International Urogynecology Journal
https://doi.org/10.1007/s00192-021-04963-z

REVIEW ARTICLE

The effect of vitamin D deficiency and supplementation on urinary incontinence: scoping review

Ronnie Baer [1] · Lea Tene [1] · Adi Y. Weintraub [2] · Leonid Kalichman [1]

Received: 14 April 2021 / Accepted: 27 July 2021

Abstract

Introduction and hypothesis Vitamin D receptors are found in skeletal and smooth muscle cells throughout the body, specifically in the bladder detrusor muscle. We reviewed the current literature on the association between vitamin D deficiency and urinary incontinence (UI), and whether vitamin D supplementation plays a role in the treatment of UI symptoms.

Methods We performed a scoping review of all available studies. PubMed, Google Scholar, and PEDro databases were searched from inception until August 2020 with the keywords "urinary incontinence," "pelvic floor disorders," "lower urinary tract symptoms," "overactive bladder," and various terms for vitamin D. No language restrictions were imposed. The reference lists of all retrieved articles were also searched.

Results The search revealed 12 studies of different research methodologies after elimination. In 6 out of the 7 cross-sectional studies reviewed, a significant association between vitamin D deficiency or insufficiency and the onset and severity of UI was found. In 2 out of the 3 prospective studies included, no association between vitamin D intake and UI was found; however, both randomized controlled trials that were reviewed found that vitamin D supplementation is effective for the treatment of UI.

Conclusions The existing literature supports an association between low levels of serum vitamin D and UI. Initial evidence regarding the effect of vitamin D supplementation on UI is accumulating, yet additional, comprehensive research is warranted to establish these findings.

Keywords Urinary incontinence · Stress incontinence · Urge incontinence · Vitamin D · Review

Introduction

Urinary incontinence (UI) is a medical disorder defined as an involuntary loss of urine. Between 24% and 45% of women and between 1% and 39% of men report that they have suffered from some degree of UI, at some period in their life. The main known risk factors for UI in women are pregnancy, childbirth, increased body mass index, menopause, and type 2 diabetes. In men, urinary tract infections and cystitis, previous stroke, and prostate surgery are associated with an increased risk for UI. The prevalence of UI increases with age for both genders [1–3]. Race and ethnicity also affect the prevalence of UI, with Black non-Hispanic women reporting UI less than other ethnicities. No significant difference was found between different ethnic groups in men.

The implications of UI for quality of life (QoL) are extensive and may include depression, anxiety, impaired sexual function, avoidance of social interactions, and in severe cases, even loss of independence [4]. Furthermore, UI has substantial economic ramifications from both a societal and a patient perspective [5].

Recently, it has been suggested that one of the factors that might contribute to the incidence of UI is vitamin D deficiency. Vitamin D is a group of fat-soluble secosteroids responsible for increasing intestinal absorption of calcium, magnesium, and phosphate, and has many other biological effects. Vitamin D is available from the diet or skin synthesis; however, it is biologically inactive. It becomes activated after it undergoes two steps of hydroxylation, in the liver and in the kidneys [6, 7]. Vitamin D status is identified through measurement of serum

✉ Lea Tene
leatene1@gmail.com

[1] Department of Physical Therapy, Recanati School for Community Health Professions, Faculty of Health Sciences, Ben-Gurion University of the Negev, P.O.B. 653, 84105 Beer Sheva, Israel

[2] Department of Obstetrics and Gynecology, Soroka University Medical Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel

Published online: 07 September 2021

vitamin D. Vitamin D deficiency is considered as serum vitamin D levels of <20 ng/ml, insufficiency is considered as levels ranging between 20 and 30 ng/ml, and normal levels of vitamin D are considered to be >30 ng/ml [8].

Vitamin D receptors are found in skeletal and in smooth muscle cells [9] throughout the body, and specifically in the bladder detrusor muscle [10]. Vitamin D deficiency or insufficiency affects muscle strength, volume, and overall function [11]. In addition, vitamin D supplementation has a positive impact on muscle strength in various populations [12–14]. The possible effect of vitamin D on the detrusor muscle and on the levator ani muscles, which contain both smooth and striated muscle fibers, could explain the association between vitamin D deficiency and UI [10]. Morelli et al. [10] have demonstrated that a vitamin D receptor agonist can regulate calcium entry through L-type Ca2+ channels in the human bladder smooth muscle cells. This suggests a possible effect of the vitamin D receptor agonist on the modulation of bladder contractile mechanisms [10].

