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The effect of vitamin D on sexual function: A systematic review

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Abstract

Background and Aim: Sexual function is one of the important aspects of human health and quality of life that is affected by various factors. Recently, some evidence reported the relationship between hypovitaminosis and sexual dysfunction, and some studies show the effect of vitamin D supplementation on sexual function. The aim of this study was to evaluate the effect of vitamin D on sexual function in both men and women.

Methods: This systematic review study assessed all clinical trial articles found in search databases (Cochrane, PubMed / Medline, Embase via Ovid, ProQuest, Scopus, and WOS) without language restriction, until 24/01/2022. Article extraction was performed using the Endnote X8.2 software and duplicate titles were excluded. After screening the titles and abstracts, the two researchers independently conducted quality assessments of studies using the Cochran's risk of bias tool and RevMan 5.4 software. Then, the data were extracted by three authors independently using a researcher-made form.

Results: This systematic review, included 8 final articles with a total sample size of 464 (including 217 women and 247 men). Four studies evaluated the effect of vitamin D on male sexual function and 4 studies evaluated the effect of vitamin D on female sexual function. Vitamin D supplementation has been shown in studies to improve both men's and women's sexual function.

Conclusion: In general, the current study's findings show that vitamin D supplementation had a significant positive effect on both men and women's sexual function. More research in larger and more diverse populations, however, is required to establish the definitive causal relationship and the importance of measuring and prescribing vitamin D in the protocol for the diagnosis and treatment of sexual disorders.

Background

Sexual function is an important component of quality of life [1] and is influenced by several factors, including neurologic, vascular, endocrine, and psychological factors [2]. Sexual dysfunction is very common in both men and women, affecting approximately 43% of women and 31% of men [3]. Sexual dysfunction in women includes disorders of sexual desire and arousal, orgasmic disorders, pelvic pain, and penetration disorders, and in men lack of libido, erectile dysfunction, late and premature ejaculation [4, 5]. These sexual problems can negatively affect mood, self-esteem, interpersonal relationships, and life satisfaction leading to decreased quality of life, fertility problems, marital disputes, and even divorce [2, 3]. In sexual dysfunction, normal sexual response is disrupted; sexual response is highly dependent on neuroendocrine and neural activity [6]. Vitamin D is a neurosteroid hormone that plays a role in metabolic and physiological processes of the body [7, 8]. The most important and well-known role of vitamin D is related to calcium homeostasis and bone growth. However, due to the widespread expression of receptors for this vitamin, there are also several non-calcium related effects of this vitamin [1, 9]. In this context, numerous studies have been conducted to investigate the effects of vitamin D deficiency [9]. The results of such studies show that low serum levels of vitamin D increase the risk of certain diseases such as depression, cardiovascular disease, type 2 diabetes, metabolic syndrome and some cancers [7, 8, 10].

Vitamin D receptors are also present in reproductive organs such as the ovaries and uterus [2]. Thus, hypovitaminosis D is associated with an increased risk of obstetric and gynecologic problems such as endometriosis, polycystic ovaries, infertility, gestational diabetes, preeclampsia, and ovarian and breast cancer [11]. On the other hand, recent research has shown that vitamin D is involved in the prevention of vaginal atrophy and the regulation of vaginal epithelial growth and differentiation, and reduces vaginal dryness [8, 12]. Decreased levels of vitamin D in the body may also lead to a decrease in sex hormones, particularly testosterone [13]. Therefore, the possible role of vitamin D in regulating sexual function has been investigated and low vitamin D levels have been shown to be associated with severe sexual dysfunction in both women and men (especially erectile dysfunction)[10, 14]. Deficiency of this vitamin depends on its severity [15]. Despite the special importance of vitamin D for body health, vitamin D deficiency is one of the most common public health problems that has become an undiagnosed epidemic [16]. Today, about one billion people in the world are deficient in vitamin D [17]. The beneficial effects of vitamin D supplements on sexual function have been reported [14]. Because of the high prevalence of vitamin D deficiency and the association between hypovitaminosis D and sexual dysfunction, a number of studies have investigated the effect of vitamin D supplementation on sexual function. One of these studies showed that vitamin D intake improved erectile function in middle-aged men, which was associated with increased serum testosterone levels and had a positive effect on the components of the metabolic syndrome [18]. The result of a clinical trial, also revealed that vitamin D supplementation improves sexual function in women with impaired sexual function and vitamin D deficiency [2].

