficiency, but not in women with vitamin D insufficiency, than in healthy subjects. Compared to women with normal vitamin D status, women with vitamin D deficiency were characterized by lower scores for three domains: sexual desire, orgasm and satisfaction, while women with vitamin D insufficiency were characterized by a lower score only for desire. Desire and in women with vitamin D deficiency also orgasm, sexual satisfaction and the overall FSFI score negatively correlated with 25-hydroxyvitamin D levels.

Conclusion: The obtained results indicate that low vitamin D status is associated with abnormal female sexual functioning, the severity of which depends on the degree of vitamin D deficiency.

Introduction

There is an increasing interest in the role of vitamin D as a potential treatment for a number of disorders. Vitamin D is a prohormone that is converted to 25-hydroxyvitamin D by the liver-derived enzyme 25-hydroxylase, and 25-hydroxyvitamin D is then hydroxylated to biologically active calcitriol by kidney-derived 1-hydroxylase [1]. Apart from its favorable effects on calcium and bone metabolism [2], hormonal active form of vitamin D, calcitriol seems to exert pleiotropic effects in various tissues and organs [3,4]. These effects, including the regulation of cellular growth and differentiation, glucose metabolism and immune function [5–7], are mediated through specific receptors, which are present in numerous organs, including the brain, the chest, bones, muscles and the gastrointestinal tract [8]. The results of observational studies suggest that inadequate serum 25-hydroxyvitamin concentrations correlate with increased morbidity and mortality [9]. Vitamin D deficiency is associated with various cardiovascular and metabolic diseases, including hypertension, myocardial infarction, stroke, as well as with type 1 and type 2 diabetes [4,10,11]. Moreover, low vitamin D status is related to several autoimmune diseases, particularly to rheumatoid arthritis, systemic sclerosis and systemic lupus erythematosus, neuromuscular disorders, respiratory infections and cancer [5,7,12]. Observational studies indicate that low vitamin D status may make women more prone to the development of some gynecological and obstetric diseases including polycystic ovary syndrome, gestational diabetes mellitus, preeclampsia, infertility, endometriosis, and breast and ovarian cancer [13].

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To the best of our knowledge, no study has investigated a relationship between sexuality in women and vitamin D status. However, a significant proportion of patients with erectile dysfunction had vitamin D deficiency and that this condition was more frequent in patients with the arteriogenic etiology [14]. Moreover, a significant association between 25-hydroxyvitamin D

Abbreviations: BDI-II, Beck Depression Inventory-Second Edition; FSFI, Female Sexual Function Index; SD, standard deviation.

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deficiency and erectile dysfunction was found in men with type 2 diabetes [15]. Therefore, the aim of this study was to investigate whether low vitamin D status and its severity determines female sexual functioning and depressive symptoms.

Methods and materials

The study population consisted of 28 women (20–40 years old) screened for the presence of thyroid disease, in whom thyroid function tests were within normal limits. Based on serum 25-hydroxyvitamin D levels, these women were divided into three groups. Vitamin D deficiency was diagnosed in 14 women in whom serum 25-hydroxyvitamin D levels were below 20 mg/dL, while vitamin D insufficiency was diagnosed in 14 women with serum 25-hydroxyvitamin D levels in the range between 20 and 30 ng/mL. The control group included 14 age- and weight-matched healthy women with normal vitamin D status defined as serum 25-hydroxyvitamin D levels above 30 ng/mL but less than 75 ng/mL. We also excluded women with any acute or chronic disorder, a history of urogynecological operations that might affect sexual function, pregnant or breastfeeding women, sexually inactive women, as well as women receiving any treatment. The study protocol was approved by the local ethical committee, and all participants were required to provide written informed consent.

Blood samples were taken from the antecubital vein between 8 and 9 a.m. after an overnight 12 h fasting, while all assays were performed in duplicate to minimize analytical errors. All blood samples were collected in January and February to avoid seasonal fluctuations in vitamin D status. Serum levels of 25-hydroxyvitamin D were determined by enzyme immunoassay using reagents obtained from ALPCO Diagnostics (Windham, NH, USA). Soon after that, all participants were asked to fill in a questionnaire assessing their demographic characteristics, marital state, education, general health, medical and sexual history and physical activity, as well as to complete questionnaires investigating their sexual function and depressive symptoms. This means that during completing the questionnaires both participants and researchers were unaware of the vitamin D status of the patient.