Vitamin D deficiency is recognized as a global epidemic. Nevertheless, the prevalence differs in different parts of the world owing to limited sun exposure due to cultural practices, dress codes, culinary habits, climate changes, and prolonged breastfeeding [15]. Even in Middle Eastern countries, despite ample sunshine, studies have shown a surprisingly high incidence of vitamin D deficiency [16–19].

It is not clear whether an association exists between the geographic variability of UI and vitamin D deficiency.

We reviewed the current literature on the association between vitamin D deficiency and UI. Moreover, we investigated the role of vitamin D supplementation in the treatment of UI symptoms.

Materials and methods

PubMed, Google Scholar, and Physiotherapy Evidence Database (PEDro) were searched without search limitations from inception until August 2020 using keywords relating to UI, and various terms for vitamin D (vitamin D; vitamin D2; vitamin D3; 1-alpha hydroxyvitamin D3; 1-alpha hydroxycalciferol; 1,25-dihydroxyvitamin D3; 1,25-dihydroxycholecalciferol; 25 hydroxycholecalciferol; 25-hydroxyvitamin D; hypovitaminosis D; alfacalcidol; calcidiol; calcitriol; calcifediol; calciferol; ergocalciferol; cholecalciferol), or a combination of these terms.

Criteria for inclusion were studies of any design and methodological quality dealing with the effect of vitamin D deficiency or supplementation on UI. No language restrictions were imposed. The reference lists of all included articles were also searched. After the elimination of duplicates, the titles and abstracts of all articles were reviewed. Articles concerning the correlation between vitamin D deficiency or insufficiency and UI, and articles regarding the effect of vitamin D supplementation on urinary incontinence were defined as potentially relevant. Full texts of potentially relevant papers were read, and their reference lists searched for additional relevant articles. Twenty articles met search terms. After excluding all irrelevant papers, a total of 12 publications were included in this review. The study design types that were included are randomized control trials, prospective studies, retrospective studies, and cross-sectional studies. All published material was critically analyzed.

Results

Association between vitamin D deficiency or insufficiency and UI

The association between vitamin D deficiency or insufficiency and UI has been examined in five cross-sectional studies and one prospective study (Tables 1 and 2). Two of the cross-sectional studies evaluated whether low levels of vitamin D are associated with lower urinary tract symptoms (LUTS) in men [20], and with pelvic floor disorders (PFDs) in women [21]. In both studies, all data were drawn from the 2005–2006 National Health and Nutrition Examination Survey, using a sample size of 2,387 men [20] and 1,881 women [21] from the USA. LUTS were defined through questions on nocturia, difficulty emptying, hesitancy, and incontinence. PFD was defined through questions on pelvic organ prolapse, fecal incontinence, and UI. Incontinence severity was evaluated by the Incontinence Severity Index (ISI)—two questions from the NHANES regarding frequency and amount of leakage.

In men, vitamin D insufficiency was defined as a serum vitamin D (25(OH)D) level of 20–30 ng/ml and vitamin D deficiency as a 25(OH)D level of <20 ng/ml. In women, vitamin D insufficiency was defined as a 25(OH)D level of 10–30 ng/ml and vitamin D deficiency as a 25(OH)D level of <10 ng/ml. Vitamin D levels were measured by the DiaSorin radioimmunoassay (RIA) method. Vaughan et al. [20] found that there was a nonsignificant trend toward an association between vitamin D deficiency and moderate to severe UI and that the presence of at least one LUTS in men correlated with vitamin D deficiency (p = 0.007). Badalian and Rosenbaum [21] found that lower levels of vitamin D were associated with an increased risk for PFD in women (p = 0.043). Moreover, a decreased risk of UI was found if vitamin D levels were within the normal range (at least 30 ng/ml; p = 0.022).