Because promising results have been reported in studies on the use of vitamin D as a non-hormonal supplement to promote sexual function in men and women, a systematic review is needed to evaluate and summarize the results. Therefore, this study was conducted to "determine the effect of vitamin D on improving sexual function."

Materials And Methods

The present study was conducted as a systematic review with the aim of investigating the effect of vitamin D on sexual function.

Search strategy

To obtain all valuable data, all published and unpublished articles from clinical trials were searched in the international databases Cochrane Central Register, PubMed / Medline via PubMed, Embase via Ovid, ProQuest, Scopus and WOS without language restriction. Data were collected from 01/01/1990 to 24/01/2022. For the search of English sources for each database, words and phrases were selected from specific terms from MeSH and Emtree, including "Sexual Dysfunction", "Sexual Disorder", "Hypoactive Sexual Desire Disorder", "Sexual Aversion Disorder", " "Orgasmic Disorder", "Erectile Dysfunction", "Male Sexual Impotence", "Premature Ejaculation", "Dyspareunia", "Vaginismus", "Vitamin D" and Cholecalciferol, which were combined using the Boolean operator OR and AND. The primary search was performed using some keywords in Medline and Embase. Titles, abstracts and keywords were evaluated. After analysis of the texts, the search was continued using keywords in other sources. To make the search as comprehensive as possible, the search, was performed

manually (hand searching). The final articles related to the topic were evaluated to find other possible sources. Papers presented at national seminars and congresses, national reports and related dissertations were also reviewed.

Inclusion and exclusion criteria based on PICO

This systematic review considered, clinical trials with at least two groups of vitamin D (as intervention group) and standard methods (as comparison group) which have one or more other groups or arms in addition to the above two groups and conducted the intervention in both groups with a parallel or cross-over design. In the intervention and control group, vitamin D was administered as follows:

1. Treatment group: vitamin D3 1,000 IU/ day orally & control group: zinc 12mg/ day for 3 or 12 months in men
2. Treatment group: vitamin D3 100,000 IU/ week orally & control group: tadalafil 5 mg daily for 1 month in men
3. Treatment group: oral solution ergocalciferol 600,000 IU/ 1.5 ml & control group: no medication for 3, 6, 9 and 12 months in men
4. Treatment group: cholecalciferol treatment group 300,000 IU intra muscle injection& control group: placebo for at least 4 to 8 weeks in women
5. Treatment group: vitamin D 4000 IU daily orally & control group: no medication for 6 months in women
6. Treatment group: 1000 IU vitamin D suppository & control group: placebo suppository for 2, 4 and 8 weeks in women
7. Treatment group: vitamin D (300 UI) & control group: isoflavones (40 mg), calcium (500 mg), inulin (3 gr) for 3, 6 and 12 months in women.

A low dose of 1000 units and a high dose of 600000 units were considered. Participants included: All healthy men and women without chronic diseases such as heart disease, kidney disease, diabetes, etc. and without age restriction.

Exclusion criteria included: lack of access to full text, unrelated and duplicate results, experimental studies conducted in animals, nonrandomized clinical trials or clinical trials with an internal control group (before and after designs with only one group), observational studies, reviews, case reports and letters to the editor. Methods of data presentation including analysis and interpretation, problem definition, and data collection were based on the Reporting System for Systematic Reviews (PRISMA).

Outcomes

Primary outcome includes:

The effect of vitamin D consumption on sexual function in men and women.

Secondary outcome includes:

1. The effect of vitamin D consumption on sexual desire of men and women
2. The effect of vitamin D consumption on female sexual arousal
3. The effect of vitamin D consumption on vaginal lubrication
4. The effect of vitamin D consumption on female orgasm
5. The effect of vitamin D consumption on women's sexual satisfaction
6. The effect of vitamin D consumption on female sexual pain
7. The effect of vitamin D consumption on erectile dysfunction
8. The effect of vitamin D consumption on ejaculation disorder (premature ejaculation - late ejaculation)

Selection of studies and Data extraction

In the present study, we used EndNote X8.2 software to integrate the extracted data and exclude duplicate titles, and then the titles and abstracts of all articles screened. Four authors reviewed the inclusion criteria for all relevant eligible studies. Two authors searched the database independently, and other authors assessed the full text of the articles and validated the eligible studies before data extraction. In case of disagreement between authors, the discussion method and an external reviewer were used to reach agreement.

