



# The effect of vitamin D on urgent urinary incontinence in postmenopausal women

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## Abstract

**Introduction and hypothesis** Conflicting results have been reported on the effect of vitamin D supplementation on urinary incontinence (UI). Therefore, the aim of this study was to evaluate the effect of consuming vitamin D oral supplements on improving urge UI (UUI) in postmenopausal women with vitamin D deficiency.

**Methods** This randomized clinical trial was conducted in 2019–2020 in postmenopausal women with UUI or nocturia more than once at night with vitamin D levels less than 30 ng/ml. After recording the severity of UI and its impact on the patient's daily life, patients were randomly divided into two groups of 45 patients: one taking vitamin D<sub>3</sub> (50,000 IU) tablets and one taking placebo weekly for 8 weeks.

**Results** There was no significant difference between the two groups in terms of the severity of UI and the frequency of nocturia before treatment. However, after treatment, in the vitamin D group, the severity of UI and the frequency of nocturia significantly reduced. Before treatment, the impact of UI on patients' daily life was reported to be high in more than 70% of patients in both groups, which was not significantly different; however, after treatment, its impact was significantly reduced in the vitamin D group.

**Conclusions** The findings of the present study showed that in postmenopausal women with UUI or nocturia, weekly use of vitamin D 50,000 IU tablets for 8 weeks can reduce the severity of UI and the frequency of nocturia, and reduce their impact on disruption in daily life.

**Keywords** Menopausal women · Urge urinary incontinence · Vitamin D

## Introduction

Lower urinary tract symptoms (LUTS) are symptoms related to urinary retention and urination, which include incontinence, the urgency to urinate, and waking up at night to urinate [1], occurring in approximately 30–50% of peri- and postmenopausal women [2, 3]. LUTS cause problems for the person, impose costs on society [4], and causes depression, anxiety, and reduced quality of life in individuals [4, 5].

Treatment of urinary incontinence (UI) in elderly patients is a challenge owing to some factors, including lifestyle and behavioral pattern modification, and drug therapies are associated with possible complications [6]. These drugs may

incur a heavy cost to the patient that will only allow her to continue treatment for a limited time [7, 8]. Considering all these issues, it is important to consider new treatments that may affect the factors involved in the development of UI and reduce the likelihood of drug side effects.

Vitamin D receptors at the level of many cells in the body play a regulatory role in the function of organs. These receptors are found in the detrusor muscles and the striated muscles of the bladder. Vitamin D appears to reduce the sense of urgency to urinate and improve urgency UI by regulating smooth muscle growth and bladder wall stroma [9, 10].

On the other hand, in the menopausal period, vitamin D deficiency is common for various reasons, such as a decrease in 7-dehydrocholesterol levels in the skin, an increase in body fat density with age, a decrease in the bioavailability of vitamin D, which is a fat-soluble vitamin, and a decrease in alpha 1-hydroxylase activity in the kidneys. It has also been shown that the improvement in muscle strength with the use of vitamin D supplementation at serum levels less than 30 nmol/l has been greater and more effective [11].

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Some studies have shown a higher prevalence of UI among the elderly, with low serum levels of vitamin D [12, 13] and other studies have examined the effect of vitamin D supplementation on urinary problems in the elderly [14, 15]. However, the results of the studies are contradictory, in some cases, its effect on improving the patient's symptoms has been mentioned, whereas in others, this effect has not been proven. Therefore, the aim of this study was to evaluate the effect of consuming oral vitamin D supplements in comparison with the placebo in improving urge UI (UUI) in postmenopausal women with vitamin D deficiency.

## Materials and methods

This randomized clinical trial was performed in 2019–2020 on postmenopausal women aged 50 to 80 years who were referred to the obstetrics and gynecology clinic of Mahdih Hospital, Tehran. Patients with incontinence or nocturia more than once at night, from whom a complete medical, pharmacological, and surgical history and complete examinations (height, weight, BMI, and pelvic examination), were obtained, requesting tests, including urinalysis, fasting blood sugar (in the absence of blood glucose testing in the last 3 years) and vitamin D levels, if their serum vitamin D levels were less than 30 ng/ml and did not meet the exclusion criteria, they were included in the study. Exclusion criteria were underlying diseases that led to impaired vitamin D absorption, such as inflammatory bowel disease, a history of gastric bypass surgery, chronic liver or kidney disease, neurological disorders that affect the urinary system, such as multiple sclerosis, neurogenic bladder, degenerative muscular disorders, a history of CVA and spinal cord injury, uncontrolled diabetes, a history of chronic cough or chronic constipation, a history of vesicovaginal fistula, consuming estrogen or progesterone supplements in the last month, urinary tract infection, severe vaginal prolapse (grades 3 and 4, cystocele and apical), and treatment with diuretics. Written consent was obtained from the patients. The study was ethically approved by the ethics committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.RETECH.REC.1399.435) and was registered on the Iran Clinical Trials registration website (IRCT20200417047109N1).

