

Calcium and Vitamin D Supplementation and Risk of Kidney Stone Formation in Postmenopausal Women

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Introduction. Calcium and vitamin D are essential structural components of the skeletal system, which prevent osteoporosis after menopause. However, there is a controversial debate on the association between the intake of calcium and vitamin D supplements and the increased risk of formation of kidney calculi in postmenopausal women, which yet have to be confirmed. This study aimed to compare the metabolic changes after supplementation of calcium and vitamin D and examine the risk of stone formation.

Materials and Methods. Fifty-three postmenopausal women referred to rheumatology clinic who had no history of kidney calculi, bone diseases (apart from osteoporosis), metabolic, and rheumatic disorders and had not been receiving calcium, diuretics and calcitonin were investigated. Renal ultrasonography and blood tests were performed and the urine calcium levels were measured for a period of 24 hours for all patients. The examinations were repeated after a 1-year period of treatment with supplemental calcium (100 mg/d) and vitamin D (400 IU/d) and compared with the data before the treatment.

Results. After 1 year, asymptomatic lithiasis was confirmed in 1 of 53 patients (1.9%) using ultrasonographic examination. No significant differences were found between the 24-hour urine and blood calcium levels before and after the treatment.

Conclusions. Our findings showed that oral intake of calcium and vitamin D after 1 year has no effect on the urinary calcium excretion rate and the formation of kidney calculi in postmenopausal women.

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INTRODUCTION

Osteoporosis, a systemic bone disease, is characterized by reduction in bone mass and its normal mineral structure, imposing a higher risk of fractures.^{1,2} Osteoporosis and bone density can be determined using dual energy radiographic absorptiometry. Bone mass degeneration increases with advancing age and speeds up in women after menopause.³ In the United States, 4 to 6 million postmenopausal women are suffering from osteoporosis,⁴ costing \$ 17 billion to treat these patients annually.⁵ In China, the prevalence of

osteoporosis in the spine, pelvic bone, and femoral neck bones in postmenopausal women has been reported to be 29.3%, 18%, and 14.9%, respectively.⁶ These demonstrate why osteoporosis and its consequences, including fractures, are considered as a major public health concern.⁷

Calcium and vitamin D are essential for maintenance of the skeletal system. The level of calcium in the body depends on the balance between dietary calcium intake and renal excretion. The reasons for menopause and aging imbalance between intake and excretion of calcium are not

well understood. Insufficient calcium supply increases the risk of bone loss and takes longer time to rebuild.⁸⁻¹⁰ Sufficient levels of vitamin D is necessary for normal bone mineralization, muscle contraction, and nerves and cellular functions.^{8,10}

Adequate intake of calcium and vitamin D supplements is used to prevent or treat bone loss in high-risk individuals, particularly, in women suffering from postmenopausal osteoporosis.⁸ However, it has been argued that the intake of calcium supply may increase the kidney stone formation by elevating urinary calcium levels.¹¹ There are some reports about the relationship between serum and urine calcium and stone formation.¹² It has also been shown that dietary calcium intakes could bind to oxalate in the gastrointestinal system and reduce urinary excretion of calcium oxalate, which plays a role in kidney stone formation.^{11,13} In North America, 74% of kidney calculi are composed of calcium oxalate, and it has been shown that reduction in the levels of calcium or calcium oxalate in urine lowers the risk of kidney stone formation.¹⁴

Studies on the relationship between dietary calcium intake and kidney calculi in postmenopausal women are scarce. Calcium and vitamin D supplements are frequently used to reduce the risk of fractures and its debilitating consequences in postmenopausal women, but its role in kidney stone formation is not yet well understood. This study was intending to investigate the role of dietary intakes of calcium and vitamin D in formation of kidney calculi.

MATERIALS AND METHODS

This clinical trial was performed on 53 postmenopausal women referred to the rheumatology clinic of Rasoul Akram Hospital in Tehran, Iran, during 2010. The study was conducted in accordance with the Declaration of Helsinki. Postmenopausal women suffering from osteoporosis that had not been receiving calcium, diuretics, or calcitonin prior to study and had no history of kidney calculi, kidney diseases, or bone-involving disorders (malignancies, osteomalacia, metabolic diseases, hyperparathyroidism, and rheumatic diseases) were included in this study. All patients who provided written informed consent were examined for the presence of kidney calculi by means of ultrasonography. The blood and 24-

hour urine test were analyzed to determine the levels of calcium, sodium, uric acid, creatinine, and urine volume. Patients who had evidence of calculi or had more than 300 mg urinary calcium in 24 hours were excluded from study.

The participants were treated with oral calcium-vitamin D tablets (Iran-daru, Tehran, Iran), twice a day, which contained 500 mg of calcium and 200 U of vitamin D. All patients were educated for a proper daily exercise and were observed by a dietitian for a healthy diet, containing not more than 500 mg/d of calcium, for 1 year, during which they did not consume alcohol or smoked.

After the follow-up period, all patients were examined for the presence of kidney calculi, using ultrasonography, and the blood and 24-hour urine test were analyzed and the data of the before and after treatment were compared. All the sampling and analysis were performed at the same laboratory and by the same persons.

To compare the normally and non-normally distributed variables before and after the treatment, paired sample *t* test and Wilcoxon rank sum test were used, respectively. The SPSS software (Statistical Package for the Social Sciences, version 19.0, SPSS Inc, Chicago, Ill, USA) was used for these data analyses. To determine the link between the changes in the levels of calcium in blood and urine and the duration of follow-up period, the Pearson correlation coefficients were calculated. *P* values less than .05 were considered significant.