To data extraction, three authors independently extracted the article data by using researcher-made checklist. This checklist includes the following:

1. General characteristics of the article (first author, publication date, year of publication, drug´s name, article code, review date)
2. Type of study (experimental or quasi-experimental clinical trial)
3. Sampling location (hospitals, community, medical centers, clinics, etc.)
4. Number of samples and target group
5. Sample characteristics (demographic, age, gender)
6. Sample collection (sampling location and tools used)
7. Outcome criteria (how to measure the results)

After data collection, 4 author independently assessed the data extraction checklist, and in case of disagreement, an external reviewer was used to reach agreement.

Data analysis

Because the integration of studies is inappropriate, we provide only a qualitative discussion of the results.

Quality assessment

The three authors independently assessed quality assessment using the Cochrane Collaboration Risk of bias and RevMan 5.4. The standard risk of bias instrument is a valid and reliable tool for assessing all randomized clinical trials, regardless of language, time, or place of publication. This instrument consists of six items. These items include: The random and consequence generation, allocation concealment, blinding outcomes assessment, blinding of participant and personnel, selective reporting and incomplete outcome data [19]. Each item was listed in three reports: low bias, high bias, and unclear bias.

Results

In this study, all English-language articles published in electronic databases that were related to the research objective were evaluated. In the first phase, 2132 articles (databases = 2038) and (registers = 94) /one article in manual search) were extracted by primary search. Finally, after excluding duplicate articles, 8 articles were analyzed with a total sample size of 464. (Including 217 women and 247 men). (Table 1). The search was conducted without time limitation. Four studies reported the effect of vitamin D on male sexual function, and 4 studies reported the effect of vitamin D on female sexual function (Tables 1 and 2, respectively). Based on the search of the Cochrane Library database, 7 clinical trial protocols related to the present study were published. After electronic connection with the authors of the correspondence, only one of the authors sent the published article, which was excluded because it did not meet the inclusion criteria.

Table 1. Summary of studies on men's sexual function

Author/year/country/trial design	Participants (T^1/C^2)	Mean age (range)	Trial duration (Weeks or months)	Vitamin D-25OH level (nmol/L)	Intervention vitamin D type, dose, frequency	Co interventions	Outcome measures	Outcome
Ahn et al. 2019 Korea, single-arm pilot study [29]	28 men with erectile dysfunction	65.1 ± 6.5; (54-84)	3 months or 12 months	11.2 ± 3.9 ng/mL	vitamin D3 1,000 IU/day	zinc 12mg/day	IIEF-5[3]	The IIEF-5 score was increased significantly in men with VD deficiency (from 11.2 ± 4.9 to 14.2 ± 5.8, p<0.01), while it does not observe in men without VD deficiency (from 9.3 ± 6.4 to 8.3 ± 4.6, p <0.526).
Culha et al. 2019 Turkey, single-arm study [25]	42 men with erectile dysfunction	51.10 ± 9.71 (31-70)	1 month	-	100,000 IU / week Vitamin D3 oral	tadalafil 5 mg daily	IIEF-EF IPSS[4]	IIEF-EF (pre-treatment: 11.02 ± 5.50, post-treatment:23.00 ± 4.96; p = 0.001) and IPSS (pretreatment: 7.81 ± 5.67, post-treatment: 3.43 ± 1.13; p = 0.003) scores were significantly improved.
Canguven et al. 2017 a prospective, Interventional trial [18]	102 men with deficient serum VD level	53.2 ± 10.4	three, six, nine, and 12 months	Baseline:15.16 ± 4.64 ng/mL 3 m: 31.90 ± 15.99 ng/mL 6 m: 37.23 ± 12.42 ng/mL 9 m: 44.88 ± 14.49 ng/mL 12 m: 48.54 ± 11.62 ng/mL	Ergocalciferol; oral solution 600 000 IU/1.5 ml	-	(IIEF)-5	Serum VD exhibited significant increments from baseline (15.16 ± 4.64 ng/mL) to three (31.90 ± 15.99 ng/mL), six (37.23 ± 12.42 ng/mL), nine (44.88 ± 14.49 ng/mL), and 12 (48.54 ± 11.62 ng/mL) months, and there was significant stepladder increases in both serum TT level (12.46 ± 3.30 to 15.99 ± 1.84 nmol/L) and erectile function scores (13.88 ± 3.96 to 19.85 ± 3.24).