Out of 116 patients studied, 14 patients did not meet the inclusion criteria and 5 patients did not want to participate in the study. Finally, 97 patients were randomly divided into two groups, including vitamin D ( $n=48$ ) and placebo ( $n=49$ ), and finally, 45 patients in each group completed the study (Fig. 1).

After obtaining the patient's consent to participate in the study, patient data, including age, BMI, and vitamin D levels were recorded at baseline. Then, the severity of UI was measured and recorded using the Modified LUTS

EPINCONT questionnaire. In the questionnaire, there are two questions about the severity of UI. How often (less than once a month, one or more times in month, one or more times in week, and every day or night) and its amount (a few drops or more). According to grading, the first question is scored from 1 to 4 and the second question is scored 1 or 2. From the sum of the two scores, the intensity of UI is divided into mild (1–2), moderate (3–4), and severe (5–6). The patient was also asked about the frequency of nocturia and the impact of incontinence and nocturia on the patient's daily life (low or high) and this was recorded on the form. Then, the patients were divided into two groups based on a random number table. In one group, patients took 50,000 IU of vitamin D<sub>3</sub> tablets made by Zahravi Company, Iran, and in another group, patients took a placebo pill, which was made mainly from starch and similar to vitamin D tablets without an active ingredient. Patients received drugs weekly for 8 weeks. After 8 weeks, the patients' serum vitamin D levels were measured again. Also, the status of incontinence and its severity, nocturia and its frequency, as well as their impact on the patient's daily life, were recorded again. Patients' satisfaction with treatment and sense of improvement and change in symptoms were asked using a five-point Likert scale from (very satisfied) to (very dissatisfied) and recorded on the form. Finally, the rate of change in the severity of UI, the frequency of nocturia, and their impact on the patient's daily life, as well as patients' satisfaction with treatment, of the two groups were compared. During the treatment period, the patients were monitored for medication use and side effects by phone call.

The software SPSS 25 was used for data analysis. Qualitative variables were described using frequency and percentage and quantitative variables were described using mean and standard deviation. The Chi-squared, independent, and paired *t* test, McNemar test, and Marginal Homogeneity test were used to analyze the data. A *p* value <0.05 was considered a significant level.