The Female Sexual Function Index (FSFI) is a questionnaire addressing all phases of the female sexual cycle, sexual satisfaction and dyspareunia in the previous four weeks and evaluates sexual activity on a five-point scale. The test consists of 19 items divided into six collective domains (subscales): I – sexual desire, II – sexual arousal, III – lubrication, IV – orgasm, V – sexual satisfaction and VI – dyspareunia [16,17]. Each answer is rated from 0 to 5 or 1 to 5 (0 means no sexual activity in the past four weeks). The total FSFI score is obtained from the sum of the items in each domain multiplied by the domain factor (0.6 for desire, 0.3 for arousal and lubrication, and 0.4 for orgasm, satisfaction, and pain). The total score may range from 2.0 to 36.0. Higher scores are suggestive of better sexual function, while total FSFI score less than 26.55 is indicative of sexual dysfunction [16,17].

The presence and severity of depressive symptoms were measured with the Beck Depression Inventory Second Edition (BDI-II), which is a valid and reliable indicator of a depressive state [18]. The questionnaire consists of 21 items, adjusted to correspond with the diagnostic criteria for depressive disorders outlined in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [19]. Each item is rated on a 4-point Likert scale, with higher scores representing greater severity of depression. The total score, which is a sum of the item scores, may range from 0 to 63. The total score of 0–13 is considered minimal range, 14–19 as mild, 20–28 as moderate, and 29–63 as severe depression [18].

Quantitative data were natural log transformed to yield a normal distribution for statistical analyses. Comparisons between the groups were performed using analysis of covariance followed by Bonferroni *post-hoc* tests after consideration of age, smoking, body mass index, blood pressure, marital status, education, occupational activity, type of work, profession, physical activity, as well as stress exposure as potential confounders. The χ^2 test was employed to compare the proportional data. Associations were calculated using Pearson's correlation coefficient (r). Probability values of p below 0.05 was regarded as statistically significant.

Results

There were no significant differences between the study groups in age, smoking, body mass index, waist circumference, education, occupational activity, a type of work, stress exposure, the number and duration of marriages, the number of deliveries, the number of sexual partners and blood pressure. Women with low and normal vitamin D status differed in physical activity (Table 1).

The mean total FSFI score was lower in women with vitamin D deficiency than in women with normal vitamin D status, as well as

Table 1
Baseline characteristics of the study population.

	Vitamin D deficiency	Vitamin D insufficiency	Normal vitamin D status
Number of patients	14	14	14
Age [years; mean (SD)]	31 (4)	32 (4)	30 (5)
Body mass index [kg/m^2; mean (SD)]	27.5 (3.2)	27.2 (2.9)	26.9 (3.1)
Smokers [%]/number of cigarettes a day [n; mean (SD)]/duration of smoking [months, mean (SD)]	29/10 (4)/82	36/12 (5)/88 (30)	29/10 (5)/75 (24)
Physical activity: total/once a week/several times a week/once a month [%]	64/29/21/14**	64/21/29/14**	86/36/43/7
Primary or vocational/secondary/university education [%]	29/43/29	36/36/29	36/43/21
Occupational activity/blue-collar/white-collar/pink-collar workers [%]	86/14/36/36	86/21/29/36	79/21/21/36
Number of sexual partners [n; mean (SD)]	1.9 (1.1)	1.8 (0.7)	1.9 (0.6)
Number of marriages [n; mean (SD)]/duration of marriages [months; mean (SD)]	1.2 (0.6)/72 (28)	1.4 (0.5)/78 (24)	1.3 (0.5)
Number of deliveries [n; mean (SD)]/number of abortions [n; mean (SD)]	1.8 (0.7)/0.6 (0.8)	1.9 (0.7)/0.5 (0.7)	1.8 (0.8)/0.4 (0.5)
Stress exposure [%]	79	79	71
Systolic blood pressure [mmHg; mean (SD)]	124 (12)	122 (13)	120 (14)
Diastolic blood pressure [mmHg; mean (SD)]	78 (8)	76 (7)	75 (8)
25-Hydroxyvitamin D levels [ng/dL; mean (SD)]	12 (4)*,***	25 (3)*	46 (8)

SD – standard deviation.
* $p < 0.001$ *vs.* women with vitamin D insufficiency.
** $p < 0.05$.
*** $p < 0.001$ *vs.* women with normal vitamin status.

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Table 2
Sexual function in young women with low and normal vitamin D status.