Author/year/country/trial design	Participants (T^1/C^2)	Mean age (range)	Trial duration (Weeks or months)	Vitamin D-25OH level (nmol/L)	Intervention vitamin D type, dose, frequency	Co interventions	Outcome measures	Outcome
Pandey et al. 2021 India, [22]	75 Erectile dysfunction Patients with Vitamin D Deficiency	A: 37.44±10.85 B: 39.08±9.78 C: 37.96±9.66	Baseline, 12 weeks	-	T1: Tadalafil 10mg once a day plus Vitamin D 60,000 IU once a week T2: Vitamin D 60,000 IU once a week only C: Tadalafil 10mg once a day	C: Tadalafil 10mg once a day	IIEF-5	After 12 weeks of treatment, in group C patients, IIEF-5 scoring was nearly same as that of the base line with no significant difference. However, IIEF-5 scoring was significantly improved in group A and B patients (P<0.001). On comparing group A and B patients there was significant improvement in group B compared to group A (P < 0.05).

[1] T= Treatment group

[2] C= Control group

[3] International Index of Erectile Function

[4] International Prostate Symptom Score

Table 2. Summary of studies on women's sexual function

Author/year/country/ trial design	Participants (T[5]/C[6])	Mean age (range)	Trial duration (Weeks or months)	Vitamin D-25OH level (nmol/L)	Intervention vitamin D type, dose, frequency	Co-interventions	Outcome measures	Outcome
Jalali-Chimeh et al. 2019 Iran, randomized, double-blind, placebo-controlled trial [26]	76 women (38/38)	T: 34.9±6.2 C: 35.9±6.7	Baseline, 4 and 8 weeks	14.4 ± 3.2 ng/ml	T: intramuscular injection of 300,000 IU cholecalciferol C: placebo	-	FSFI[7]	The Female Sexual Function Index score was higher in the intervention group at the 4th (19.6 vs. 16.3, P=0.002) and 8th (25.0 vs. 17.1, P <0.001) weeks of the study
Krysiak et al. 2018 Poland, RCT [30]	47 women (16/17/14)	T1: 30±6 T2: 31±5 C: 30±5	Baseline and 6 months	T1: 11±4 ng/dl T2: 24±3 ng/dl C: 24±4 ng/dl	T1: oral vitamin D (4000 IU daily) T2: oral vitamin D (4000 IU daily) C: not receiving vitamin D therapy	-	FSFI	Vitamin D improved sexual desire in women with both vitamin D deficiency and vitamin D insufficiency, increased the total FSFI score and scores for orgasm and sexual satisfaction, and decreased the total BDI-II score, in women with vitamin D deficiency.
Rad et al. 2015 Iran, double-blind clinical trial [24]	44 women (22/22)	T: 54.04±5.2 C:54.38±3.2	Baseline,2, 4 and 8 weeks	-	T: vitamin D suppositories 1000 IU vitamin D C: placebo suppositories	-	VAS[8]	The mean pain significantly reduced after 8 weeks in the treatment group (1.23 ± 0.53) compared to the control group 1.95 ± 0.74 (P < 0.001).
Vitale et al. 2018 Italy, a prospective, randomized, placebo-controlled, parallel-group study [27]	50 menopausal women (25/25)	T: 52.72±4.02 C: 52.48±3.4	Baseline,3 ,6 and 12 months	T: 30.48±5.15 ng/ml C: 31.32±5.46 ng/ml	T: vitamin D (300 UI) C: -	T: isoflavones (40 mg), calcium (500 mg) and inulin (3 g) C: placebo	MENQOL[9] FSFI	After 12 months, sexual domain scores (p<0.05) and a significant increase in all FSFI domain scores (p<0.05) were observed in treatment group.