Another cross-sectional study assessed whether low levels of serum vitamin D correlates with UI symptoms in adult women [22]. Korean women over the age of 20 were evaluated (n = 6,451). UI was determined by a single question: “Do you have current UI?”. Vitamin D level was divided into three categories: <20 ng/ml, 20–30 ng/ml, and > 30 ng/ml. Vitamin

Table 1 Characteristics of the studies reviewed

Reference	Design	Participants (*N*)	Participants (special characteristics)	Age	Sex, females (*N*)	Vitamin D deficiency and insufficiency definition	Vitamin D consumption method
Vaughan et al. [20]	Cross-sectional	2,378	–	≥20	0	Insufficiency 20–30 ng/ml Deficiency < 20 ng/ml	– –
Badalian & Rosenbaum [21]	Cross-sectional	1,881	Nonpregnant	≥20	1,881	Insufficiency 10–30 ng/ml Deficiency < 10 ng/ml	– –
Lee and Lee [22]	Cross-sectional	6,451	–	≥20	6,451	Insufficiency 20–30 ng/ml deficiency <20 ng/mL	– –
Li et al. [23]	Cross-sectional	2,671	–	≥40	0	Deficiency <20 ng/ml	–
Stafne et al. [24]	Cross-sectional	851	Mid-pregnant	30.5 ± 4.4	851	Insufficiency <20 ng/ml	–
Vaughan et al. [25]	Prospective	350	Community-dwelling older adults	73.6 ± 5.8	175	Insufficiency 20–30 ng/ml Deficiency <20 ng/ml	– –
Parker-Autry et al. [26]	Retrospective	394	–	>19	394	Insufficiency 15–29 ng/ml Deficiency < 15 ng/mL	– –
Dallosso et al. [27]	Prospective	5,816	–	≥40	5,816	–	Diet
Vaughan et al. [28]	Prospective	33,133	Suffering from mild/moderate UI	42–73	33,133	–	Diet + oral supplement
Markland et al. [29]	Prospective	73,291	Not suffering from UI	40–71	73,291	–	Diet + oral supplement
Digesu et al. [30]	RCT	Treatment group 1 (87) Treatment group 2 (84) Control group (86)	Suffering from OAB symptoms	55.1	257	–	Oral supplement
Oberg et al. [31]	RCT	Treatment group (134) Control group (139)	Post-menopausal, low bone density	50–80	273	–	Oral supplement

RCT randomized control trial, *UI* urinary incontinence

D levels were measured by RIA. Low serum vitamin D levels were not found to be independently associated with UI.

Vitamin D deficiency and UI in obese and non-obese men

Li et al. [23] investigated factors that may be associated with UI in obese and non-obese adult men from the USA. A total of 2,671 men participated in the study. To determine whether the subjects suffer from UI, each subject answered two questions: the first regarding stress UI and the second regarding urge UI. Subjects who responded "yes" to one or both questions were then evaluated using the ISI, to measure the severity of the condition. A 25(OH)D level of <20 ng/ml was defined as vitamin D deficiency. Vitamin D levels were measured by RIA. Vitamin D deficiency was found to be associated with urge UI in non-obese men ($p < 0.05$). In obese men, no statistically significant association between vitamin D deficiency and UI was found.

Vitamin D insufficiency and UI in pregnant women

A recent cross-sectional study by Stafne et al. [24] evaluated the association between UI and insufficient levels of vitamin D in 851 European, mid-trimester pregnant women (mean age 30.5 ± 4.4). UI was evaluated using the ISI. Participants with 25(OH)D <20 ng/ml were defined as having vitamin D insufficiency. Vitamin D levels were measured using the Electrochemiluminescence Immunoassay method. Vitamin D insufficiency was found to be associated with UI (p = 0.03), particularly stress UI (p = 0.01).

Vitamin D insufficiency and UI in older adults

One prospective study examined whether vitamin D status is associated with UI in community-dwelling older adults from the USA [25]. Three hundred and fifty participants (175 male, mean age 73.6 ± 5.8) were evaluated for the incidence of UI