## Results

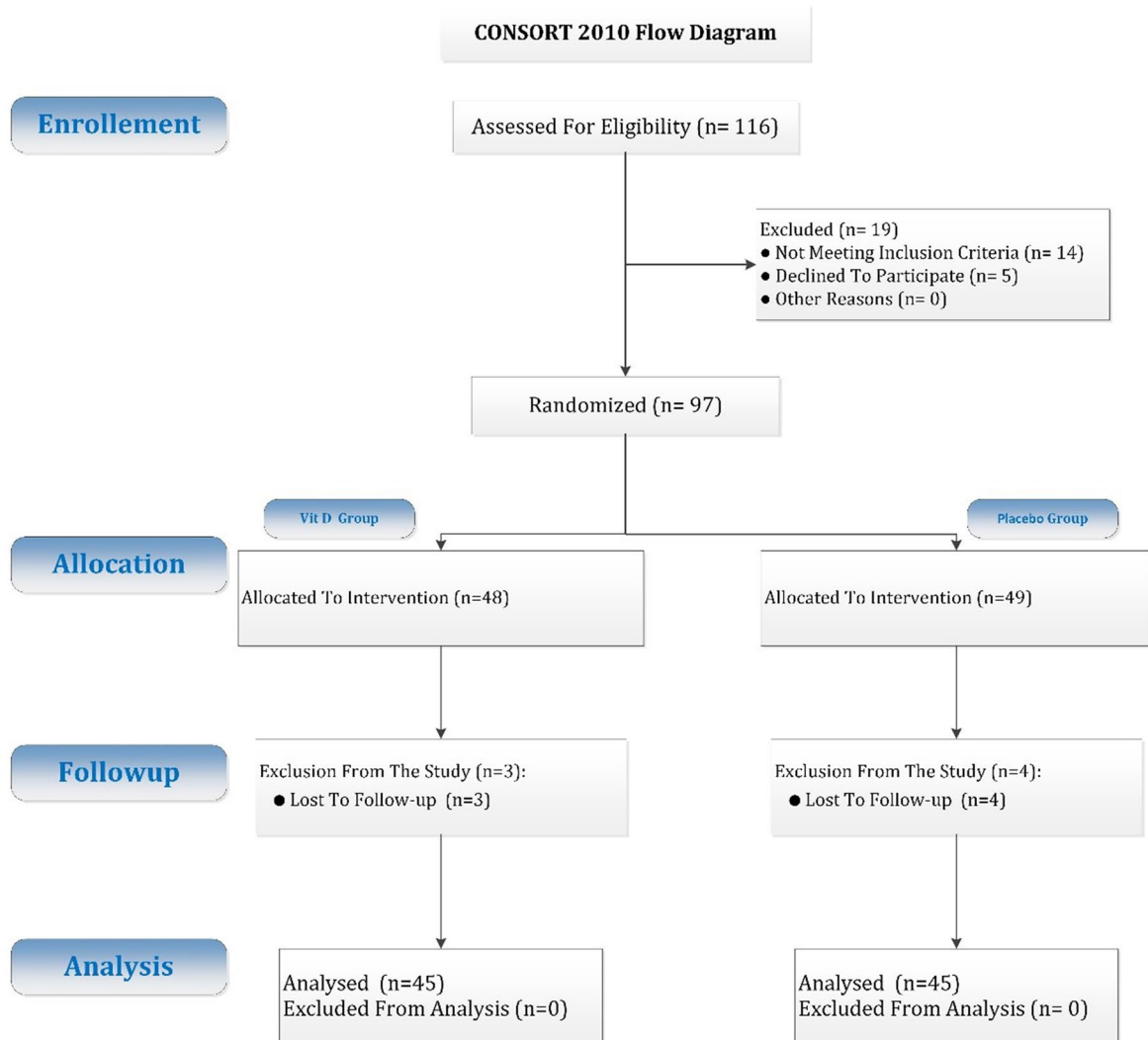
### Age and BMI

The range and mean (SD) of the age of patients were 50–69 years and  $57 \pm 5$  years respectively, which was not significantly different between the vitamin D and placebo groups ( $58 \pm 5$  years and  $57 \pm 5$  years,  $p=0.889$  respectively). Also, the range and mean (SD) of patients' BMI were 22.2–40 kg/m<sup>2</sup> and  $28.9 \pm 4.1$  kg/m<sup>2</sup> respectively, which was not significantly different between the two groups of vitamin D and placebo ( $29.1 \pm 4.5$  kg/m<sup>2</sup> and  $28.8 \pm 3.5$  kg/m<sup>2</sup> respectively,  $p=0.697$ ).



# CONSORT

TRANSPARENT REPORTING of TRIALS



**Fig. 1** Consolidated Standards of Reporting Trials (*CONSORT*) algorithm of the study

### Vitamin D levels

There was no significant difference in the vitamin D levels in patients before treatment between the two groups, but after treatment, vitamin D levels in the vitamin D group were significantly higher than in the placebo group (Table 1). No complications were reported.

### Urinary incontinence severity

There were no significant differences in the severity of pre-treatment UI between the two groups ( $p=0.371$ ). After treatment, the severity of UI was significantly lower in the vitamin D group ( $p<0.001$ ), whereas in the placebo group, it was not significantly changed ( $p=0.083$ ). A comparison of the severity

**Table 1** Comparison of vitamin D levels in the two groups before and after treatment

Vitamin D level (ng/ml)	Vitamin D group (n=45)	Placebo group (n=45)	<i>p</i> value**
Pre-treatment	21.1±3.6	21.7±3.3	0.427
Post-treatment	30.3±2.4	21.4±3.4	<0.001
<i>p</i> value* (pre- and post-treatment comparison)	<0.001	0.118	–

\*Paired *t* test; \*\*independent *t* test

of UI after treatment between the two groups also showed a significant reduction in the severity of UI in the vitamin D group compared with the placebo ( $p=0.010$ ; Table 2).

### Nocturia frequency

There was no significant difference in the pre-treatment nocturia frequency between the two groups ( $p=0.318$ ). After treatment, the frequency of nocturia significantly reduced in the vitamin D group ( $p<0.001$ ), whereas in the placebo group, it was not significantly changed ( $p=0.102$ ). A comparison of the frequency of nocturia after treatment between the two groups also showed a significant reduction in the vitamin D group compared with the placebo group ( $p<0.001$ ; Table 3).