Variable	Vitamin D deficiency	Vitamin D insufficiency	Normal vitamin D status
FSFI score [mean (SD)]	30.26 (3.75)*	31.71 (4.01)	34.02 (2.68)
FSFI score ≤26.55 [%]	36**	21	7
Sexual desire [mean (SD)]	4.61 (0.48)***	5.07 (0.39)**	5.69 (0.38)
Sexual arousal [mean (SD)]	5.12 (0.46)	5.34 (0.69)	5.56 (0.55)
Lubrication [mean (SD)]	5.31 (0.63)	5.43 (0.67)	5.70 (0.42)
Orgasm [mean (SD)]	4.92 (0.62)**	5.36 (0.53)	5.73 (0.47)
Sexual satisfaction [mean (SD)]	5.03 (0.47)**	5.26 (0.51)	5.62 (0.40)
Dyspareunia [mean (SD)]	5.27 (0.50)	5.32 (0.64)	5.72 (0.48)

SD – standard deviation.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$ *vs.* women with normal vitamin status; $p < 0.001$ *vs.* women with vitamin D insufficiency.

insignificantly lower in women with vitamin D insufficiency than in control subjects ($p = 0.083$) (Table 2). Sexual dysfunction was found in five subjects (36%) with vitamin D deficiency, three subjects (21%) with vitamin D insufficiency and in one person (7%) with normal vitamin D status. Women with vitamin D deficiency obtained lower scores in three domains (sexual desire, orgasm and sexual satisfaction), while women with vitamin D deficiency only in one domain (sexual desire). There were differences between subjects with vitamin D deficiency and with vitamin D insufficiency in desire (Table 2).

The overall BDI-II score and a percentage of subjects women with total and mild depressive symptoms were higher in subjects with vitamin D deficiency than in control women. Compared to women with normal vitamin D status, women with vitamin D insufficiency had insignificantly higher values of the BDI-II score ($p = 0.062$) (Table 3).

In all study groups, the mean total FSFI score inversely correlated with the total BDI-II score and the number of women with total and mild depressive symptoms (vitamin D deficiency: r values between −0.30 [$p < 0.05$] and −0.49 [$p < 0.001$]; vitamin D insufficiency: r values between −0.31 [$p < 0.05$] and −0.47 [$p < 0.001$]; normal vitamin D status: r values between −0.26 [$p < 0.05$] and −0.40 [$p < 0.001$]). In all groups of patients, the BDI-II score inversely correlated with body mass index (vitamin D deficiency: $r = -0.42$ [$p < 0.001$]; vitamin D insufficiency: $r = -0.46$ [$p < 0.001$]; normal vitamin D status: $r = -0.52$ [$p < 0.001$]). In subjects with low vitamin D status, 25-hydroxyvitamin D levels inversely correlated with physical activity (vitamin D deficiency: $r = -0.40$ [$p < 0.001$]; vitamin D insufficiency: $r = -0.37$ [$p < 0.01$]). In women with vitamin D deficiency, there were negative correlations between serum levels of 25-hydroxyvitamin D and sexual desire ($r = -0.50$ [$p < 0.001$]), orgasm ($r = -0.30$ [$p < 0.05$]) and sexual satisfaction ($r = -0.29$ [$p < 0.05$]). In women with vitamin D insufficiency, circulating levels of 25-hydroxyvitamin D negatively correlated with a domain score for orgasm ($r = -0.38$ [$p < 0.01$]). No other correlations were found.

Comments

In this study, we have found for the first time that low vitamin D status is associated with impaired sexual functioning and that a degree of sexual dysfunction depends on the severity of vitamin D deficiency. Consequently, women with vitamin D deficiency presented worse scores in three domains of FSFI: desire, orgasm and satisfaction, whereas women with vitamin D insufficiency were characterized only by disturbed sexual desire. Based on these observations, we may assume that even in females with 25-hydroxyvitamin D levels below 20 ng/mL, sexual dysfunction is at most moderate. The obtained results are in line with recent studies which showed that low vitamin D status was associated with erectile dysfunction in men [14,15].

The only dysfunction observed in women with low vitamin D status irrespective of its severity was sexual desire. Moreover, a domain score for desire, but not other domain scores, correlated with 25-hydroxyvitamin D levels in women in whom these levels were in the range between 20 and 30 ng/mL while in vitamin D-deficient women inverse correlations with 25-hydroxyvitamin D levels were stronger for sexual desire than for other domain scores of FSFI. Based on these finding we can conclude that hormonal and/or metabolic changes caused by hypovitaminosis D preferentially affects the need to engage in sexual activities. This observation is not surprising in light of our previous studies. Impaired desire was the only sexual dysfunction in women with macroprolactinemia [20], as well as, beyond arousal, the only dysfunction observed in women with subclinical hypothyroidism, irrespective of its nature, as well as in women with euthyroid Hashimoto's thyroiditis [21].