[5] T= Treatment group

[6] C= Control group

[7] Female Sexual Functioning Index

[8] Visual Analouge Scale

[9] Menopause-Specific Quality of Life Questionnaire

The effect of vitamin D on male sexual function

A randomized trial by Canguven et al (2017) reported the effect of vitamin D supplementation on improving sex hormones, metabolic syndrome, and erectile dysfunction in 102 middle-aged men with vitamin D deficiency. Erectile dysfunction status was assessed with the International Erectile Function Index (IIEF-5) at baseline and then at 3, 6, 9 and 12 months after the intervention. Vitamin D was administered as ergocalciferol at a dose of 600,000 units in 1.5 ml. The results of this study showed that with the administration of vitamin D, serum levels of vitamin D, testosterone, and erectile function index increased significantly (P < 0.001) [18].

Ahn et al (2019) reported the efficacy of vitamin D and zinc supplements for erectile dysfunction in a single arm study. In this study, 28 men with erectile dysfunction received 1000 units of vitamin D and 12 units of zinc daily as dietary supplement for 12 weeks. The International Erectile Performance Index (IIEF-5) was used to assess erectile dysfunction status at baseline and then 12 weeks after the intervention. The results of this study showed that 67.9% of patients were vitamin D deficient and the mean vitamin D level at baseline was 11.2 ± 3.9 ng/ml. In patients with vitamin D deficiency, the IIEF-5 score increased significantly with vitamin D and zinc supplementation (p < 0.01), whereas this change was not significant in the group with normal vitamin D levels [20].

In the study by Culha et al (2019), conducted with the aim of investigating the effect of vitamin D supplementation on sexual dysfunction as a single-arm study, 42 men with erectile dysfunction were studied. These men received oral vitamin D supplementation of 100,000 units per week for 4 weeks; in addition

to the vitamin D supplementation, they received 5 mg of oral tadalafil tablets. The International Erectile Dysfunction Index (IIEF-5) and the International Score of Prostate Symptoms (IPSS) were used to assess the erectile dysfunction status at baseline and then 4 weeks after the intervention. The results of this study showed that one month after taking vitamin D, the IIEF-5 and IPSS improved significantly ($p = 0.001$ and $p = 0.003$, respectively) [21].

In the study by Ali et al (2021), which aimed to evaluate the efficacy of vitamin D supplementation in erectile dysfunction patients with vitamin D deficiency, 75 patients in the age group of 20 to 60 years had severe vitamin D deficiency and erectile dysfunction. They were randomly divided into three groups. The first group (A) with tadalafil 10 mg once a day, the second group (B) tadalafil 10 mg once a day with vitamin D 60,000 international units once a week and the third group (C) vitamin D 60,000 units was given only once a week. The efficacy of the drugs was assessed at baseline and after 12 weeks based on the IIEF-5. After 12 weeks of treatment, the IIEF-5 value in group C patients was almost the same as the baseline value and there was no significant difference. On the other hand, the IIEF-5 score improved significantly in patients in group A and B ($P < 0.001$). When patients in groups A and B were compared, significant improvement was observed in group B compared with group A ($P < 0.05$) [22].

The effect of vitamin D on female sexual function

In a double-blind clinical trial by Jalali-Chimeh et al (2019), aimed at investigating the effect of vitamin D on female sexual function, 76 women in the intervention and control groups (38 in each group) were studied. The Female Sexual Function Index (FSFI) was used at baseline, and 4 and 8 weeks after the intervention. The intervention group received 300,000 units of vitamin D (intramuscular injection) and the control group received placebo. Female sexual function index score in the intervention group were significantly higher at 4 and 8 weeks after the intervention ($P = 0.002$ and $P < 0.001$, respectively [2].

Krysiak et al (2018) conducted a study in the Netherlands to investigate the effect of vitamin D supplementation on sexual function and depressive symptoms in young women with low vitamin D levels. This study was conducted in three groups: The first group consisted of 16 women with vitamin D deficiency (serum vitamin D level below 20 ng/ml) who received vitamin D supplementation at a dose of 400,000 units per day, the second group consisted of 17 women with insufficient vitamin D level (serum vitamin D level 20–30 ng/ml) who received vitamin D supplementation at a dose of 400,000 units per day and the third group includes 14 women with insufficient vitamin D level who did not receive any supplementation. To assess the women's sexual function, the Female Sexual Performance Index (FSFI) was used at baseline and 6 months after the intervention. Results showed that the FSFI total score and scores in the three domains of libido, orgasm, and sexual satisfaction were lower in women with vitamin D deficiency than in women with inadequate vitamin D levels. Vitamin D supplementation improved libido in both intervention groups and increased total FSFI score, orgasm, and sexual satisfaction in vitamin D deficient women ($P < 0.05$) [11].