**Table 2** Severity of urinary incontinence

Severity of urinary incontinence	Vitamin D group (n=45)			Placebo group (n=45)			<i>p</i> value***	<i>p</i> value****
	Pre-treatment	Post-treatment	<i>p</i> value*	Pre-treatment	Post-treatment	<i>p</i> value**		
Mild	1 (2%)	14 (31%)	<0.001	2 (4%)	4 (9%)	0.082	0.371	0.010
Moderate	35 (78%)	26 (58%)		29 (65%)	28 (62%)			
Severe	9 (20%)	5 (11%)		14 (31%)	13 (29%)			

\*Marginal homogeneity test, pre- and post-treatment comparison in the vitamin D group, \*\*marginal homogeneity test, pre- and post-treatment comparison in the placebo group, \*\*\*Chi-squared test, pre-treatment comparison between the vitamin D and placebo groups, \*\*\*\*Chi-squared test, post-treatment comparison between vitamin the D and placebo groups

**Table 3** Frequency of nocturia

Frequency of nocturia	Vitamin D group (n=45)			Placebo group (n=45)			<i>p</i> value***	<i>p</i> value****
	Pre-treatment	Post-treatment	<i>p</i> value*	Pre-treatment	Post-treatment	<i>p</i> value**		
0–1	5 (11%)	27 (60%)	<0.001	5 (11%)	8 (18%)	0.102	0.318	<0.001
2	27 (60%)	16 (36%)		19 (42%)	17 (38%)			
3	11 (25%)	2 (4%)		19 (42%)	18 (40%)			
4 or more	2 (4%)	0 (0%)		2 (4%)	2 (4%)			

\*Marginal homogeneity test, pre- and post-treatment comparison in the vitamin D group, \*\*marginal homogeneity test, pre- and post-treatment comparison in the placebo group, \*\*\*Chi-squared test, pre-treatment comparison between the vitamin D and placebo groups, \*\*\*\*Chi-squared test, post-treatment comparison between the vitamin D and placebo groups

### Impact on daily life

The impact of nocturia and UI on daily life showed no significant difference between the two groups before treatment ( $p=0.814$ ). After treatment, its impact was significantly reduced in the vitamin D group ( $p<0.001$ ), whereas in the placebo group, it did not change significantly ( $p=0.500$ ). A comparison of the impact on the patients' daily life after treatment between the two groups also showed a significant decrease in the vitamin D group compared with the placebo group ( $p<0.001$ ; Table 4).

### Satisfaction with treatment

Satisfaction with treatment in the vitamin D group was significantly higher than in patients in the placebo group (Table 5).

### Discussion

The findings of the present study showed that in postmenopausal women with complaints of UUI or nocturia, weekly consumption of 50,000 IU of vitamin D<sub>3</sub> tablets for 8 weeks can reduce the severity of UI and the frequency of nocturia and reduce their impact on disruption in daily life. It also provides a high level of treatment satisfaction.

**Table 4** Impact on patients' daily life

Impact on patients' daily life	Vitamin D group (n=45)			Placebo group (n=45)			p value***	p value****
	Pre-treatment	Post-treatment	p value*	Pre-treatment	Post-treatment	p value**		
Low	13 (29%)	34 (76%)	<0.001	12 (27%)	14 (31%)	0.500	0.814	<0.001
High	32 (71%)	11 (24%)		33 (73%)	31 (69%)			

\*McNemar test, pre- and post-treatment comparison in the vitamin D group, \*\*McNemar test, pre- and post-treatment comparison in the placebo group, \*\*\*Chi-squared test, pre-treatment comparison between the vitamin D and placebo groups, \*\*\*\*Chi-squared test, post-treatment comparison between the vitamin D and placebo groups