RESULTS

A total of 53 postmenopausal osteoporotic women completed the study. The mean age was 55.57 ± 11.09 years (range, 35 to 85 years). At the commencement of the study, all patients had a normal ultrasonographic findings and blood and urine test results. The mean blood and urine calcium levels were 9.55 ± 0.54 mg/dL and 178.8 ± 76.5 mg/d, respectively. Other parameters were in the normal range as shown in the Table.

The average duration of follow-up was 13.5 ± 4.17 months, during which no patients required to receive any medication. At the end of study, the average blood and urinary calcium levels were 9.44 ± 0.47 mg/dL and 183.4 ± 68.6 mg/d, respectively. As shown in the Table, no significant differences were found between the values before and after the study.

Mean Values of Blood Parameters Before and After the Study

Parameter	Before	After	P
Blood calcium, mg/dL	9.55 ± 0.54	9.44 ± 0.47	.14
Blood sodium, mmol/L	142.08 ± 3.74	142.22 ± 2.82	.87
Blood uric acid, mg/dL	4.78 ± 1.15	4.93 ± 1.56	.24
Blood creatinine, ng/mL	0.84 ± 0.14	0.98 ± 1.02	.923
Urine volume, mL	1478.0 ± 607.2	1594.0 ± 536.2	.10
Urine calcium, mg/d	178.8 ± 76.5	183.4 ± 68.6	.71
Urine sodium, mmol/d	130.0 ± 58.3	132.4 ± 62.8	.87
Urine uric acid, mg/d	474.5 ± 196.3	418 ± 145.6	.06
Urine creatinine, g/d	0.84 ± 0.21	0.85 ± 0.25	.98

During the follow-up period, no symptoms or signs of kidney calculi, reduced urine volume, and abdominal or flank pain were noticed. Ultrasonography at the end of the study showed the evidence of urinary calculi in 1 patient (1.9%) and the 52 remaining patients (98.1%) had no evidence of stone formation or hydronephrosis.

Correlation analysis did not show any link between the follow-up duration and the changes in the calcium levels in both urine and blood ($P = .68$ and $P = .78$, respectively).

DISCUSSION

The present study examined the effect of calcium and vitamin D supplementation on the incidence of kidney calculi in postmenopausal women. The outcomes of this study showed that administration of 1000 mg/d of dietary calcium and vitamin D had a weak association with the formation of kidney calculi (only 1.9% of 53 patients). No significant differences were found between the amount of calcium in blood and urine between before and after the 1-year course of observation, during which no other symptoms, or clinical signs of kidney calculi were noticed. Other serum and urine parameters, including sodium, creatinine, and uric acid remained unchanged before and after treatment.

There is a controversy over the association between the content of dietary calcium and lithiasis in postmenopausal women. In a study by Jackson and colleagues, 36 282 postmenopausal women, aged 50 to 79 years, were treated with 1000 mg of calcium and 400 IU of vitamin D per day, and a 17% higher rate of kidney calculi was shown in the treated group after 7 years of follow-up.¹⁵ Other studies contradicted this result, suggesting no association between the consumption of calcium and vitamin D and formation of kidney calculi.¹⁶

Normally, urine is saturated with calcium salts, but stone formation in a normal kidney is relatively rare and it usually occurs in people with a kidney disorder and following imbalance between the excreted and retained calcium within the kidneys. The main metabolic causes of kidney calculi are hypercalciuria (30% to 70%) followed by metabolic hyperoxaluria.¹⁴ Recently, it has been shown that urinary oxalate has a greater role in calcium stone formation.^{11,13} In the intestines, the unabsorbed calcium can bind with oxalate, which reduces the risk of stone formation. Despite the higher concentrations of oxalate in the urine, this may explain the reason for the lower risk of kidney calculi in those studies that patients received higher concentrations of calcium intake.^{17,18} Other environmental factors can also increase the risk of kidney calculi, including low fluid intake as the most common reason, and consumption of foods containing high levels of oxalate, proteins, and salt.¹⁹ It has also been shown that obesity and a body mass index greater than 30 kg/m² can double the risk of kidney stone formation. Finally, high blood pressure and reduced intake of magnesium can increase the risk of kidney stone formation.^{20,21}

The higher incidence of lithiasis in some studies might be caused by the effect of calcium or other predisposing factors in the investigated populations. Consistent with the outcomes from the current study, in a review covering 12 different randomized controlled trials, investigating the effect of calcium supplements on the lithiasis in postmenopausal women, the average incidence of calculi in the treatment group receiving calcium was 77.3 ± 24.7 per 100 000 persons, compared to 80.4 ± 28.7 per 100 000 persons in the control group, which were not significantly different.¹⁴

A great number of women receive oral calcium to reduce the progression of osteoporosis. Several studies recommended at least 1 g/d of dietary calcium in postmenopausal women,²²⁻²⁶ and a significant association has been shown between the calcium intake and bone density in postmenopausal women.²³ The current study showed that there is no link between the dietary calcium and vitamin D supplement and the levels of blood and urine calcium. Our findings opposed the results from Jackson and colleagues.¹⁵ The difference between the two studies could be caused by the differences in the sample size or follow-up period of the study.

As shown in the current study, the postmenopausal women receiving calcium and vitamin D supplements had a low incidence of kidney calculi. However, performing further investigations using greater sample size and longer follow-up period can provide better insights towards the benefits of using calcium in postmenopausal women suffering from osteoporosis.

CONCLUSIONS

Our findings showed that oral intake of calcium and vitamin D after 1 year has no effect on the urinary calcium excretion rate and the formation of kidney calculi in postmenopausal women.

CONFLICT OF INTEREST

None declared.

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