Table 2 Studied variables and findings

Study	Outcome measures	Findings
Vaughan et al. [20]	Incontinence Severity Index Questions on nocturia, difficulty emptying, hesitancy, and UI	Association between at least one LUTS and vitamin D deficiency, $p = 0.007$
	Serum vitamin D level	
Badalian & Rosenbaum [21]	Incontinence Severity Index Questions on pelvic organ prolapse, fecal incontinence, and UI	Association between increased risk of PFD and lower levels of vitamin D, $p = 0.043$
	Serum vitamin D level	Decreased risk of UI if vitamin D levels are within the normal range, $p = 0.022$
Lee and Lee [22]	Single question regarding the existence of UI Serum vitamin D level	No association between UI and serum vitamin D level
Li et al. [23]	Questions regarding stress and urge UI Serum vitamin D level	Association between urge UI and vitamin D deficiency in non-obese men, $p < 0.05$
Stafne et al. [24]	Incontinence Severity Index Serum vitamin D level	Association between increased risk of UI and vitamin D insufficiency, $p = 0.03$
Vaughan et al. [25]	Incontinence Severity Index Serum vitamin D level	Association between the incidence of UI and vitamin D insufficiency, $p = 0.03$
Parker-Autry et al. [26]	Incontinence Impact Questionnaire 7 Pelvic Floor Distress Inventory Short-Form 20	Association between the greater impact of UI on QoL and vitamin D deficiency, $p = 0.001$
	Medical, Epidemiologic, and Social Aspects of Aging Questionnaire	
	Serum vitamin D level	
Dallosso et al. [27]	OAB symptoms questionnaire Food Frequency Questionnaire	Association between reduced risk of OAB onset and high consumption of vitamin D, $p = 0.008$
Vaughan et al. [28]	NHS questionnaire Food Frequency Questionnaire	No association between progression of UI symptoms and vitamin D consumption
	Vitamin D supplementation self-report	
Markland et al. [29]	NHS questionnaire Food Frequency Questionnaire	No association between progression of UI symptoms and vitamin D consumption
	Vitamin D supplementation self-report	
Digesu et al. [30]	Vital signs Laboratory blood tests	No effect on bladder volume at the first involuntary detrusor contraction
	24-h urine collection Electrocardiography	Improved Patient's Perception of Bladder Condition scores ($p = 0.02$)
	Urodynamic parameters	
	3-day bladder diary Urgency Perception Scale	Decreased frequency of incontinence episodes ($p = 0.02$)
	Patient's Perception of Bladder Condition	
Oberg et al. [31]	LUTS questionnaire from the EPINCONT study	The level of serum vitamin D increased more in the high-dose group than in the standard-dose group ($p < 0.01$)
	Serum vitamin D level	Reduced reported severity of UI in the high-dose group in comparison with the standard-dose group ($p < 0.05$)

LUTS lower urinary tract symptoms, *NHS* Nurses' Health Study, *OAB* overactive bladder, *PFD* pelvic floor disorder, *UI* urinary incontinence

for up to 42 months, every 6–12 months. UI was assessed using the ISI. Vitamin D insufficiency was defined as a 25 (OH)D level of 20–30 ng/ml and vitamin D deficiency as a 25 (OH)D level <20 ng/ml. Vitamin D levels were measured by the IDS-iSYS analyzer. Cumulative incidence of UI at 42 months was found to be associated with vitamin D insufficiency ($p = 0.03$) and presented a nonsignificant trend toward vitamin D deficiency ($p = 0.07$).

Vitamin D insufficiency and UI impact on quality of life

Parker-Autry et al. [26] assessed the effect of vitamin D levels and PFD severity on QoL among adult women. To do so, a retrospective electronic health record review was conducted on 394 women from the USA. To evaluate the impact of PFD severity on quality of life, several questionnaires were used. One questionnaire was the Incontinence Impact Questionnaire, which was developed to assess the effect of UI on activities of daily living in women. Another questionnaire was the Pelvic Floor Distress Inventory Short-Form 20 (PFDI-SF-20), which was used to assess the distress of lower urinary and gastrointestinal tract dysfunction symptoms in women. The PFDI-SF-20 is divided into three subscales: the Urinary Distress Inventory, the Pelvic Organ Prolapse Distress Inventory, and the Colorectal–Anal Distress Inventory. Vitamin D insufficiency was defined as a 25(OH)D level of 15–29 ng/ml and vitamin D deficiency as a 25(OH)D level of < 15 ng/ml. Vitamin D levels were measured using liquid chromatography. Vitamin D insufficiency was found to be significantly associated with a greater impact of UI on QoL ($p = 0.001$).

Vitamin D supplementation for the treatment of UI

The effect of vitamin D consumption or supplementation on UI has been investigated in three prospective studies and two randomized control trials (RCTs; Tables 1, 2).