The study by Vitale et al (2018) aimed to determine the effect of isoflavone, calcium, vitamin D, and inulin on improving quality of life, sexual function, and metabolic parameters in postmenopausal women as a randomized controlled trial with two parallel groups. In this study, 50 postmenopausal women were studied in two intervention groups (300 units of vitamin D, 40 mg of isoflavones, 500 mg of calcium, and 3 g of inulin) and one control group (placebo). Sexual function was assessed using Female Sexual Performance Index (FSFI) at baseline, and 3, 6, and 12 months after the intervention. The results showed that scores on all domains of the sexual function index and its total score had increased after the intervention ($P < 0.05$) [23].

A double-blind study by Rad et al (2015) examining the effect of vitamin D on vaginal atrophy in postmenopausal women was conducted with 44 women who had been menopausal for at least one year. In this study, vitamin D was administered at a dose of 1000 units in the vaginal suppository intervention group and placebo in the control group for 8 weeks (every night for the first 2 weeks, and every night in between for the next 6 weeks). The visual analog scale (VAS) was used to assess the degree of pain during intercourse before the intervention and at the end of 2, 4, and 8 weeks after the intervention. In this study, the mean score of pain during intercourse was significantly lower in the intervention group than in the placebo group ($p = 0.001$) [24].

Quality Assessment Report

The assessment of the quality of the studies is based on the Review Manager program (RevMan 5.3), which presents the quality of the studies in Fig. 2. Selection bias in 5 articles was low risk [18, 25–28], and 3 article was unclear [25, 29, 30]. Performance bias was low risk in 4 articles [18, 26–28], high risk in 3 article [25, 30, 31]and unclear in 1 articles [29]. The process of key individuals blinding was low risk in 3 articles [26–28], high risk in 3 articles [18, 25, 29], and unclear in 2 article [30, 31]. Detection bias was low-risk in 5 articles [26–28, 30, 31] and unclear in 3 articles [18, 25, 29]. Attrition bias was low risk in 6 studies [18, 26–28, 30, 31] and unclear in 2 study [25, 29], and all of predetermined outcomes were reported [18, 25–31]. Other biases were unclear in 6 studies [18, 25, 26, 28–31] and low risk in 1 studies [27].

Discussion

The aim of this systematic review was to determine the effects of vitamin D on sexual function. The study included seven articles with a total sample size of 389 subjects (including 217 women and 172 men) after a thorough search of six electronic databases and screening of obtained articles. Studies have shown that vitamin D supplementation can improve sexual function in both sexes. Three studies, including those by Canguven et al. (2017), Ahn et al. (2019), and Culha et al. (2019), examined the effect of vitamin D on erectile function, and according to their results, vitamin D supplementation improved the International Index of Erectile Function [18, 20, 21]. Previous research has shown that vitamin D deficiency is significantly higher in patients with erectile dysfunction and that low vitamin D levels may increase the risk of erectile dysfunction due to endothelial system dysfunction. Endothelial dysfunction impairs nitric oxide bioavailability, decreases vasodilation, and causes atherosclerotic lesions in the vessel wall, making it an important biological risk factor for erectile dysfunction [32]. Vitamin D deficiency, in turn, may impair erectile function by increasing the risk of cardiovascular disease and being associated with obesity, diabetes, dyslipidemia, and hypertension [10].

In addition, studies have shown that vitamin D levels have a direct effect on testosterone levels, and vitamin D receptors are found in the testes, hypothalamus, and pituitary gland [10]. In a clinical study, vitamin D supplementation was found to be associated with higher blood testosterone levels [33]

and this may play a role in improving erectile function in men after vitamin D administration. On the other hand, arterial calcification, which is one of the risk factors for erectile dysfunction, is strongly inversely related to serum vitamin D levels. Therefore, calcification is more pronounced in people with low vitamin D levels, and this factor may also play a role in the frequency and severity of erectile dysfunction in these people [34].