Mechanisms explaining the presence of sexual dysfunction in women with low vitamin D status remain speculative. Low vitamin D status seems to have an unfavorable effect of blood vessels and is regarded as a risk factor for cardiovascular diseases, including hypertension, atherosclerosis, coronary artery disease, stroke, heart failure, dyslipidemia and atrial fibrillation [10,11]. It is also associated with impaired production of nitric oxide secondary to

Table 3
Depressive symptoms in young women with low and normal vitamin D status.

Variable	Vitamin D deficiency	Vitamin D insufficiency	Normal vitamin D status
BDI-II score [mean (SD)]	12.5 (4.5)**	10.0 (3.6)	7.6 (3.0)
Depressive symptoms [*n* (%)]	6 (43)**	3 (21)	1 (7)
Mild symptoms [*n* (%)]	5 (36)*	3 (21)	1 (7)
Moderate symptoms [*n* (%)]	1 (7)	0 (0)	0 (0)
Severe symptoms [*n* (%)]	0 (0)	0 (0)	0 (0)

SD – standard deviation.
* $p < 0.05$.
** $p < 0.01$ *vs.* women with normal vitamin status.

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reduced expression of endothelial nitric oxide synthase [22,23]. In turn, exogenous preparations of this vitamin induce a significant increase in endothelial nitric oxide production [24]. Consequently, in states of its deficiency blood flow through genital organs during the sexual intercourse may be disrupted. Alternatively, low vitamin D status may affect the production of hormones implicated in the regulation of sexual functioning, particularly of testosterone. Loss of sexual desire, as well as the remaining disturbances of female sexual functioning occur more frequently in women with low testosterone levels [25]. In line with this explanation, in a group of healthy women serum 25-hydroxyvitamin D levels correlated with circulating levels of total testosterone and free androgen index [26]. Finally, it cannot be totally excluded that sexual dysfunction is secondary to its effect on nervous system. A recent systematic review and meta-analysis of patients with type 2 diabetes has demonstrated an association between vitamin D deficiency and the development of peripheral neuropathy [27]. Moreover, vitamin D deficiency slightly increased the risk of autonomic neuropathy [28]. Finally, in the central nervous system, vitamin D was found to be involved in the regulation of neuronal excitotoxicity, to reduce oxidative stress, and to play a role in the induction of synaptic structural proteins, neurotrophic factors and neurotransmitters [29].

Vitamin D receptors are widely distributed in areas of the brain, which seem to play a role in the pathogenesis of depression, including the thalamus, hypothalamus prefrontal cortex and hippocampus [30]. Despite contradictory results, according to some authors, the risk of depression depends on vitamin D status [31,32]. In line with this hypothesis, BDI-II score as well as the number of patients with total and mild depressive symptoms were higher in women with vitamin D deficiency than in females with normal vitamin D status. This finding, as well as the presence of correlations between BDI-II and FSFI scores, suggest that impaired sexual functioning and depressive symptoms are reciprocally interrelated, but do not allow to answer the question which of the two is responsible for triggering a vicious circle. However, the fact that correlations between FSFI and BDI-II scores were moderate suggest that the involvement of other factors determining worsened mood in females with vitamin D deficiency. Probably, one of the most important of them is excessive body weight because the total BDI-II score was found to correlate with body mass index. In agreement with this, body mass index inversely correlates with 25-hydroxyvitamin D levels [33]. It is likely that low self-esteem, poor self-image or a tendency toward pessimism or self-recrimination may partially explain the presence of depressive symptoms in patients with 25-hydroxyvitamin D below 20 ng/mL.

The study is not free from some limitations. The main shortcoming is the small sample size and therefore the results of our study need to be confirmed by a larger study. Low serum levels of 25-hydroxyvitamin D levels may be caused by either its decreased synthesis or enhanced degradation, two processes not addressed in our study. Because of seasonal variation in 25-hydroxyvitamin D levels at high latitudes [34], it cannot be ruled out different sexual functioning in subjects recruited at other times of the year. Finally, although well-validated, the utility of FSFI and BDI-II questionnaires is limited by their subjectivity.

In conclusion, our study shows that vitamin D deficiency and insufficiency in women are associated with impaired sexual functioning and depressive symptoms. The magnitude of these disturbances correlates with baseline vitamin D status. It may be supposed that women with vitamin D deficiency or insufficiency benefit from treatment with vitamin D preparations.

Conflict of interest

None declared.

Institutional approval

The study was approved by the Bioethical Committee of the Medical University of Silesia.

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