Dietary vitamin D and overactive bladder

One prospective study examined the association between the nutrient composition of a diet and overactive bladder (OAB) symptoms [27]. The study included 5,816 community-dwelling women from the UK, 40 years old or above. All participants answered a postal baseline questionnaire including questions regarding OAB symptoms and a food frequency questionnaire. OAB was defined as suffering from leakage of urine, urge to urinate, or both at least several times a month. It was determined by the following questions: “Do you have such a strong desire to pass urine that you leak before reaching the toilet?” and “When you need to pass urine, how strong is the urge usually?” The food frequency questionnaire contained questions on the frequency of consumption of 130 food and beverage items. The postal baseline questionnaire was sent again to all participants 1 year later. High consumption of vitamin D was correlated negatively with OAB onset ($p = 0.008$).

Supplementation of vitamin D and UI

Two recent prospective studies were aimed at determining whether vitamin D supplementation is associated with the progression of UI [28] and the development of UI [29] in women. In both studies, all data were drawn from the Nurses' Health Study (NHS) I and II, in which female registered nurses from the USA responded to mailed questionnaires regarding their medical history and lifestyle. Vaughan et al. [28] used a sample of 20,560 women from the NHSI and 12,573 women from the NHSII. Markland et al. [29] used a sample of 38,101 women from the NHSI and 35,190 women from the NHSII. Questionnaires were sent every 2 years, over 8 years. To assess vitamin D intake, the NHS questionnaires included questions about multi-vitamin dose and brand/type supplement. Additionally, once every 4 years participants answered the food frequency questionnaire. UI was initially assessed using the following question: “During the past 12 months, how often have you leaked or lost control of your urine?” Women who reported leakage or loss of control were also asked about the amount of leakage to determine the severity of the condition and about dominant symptoms to classify UI into subtypes. After multivariate adjustment, Vaughan et al. [28] found no significant association between vitamin D consumption and the progression of UI symptoms. Likewise, Markland [29] found no association between vitamin D intake and the development of UI.

Elocalcitol for the treatment of OAB

A 2012 RCT evaluated the safety and efficacy of treatment of OAB and idiopathic detrusor overactivity with Elocalcitol—a synthetic vitamin D3 analog, administered orally [30]. A total of 308 women suffering from OAB and idiopathic detrusor overactivity were recruited from 48 tertiary referral centers around Europe. Participants were randomly allocated to three groups and received either oral elocalcitol 75 mcg/day, oral elocalcitol 150 mcg/day, or oral placebo (ratio 1:1:1), for 4 weeks. The safety of the drug was assessed by measuring vital signs, laboratory blood tests, 24–h urine collection, and electrocardiography. The efficacy of the treatment was evaluated by urodynamic parameters, a 3-day bladder diary, the Urgency Perception Scale, and the Patient’s Perception of Bladder Condition. The efficacy of elocalcitol was not demonstrated on bladder volume at the first involuntary detrusor contraction, which was defined as the primary endpoint of the study. The bladder volume at first sensation to void in participants treated with elocalcitol increased in comparison with participants who received a placebo, yet results were not statistically significant. However, the frequency of incontinence episodes significantly decreased ($p = 0.02$), and the Patient’s Perception of Bladder Condition scores improved significantly ($p = 0.02$) in the elocalcitol groups, compared with the control group. No efficacy differences were found between the 75 mcg/day and the 150 mcg/day groups.

High-dose vitamin D supplementation for the treatment of LUTS

In an RCT, Oberg et al. [31] examined the effect of high-dose vitamin D3 supplementation on LUTS in post-menopausal women with low bone mineral density. In the study, 297 women aged 50–80 years were recruited from the research unit in the University Hospital of North Norway and randomly assigned to two groups: a standard-dose group and a high-dose group. Participants in both groups received

500 mg of calcium and 400 IU (10 mcg) of vitamin D to be taken twice daily. In addition, the high-dose group received another capsule containing 20,000 IU (500 mcg) of vitamin D, and the standard-dose group received a placebo capsule to be taken twice a week. Participants took the pills for 12 months. Blood samples were taken from participants every 3 months and analyzed for serum vitamin D levels. Participants filled out a questionnaire regarding LUTS from the EPINCONT study at baseline and at the end of the study. In the high-dose group, levels of serum vitamin D increased significantly more than in the standard-dose group ($p < 0.01$). In addition, a significant reduction in the reported severity of UI was found in the high-dose group, compared with the standard-dose group ($p < 0.05$).