Although some studies have suggested a role for vitamin D in patients with urinary or pelvic problems, especially in the elderly, the therapeutic role of vitamin D in urinary problems has been less frequently studied in clinical trials. In their clinical trial, Digesu et al. reported that the incidence of UI episodes was significantly reduced in the elocalcitol group compared with the placebo group, and this combination of vitamin D was an effective and tolerable drug for the treatment of women with overactive bladder and idiopathic detrusor over-activity. Their study had three groups: control, elocalcitol (75 g per day), and elocalcitol (150 g per day) for a period of 4 weeks [16]. Vaughan et al. studied the relationship between vitamin D levels and UI in older adults and reported that of 187 patients who lacked UI at baseline, 57% were deficient in vitamin D (25(OH)D <20 ng/ml) and 24% had insufficient vitamin D levels (25(OH)D 20–30 ng/ml). Also, 175 of these patients were followed for 42 months, and UI occurred in 37% of them. Therefore, the authors stated that the development of UI in the future is associated with insufficiency or deficiency of vitamin D and it is necessary to conduct studies in this field [17]. In a randomized, controlled study on 297 postmenopausal women with low bone density, Oberg et al. divided participants into two groups receiving 20,000 IU of vitamin D<sub>3</sub> capsules twice a week (high-dose group) or placebo (standard dose group). Serum 25(OH) D levels were reported to be significantly increased in the high-dose group and after 1 year, the severity of UI

was significantly reduced in this group [18]. However, Markland et al., in their two studies in 2019 and 2021, reported that the use of vitamin D is not effective in the prevalence, incidence, or progression of UI in older women with or without adequate vitamin D levels [19, 20]. In the first study, they investigated the effect of vitamin D<sub>3</sub> at a dose of 50,000 IU weekly for 12 weeks or placebo on reducing the severity of UUI in 56 postmenopausal women [19]. In the second study, they investigated the effect of vitamin D<sub>3</sub> at a dose of 2,000 units per day, along with omega-3 fatty acids at a dose of 1 g per day, versus placebo on the prevalence, incidence, or progression of urinary incontinence in elderly women in a 5-year prospective study [20]. However, Shahraki et al., in a randomized controlled trial in 60 postmenopausal women, investigated the effect of weekly 5,000-IU vitamin D supplementation or placebo for 3 months on the severity of stress UI and reported that after 8–12 weeks, the severity of stress UI, the number of its symptoms of stress incontinence, and urinary leakage decreased significantly in the vitamin D group [15]. The type of patients studied, the dose of the drug used, and the treatment duration are some reasons for the discrepancies in the results of different studies.

One of the strengths of our study was that we demonstrated the effect of vitamin D on reducing UUI symptoms in a randomized clinical trial, as, so far, few clinical trials have been conducted in this field and their results are contradictory. Because power analysis was not done before the study, post hoc power calculation was used. Considering the sample size of 45 patients in each group, the probability of type-I error ( $\alpha$ ) of 5%, and the moderate to severe severity of urinary incontinence after the intervention, in the vitamin D group equal to 69% and in the placebo group equal to 91% (Table 2), the power of the study was calculated to be 75%. Therefore, it seems that vitamin D can be used to treat UUI in this group of patients. However, because the patients were treated for only 8 weeks, it was not possible to examine the long-term effect of the treatment and the reversibility of the symptoms if the treatment was discontinued. Therefore, it is necessary to conduct more extensive studies in order to determine the method and duration of use of this drug.

**Table 5** Comparison of treatment satisfaction between the two groups

Treatment satisfaction	Vitamin D group (n=45)	Placebo group (n=45)	p value*
Very satisfied	9 (20%)	0 (0%)	<0.001
Satisfied	14 (32%)	3 (7%)	
Neither satisfied nor dissatisfied	11 (24%)	8 (18%)	
Dissatisfied	10 (22%)	23 (51%)	
Very dissatisfied	1 (2%)	11 (24%)	

\*Chi-squared test

## Conclusion

The findings of the present study showed that in postmenopausal women with complaints of UUI or nocturia, weekly use of 50,000 units of vitamin D tablets for 8 weeks can reduce the severity of UI and the frequency of nocturia, and reduce their impact on disruption in daily life. It also provides a high level of treatment satisfaction. Therefore, the use of vitamin D in the treatment of UUI in postmenopausal women can be recommended.

**Author contributions** M. Arjmand: protocol/project development, data collection, data analysis, manuscript writing; H. Abbasi: data collection, manuscript writing; A. Behforouz: protocol/project development, manuscript editing.

## Declarations

**Ethical issues** The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Shahid Beheshti University of Medical Sciences approved this study. The institutional ethics committee at Shahid Beheshti University of Medical Sciences approved all study protocols (IR.SBMU.RETECH.REC.1399.435) and was registered on the Iran Clinical Trials registration website (IRCT20200417047109N1). Accordingly, written informed consent was taken from all participants before any intervention.

**Conflicts of interest** None.

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