Overall, the results show that serum vitamin D levels and male sexual function are correlated and vitamin D supplementation is effective in improving erectile function. Therefore, it is recommended that serum vitamin D levels also be assessed when evaluating sexual dysfunction in men [10]. Studies on the effect of vitamin D on female sexual function have also shown positive effects of this supplement on improving sexual function. In the experimental studies of Jalali-Chimeh et al (2019), Krysiak et al (2018) and Vitale et al (2018), daily administration of 300, 400, and 300,000 units of vitamin D, respectively, improved the scores obtained from the female sexual function index (FSFI) [2, 11, 23]. There are several mechanisms that could explain such an effect. A study on the role of vitamin D in regulating estrogen synthesis in the gonads in animals revealed that hypovitaminosis D disrupts one or more components of the hypothalamic-pituitary-ovarian axis. Mice with VDR (Vitamin D receptor) gene mutations had lower aromatase gene expression, abnormal estradiol production, uterine hypoplasia, and follicular damage. According to the findings of this study, normal levels of vitamin D are required for the proper functioning of the gonads in both sexes [35]. There is also evidence that testosterone levels are lower in women with sexual dysfunction [36]; and laboratory studies have shown that 1,25 (OH) 2D3 significantly alters the expression of genes involved in reproduction and increases human testosterone synthesis [37]. As a result, by increasing this hormone, vitamin D can influence sexual function and, in particular, sexual desire.

The local effects of vitamin D on the vaginal surface as a functional sexual organ of women, on the other hand, should be considered. A recent systematic review found that vitamin D consumption increases the growth and proliferation of vaginal epithelial cells, modulates vaginal pH, and reduces vaginal dryness in postmenopausal women [12]. In this regard, Rad et al. (2015) discovered that a vitamin D vaginal suppository protects the vaginal squamous epithelium. Furthermore, in the group that used vitamin D vaginal suppository, the rate of superficial cells of the vaginal epithelium increased from 10 to 68 cells, and vaginal dryness decreased by about 26% [24]. As a result, the local role of vitamin D in improving vaginal conditions to prepare for sexual intimacy should not be overlooked when explaining the causes of vitamin D's positive effect on women's sexual function.

In addition, if we want to analyze the findings from a psychological standpoint, we must refer to the findings of a systematic review and meta-analysis in this field: Anglin et al. (2013) discovered a correlation between serum levels. Low vitamin D levels have been linked to depression and the severity of symptoms [7]; additionally, a population-based cohort study of 1282 people in the Netherlands found that depression and its severity are directly and significantly linked to a decrease in serum 25 (OH) D levels [38]. However, evidence suggests that depression, as well as the majority of its medications (antidepressants), play a significant role in the development of sexual dysfunction in women [39, 40]. As a result, the importance of psychological factors should not be overlooked. One of the limitations of the current study was the heterogeneity of the studies, which precluded meta-analysis, but one of its strengths is that it considers the effect of vitamin D on both female and male sexual function and its sub-domains.

Conclusion

In general, the current study's findings show that vitamin D supplementation had a significant positive effect on both men and women's sexual function. More research in larger and more diverse populations, however, is required to establish the definitive causal relationship and the importance of measuring and prescribing vitamin D in the protocol for the diagnosis and treatment of sexual disorders.

Availability of data and materials

Not applicable.

Abbreviations

RevMan: Review Manager Program; VAS: Visual pain Scale; FSFI: Female Sexual Function Index; IIEF: International Erectile Dysfunction Index; IPSS: International Score of Prostate Symptoms

Declarations

Availability of data and materials

Not applicable.

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Authors' contributions

MB, TD, VGH and BM contributed to the concept, design, drafting the article and acquisition of data. The search strategy was developed by MB and VGH and it was verified by NR and TD. The eligibility criteria were decided upon by TD, NR and LM. MB, TD and FD extracted the data and appraised the quality of the

included studies. LM, VGH and NR resolved any disagreements. MB, TD, VGH and NR developed the first draft of the manuscript, and BM, LM, FD, and VM contributed to the revisions of the manuscript. All the authors provided critical comments for revision and approved the final version of the manuscript.