Discussion

Most evidence presented in this review indicates that serum vitamin D levels correlate with the onset and worsening severity of UI. One study found no correlation between vitamin D levels and UI [22]; however, this study is of low methodological quality. Risk factors for UI are diverse and include cognitive, mental, and metabolic comorbidities, medical history, habits, and environmental factors [1, 32]. This makes isolating the effect of vitamin D levels alone very difficult. As a result, although the findings of the studies mentioned are mostly conclusive and support the association between vitamin D levels and UI, they should be treated cautiously.

Regarding the effect of vitamin D consumption and supplementation on UI, the results are less decisive. Out of three prospective studies [27–29], only one found an association between vitamin D intake and UI. The findings of these studies are based solely on self-reported questionnaires; this method of data collection could lead to biased results as self-reported questionnaires could be inaccurate. In addition, vitamin D absorption varies between different individuals, and serum vitamin D is not measured in the studies mentioned. Therefore, the findings of these studies should be interpreted with caution. Two RCTs found a significant improvement in UI because of vitamin D supplementation [30, 31]: Oberg et al. [31] found that the vitamin D dose had a significant effect on UI, whereas Digesu et al. [30] found a similar improvement in the standard-dose and high-dose groups. This discrepancy could be explained by the fact that the doses administered were closer in the study conducted by Digesu et al. [30] than in the study by Oberg et al. [31].

A limitation of this review is that as this was not a systematic review and because we were interested in the idea and proof of concept, we did not evaluate the quality of the studies presented. Most of the studies included were observational and would have received a low-quality rating.

Furthermore, it should be considered that a narrative review per se can be the source of bias by the methodology of this type of review, and our conclusions should be read with caution.

After the association between serum vitamin D and UI has been established, more high-quality RCTs should be conducted to further understand the effect of vitamin D intake on UI. Several factors must be considered in future studies. First is the study population—none of the previous studies that examined the effect of vitamin D consumption and supplementation on UI had male participants; therefore, their conclusions cannot be applied to males. We suggest including male subjects in the future, especially because several studies found that vitamin D deficiency is associated with UI in men [20, 23, 25]. A second factor is the type of vitamin D supplement used. The two types of vitamin D that are commonly administered are vitamin D2 and vitamin D3. Vitamin D3 and elocalcitol, which is a vitamin D3 analog, were the vitamin D preparations that were used in the RCTs previously presented. This choice could be based on previous animal studies, which found that vitamin D3 supplementation had a positive effect on rats suffering from bladder outlet obstruction [33] and that elocalcitol can suppress signs of detrusor overactivity in rats and mice [34]. Moreover, vitamin D3 was found to be significantly more effective than vitamin D2 in raising serum vitamin D levels [35]. In the future, we suggest comparing the effectivity of vitamin D3 and vitamin D3 analogs in UI treatment. Another factor that should be addressed in future studies is the dose of vitamin D supplements for the treatment of UI, which has not yet been determined. A fourth factor is the effect of climate, seasonal changes, and sun exposure on UI, as skin exposure to solar radiation is the main source of vitamin D [36]. However, the prevalence of vitamin D deficiency differs in different parts of the world owing to limited sun exposure due to cultural practices, dress codes, culinary habits, climate changes, and prolonged breastfeeding [15]. Even in countries such as those in the Middle East, despite ample sunshine, studies have shown a surprisingly high incidence of vitamin D deficiency [16, 17].

Conclusions

Urinary incontinence is a common condition affecting both men and women worldwide and has a major impact on the QoL. Most current evidence supports the association between vitamin D deficiency/insufficiency and UI. Based on the results of the studies presented in this review, vitamin D supplementation seems to play a role in the treatment of UI. Therefore, screening patients with UI for vitamin D deficiency should be considered. Vitamin D supplementation is cheap and safe and may assist in the prevention and treatment of UI. High-quality studies are needed to further investigate the effect of vitamin D supplementation on UI in men, and to establish the most efficient vitamin D type and dose.

Abbreviations IU, International units; LUTS, Lower urinary tract symptoms; NHS, Nurses' Health Study; OAB, Overactive bladder; PFDs, Pelvic floor disorders; RCT, Randomized control trial; RIA, Radioimmunoassay; UI , Urinary incontinence; 25(OH)D, Serum vitamin D

Contributions R. Baer: article conception and design, data collection, draft manuscript preparation;L. Kalichman: article conception and design, critical revising of the manuscript, project supervision;A.Y. Weintraub: draft manuscript preparation, critical revising of the manuscript;L. Tene: article conception and design, critical revising of the manuscript, project advising. All authors reviewed the results and approved the final version of the manuscript.

Funding The study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declarations

Conflicts of interest None.

Ethics approval Ethical review board approval was not needed.

References

1. Buckley BS, Lapitan MCM. Prevalence of urinary incontinence in men, women, and children—current evidence: findings of the Fourth International Consultation on Incontinence. Urology 2010;76(2):265–70.
2. Jackson SL, Scholes D, Boyko EJ, Abraham L, Fihn SD. Urinary incontinence and diabetes in postmenopausal women. Diabetes Care 2005;28(7):1730.
3. Aune D, Mahamat-Saleh Y, Norat T, Riboli E. Body mass index, abdominal fatness, weight gain and the risk of urinary incontinence: a systematic review and dose–response meta-analysis of prospective studies. BJOG. 2019;126(12):1424–33.
4. Farage MA, Miller KW, Berardesca E, Maibach HI. Psychosocial and societal burden of incontinence in the aged population: a review. Arch Gynecol Obstet. 2008;277(4):285–90.
5. Coyne KS, Wein A, Nicholson S, Kvasz M, Chen C-I, Milsom I. Economic burden of urgency urinary incontinence in the United States: a systematic review. J Manag Care Pharm. 2014;20(2): 130–40.
6. Bikle DD. Vitamin D metabolism, mechanism of action, and clinical applications. Chem Biol. 2014;21(3):319–29.
7. Norman AW. From vitamin D to hormone D: fundamentals of the vitamin D endocrine system essential for good health. Am J Clin Nutr. 2008;88(2):491s–9s.
8. Holick MF. Vitamin D status: measurement, interpretation, and clinical application. Ann Epidemiol. 2019;19(2):73–8.
9. Girgis CM, Clifton-Bligh RJ, Hamrick MW, Holick MF, Gunton JE. The roles of vitamin D in skeletal muscle: form, function, and metabolism. Endocr Rev. 2013;34(1):33–83.
10. Morelli A, Squecco R, Failli P, et al. The vitamin D receptor agonist elocalcitol upregulates L-type calcium channel activity in human and rat bladder. Am J Physiol Cell Physiol. 2008;294(5):C1206–C14.
11. Aspell N, Laird E, Healy M, Lawlor B, O'Sullivan M. Vitamin D deficiency is associated with impaired muscle strength and physical performance in community-dwelling older adults: findings from the English Longitudinal Study Of Ageing. Clin Interv Aging. 2019;14:1751–61.
12. Beaudart C, Buckinx F, Rabenda V, et al. The effects of vitamin D on skeletal muscle strength, muscle mass, and muscle power: a systematic review and meta-analysis of randomized controlled trials. J Clin Endocrinol Metab. 2014;99(11):4336–45.
13. Garcia M, Seelaender M, Sotiropoulos A, Coletti D, Lancha AH Jr. Vitamin D, muscle recovery, sarcopenia, cachexia, and muscle atrophy. Nutrition. 2019;60:66–9.
14. Tomlinson PB., Joseph C, Angioi M. Effects of vitamin D supplementation on upper and lower body muscle strength levels in healthy individuals. A systematic review with meta-analysis. J Sci Med Sport. 2015;18(5):575–80.
15. Salman S, Khouzami M, Harb M, Saleh B, Boushnak MO, Moussa MK, Mohsen ZH. Prevalence and predictors of vitamin D inadequacy: a sample of 2,547 patients in a Mediterranean country. Cureus. 2021;13(5):e14881.
16. Gannagé-Yared MH, Chemali R, Yaacoub N, Halaby G. Hypovitaminosis D in a sunny country: relation to lifestyle and bone markers. J Bone Miner Res. 2000;15(9):1856–62.
17. Gannagé-Yared MH, Maalouf G, Khalife S, et al. Prevalence and predictors of vitamin D inadequacy amongst Lebanese osteoporotic women. Br J Nutr. 2009;101(4):487–91.
18. Lips P, Hosking D, Lippuner K, et al. The prevalence of vitamin D inadequacy amongst women with osteoporosis: an international epidemiological investigation. J Intern Med. 2006;260(3):245–54.
19. El-Hajj Fuleihan G, Nabulsi M, Choucair M, et al. Hypovitaminosis D in healthy schoolchildren. Pediatrics. 2001;107(4):E53.
20. Vaughan CP, Johnson TM 2nd, Goode PS, Redden DT, Burgio KL, Markland AD. Vitamin D and lower urinary tract symptoms among US men: results from the 2005–2006 National Health and Nutrition Examination Survey. Urology. 2011;78(6):1292–7.
21. Badalian SS., Rosenbaum PF. Vitamin D and pelvic floor disorders in women: results from the National Health and Nutrition Examination Survey. Obstet Gynecol. 2010;115(4):795–803.
22. Lee HS, Lee JH. Vitamin D and urinary incontinence among Korean women: a propensity score-matched analysis from the 2008–2009 Korean National Health and Nutrition Examination Survey. J Korean Med Sci. 2017;32(4):661–5.
23. Li D, Xu Y, Nie Q, Li Y, Mao G. Predictors of urinary incontinence between abdominal obesity and non-obese male adults. Postgrad Med. 2017;129(7):747–55.
24. Stafne SN, Mørkved S, Gustafsson MK, et al. Vitamin D and stress urinary incontinence in pregnancy: a cross-sectional study. BJOG. 2020;127(13):1704–11.
25. Vaughan CP, Tangpricha V, Motahar-Ford N, et al. Vitamin D and incident urinary incontinence in older adults. Eur J Clin Nutr. 2016;70(9):987–9.
26. Parker-Autry CY, Markland AD, Ballard AC, Downs-Gunn D, Richter HE. Vitamin D status in women with pelvic floor disorder symptoms. Int Urogynecol J. 2012;23(12):1699–705.
27. Dallosso HM, McGrother CW, Matthews RJ, Donaldson MMK, Leicestershire MRC Incontinence Study Group. Nutrient composition of the diet and the development of overactive bladder: a longitudinal study in women. Neurourol Urodyn. 2004;23(3):204–10.
28. Vaughan CP, Markland AD, Huang AJ, Tangpricha V, Grodstein F. Vitamin D intake and progression of urinary incontinence in women. Urology 2021;150:213–8.
29. Markland AD, Vaughan C, Huang A, Tangpricha V, Grodstein F, et al. Vitamin D intake and the 10-year risk of urgency urinary incontinence in women. J Steroid Biochem Mol Biol. 2020;199: 105601.