Ethics approval and consent to participate

The Ethical Committee of Hormozgan University of Medical Sciences approved this research. All the following procedures were approved by the above-mentioned committee.

Consent for publication

The consent form for publication is filled by the authors.

Competing interests

The authors declare that they have no competing interests.

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Figures

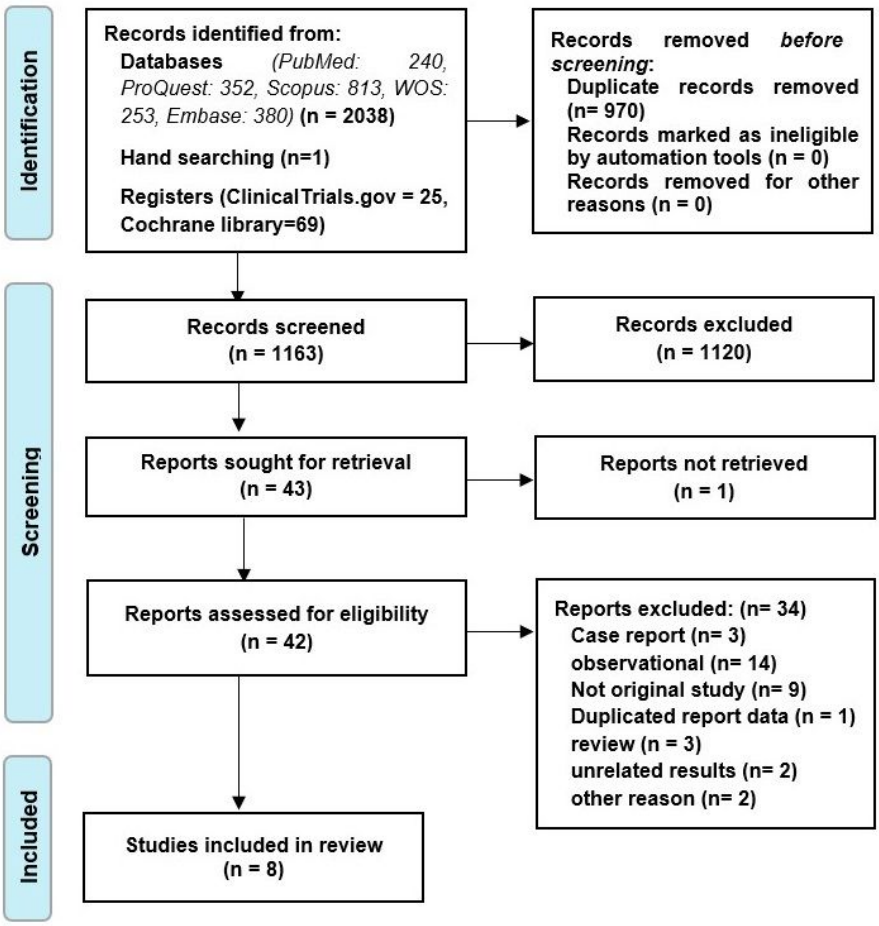

Figure 1

flowchart for selection of studies (PRISMA 2020)

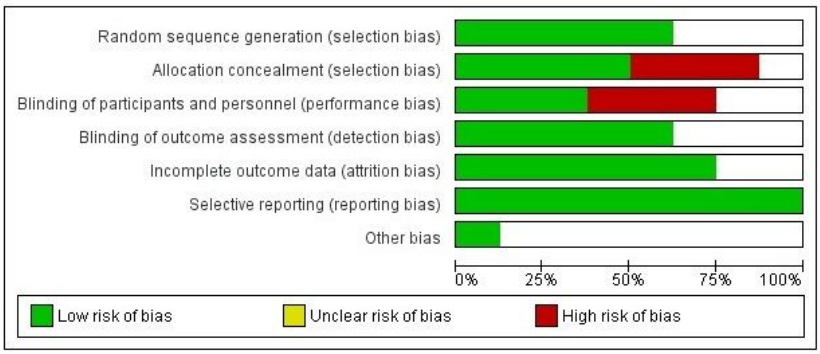

Figure 2

Risk of bias assessment

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