30. Digesu GA, Verdi E, Cardozo L, Olivieri L, Khullar V, Colli E. Phase IIb, multicenter, double-blind, randomized, placebo-controlled, parallel-group study to determine effects of elocalcitol in women with overactive bladder and idiopathic detrusor overactivity. Urology. 2012;80(1):48–54.
31. Oberg J, Verelst M, Jorde R, Cashman K, Grimnes G. High dose vitamin D may improve lower urinary tract symptoms in post-menopausal women. J Steroid Biochem Mol Biol. 2017;173:28–32.
32. Linde JM, Nijman RJM, Trzpis M, Broens PMA. Urinary incontinence in the Netherlands: prevalence and associated risk factors in adults. Neurourol Urodyn. 2017;36(6):1519–28.
33. Schröder A, Colli E, Maggi M, Andersson K-E. Effects of a vitamin D3 analogue in a rat model of bladder outlet obstruction. BJU Int. 2006;98(3):637–42.
34. Shapiro B, Redman TL, Zvara P. Effects of vitamin D analog on bladder function and sensory signaling in animal models of cystitis. Urology. 2013;81(2):466.e1–7.
35. Tripkovic L, Lambert H, Hart K, et al. Comparison of vitamin D2 and vitamin D3 supplementation in raising serum 25-hydroxyvitamin D status: a systematic review and meta-analysis. Am J Clin Nutr. 2012;95(6):1357–64.
36. Saraff V, Shaw N. Sunshine and vitamin D. Arch Dis Child. 2016;101(2):190–2.