Original Article

Anti-proteinuria effect of active vitamin D in patients with type 2 diabetic nephropathy

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Abstract

Introduction: Proteinuria is a common complication in patients with type 2 diabetic nephropathy (DN). The aim of this study was to evaluate the anti-proteinuria effect of active vitamin D in patients with type 2 DN. **Methods:** A double-blind randomized clinical trial study was conducted on 42 DN patients selected by convenience sampling method. After selecting patients based on inclusion criteria, they were randomly divided into control and intervention groups. Patients in the intervention group received 0.25 mg of active vitamin D per day for 12 weeks. The variables evaluated in the patients on the first day of the intervention included fasting blood sugar (FBS), calcium, phosphorus, creatinine, glomerular filtration rate (GFR), systolic and diastolic blood pressure, and proteinuria. These variables were also evaluated at the end of the first, second, and third month of intervention. Data were collected and analyzed in Statistical Package for Social Sciences software version 22. **Results:** Around 52.5% of the patients participating in this study were male and 47.5% were female. The mean age of the patients was 55.52 ± 6.58 years. The results of repeated measures analysis showed that active vitamin D significantly reduced proteinuria ($P = 0.000$) in patients in the intervention group. The changes in FBS ($P = 0.235$), calcium ($P = 0.393$), phosphorus ($P = 0.694$), creatinine ($P = 0.232$), GFR ($P = 0.347$), systolic blood pressure ($P = 0.615$), and diastolic blood pressure ($P = 0.115$) were not significant in patients in the intervention group. **Conclusion:** Prescription of active vitamin D can significantly reduce the incidence of proteinuria in patients with DN.

Keywords: Active vitamin D, anti-proteinuria, diabetic nephropathy, type 2 diabetes mellitus

Introduction

The prevalence of type 2 diabetes (T2D) has become a global concern. The estimates show a prevalence of approximately 382 million people with diabetes in 2013, expected to rise to 592 million by 2035 with an increase in its complications such as nephropathy.[1] Diabetic nephropathy (DN) is one of the most common and severe complications of T2D that is associated with increased mortality in diabetic patients.[2] According to studies, the estimated number of diabetic patients with chronic kidney disease (CKD) in China is 24.3 million.[3] In general, the global prevalence of diabetes is growing rapidly, especially in developing countries. With the increasing prevalence of diabetes, more cases of DN are also expected if there is no immediate improvement in the clinical strategies for DN prevention.[4] DN is a long-term complication, starting with glomerular and

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tubular epithelial hypertrophy and thickening of the glomerular basement membrane.[5] DN progression is characterized by the development of microalbuminuria in patients with normal renal function, followed by a gradual increase in urinary albumin excretion and an ultimate decrease in glomerular filtration rate (GFR).[6] Symptoms of DN include proteinuria, decreased GFR, elevated arterial blood pressure, fluid retention, and finally renal failure. The results of various studies have shown that persistent proteinuria is a clinical indicator and an independent risk predictor for DN progression. Therefore, it seems essential to protect DN patients against further loss of renal function.[7]

Recently, an increasing number of studies have shown the protective effect of active vitamin D and its analogs on renal function.[8] Other studies have also shown that 1,25 dihydroxycholecalciferol (calcitriol) improve glomerular damage and enhance kidney protection by suppressing transforming growth factor beta 1 and increasing hepatocyte growth factor. In a study by Taheri *et al.* (2018),[9] it was stated that vitamin D deficiency stimulates renin expression in healthy mice, and injection of 1,25-(OH) 2-D3 reduces renin synthesis. Song *et al.* (2021)[10] showed that calcitriol/vitamin D receptor signaling slows down DN progression by restoring podocyte autophagy and cell damage. Research has shown that diabetic mice with a lack of vitamin D receptors are more likely to develop severe nephropathy than wild-type mice. These results suggest that vitamin D promotes protection by suppressing Renin–angiotensin-aldosterone system (RAAS). In addition to the above-mentioned evidence that was mostly based on laboratory models, the results of the Third National Health and Nutrition Examination Survey showed that a decrease in 25(OH) D was associated with an increase in the prevalence of albuminuria in the general population. Evaluation of diabetic patients has demonstrated an independent association between vitamin D deficiency and DN. In patients with T2D, the greater the progression of DN, the more severe the vitamin D deficiency.[11] The results of a study by Lee *et al.*[12] showed that vitamin D levels were not significantly associated with insulin resistance and cardiovascular factors. A brief review of the sources shows that there is a large body of research on DN patients and various drug interventions to improve proteinuria in these patients. However, the effectiveness of some interventions, including vitamin D-based interventions, has not been conclusively proven. Most studies in this field are theoretical and at the laboratory level and there is a need for human studies. Thus, this study aimed to determine the anti-proteinuria effects of active vitamin D in patients with type 2 DN.

Methods

The present study was a randomized double-blind clinical trial with an ethical code of IR.AJUMS.HGOLESTAN.REC.1399.129 approved by the ethics committee of Ahvaz Jundishapur University of Medical Sciences. This study aimed to evaluate the anti-proteinuria effect of active vitamin D in diabetic patients with type 2 DN in 2021. The present study has been registered in the Iranian Registry of Clinical Trials with the code number IRCT20200802048276N1. The study population included patients with type 2 DN who had a proteinuria >500 mg per day. The patients were randomly divided into two groups of intervention and control using the block randomization method. The study population consisted of 40 patients with T2D DN who had been referred to Golestan and Imam Hospitals of Ahvaz, Iran, between 2020 and 2021. The convenience sampling method was used to select patients. Since this study had a repeated measures design, the following set of formulas was used to measure the sample size.

$$R = \left[\frac{1+(w-1)\rho_T}{w} - \frac{v\rho_T^2}{[1+(v-1)\rho_T]} \right]$$

$v \geq 0$

$w \geq 1$

$$m_{repeated} = R\left[\left(1+\frac{1}{\lambda}\right)^2 \frac{(Z_{1-\alpha/2}+Z_{1-\beta})^2}{\Delta^2_{plan}} + \frac{Z^2_{1-\alpha/2}}{4} \right]$$

$$n_{repeated} = \lambda \times m_{repeated}$$

$$N = m_{repeated} + n_{repeated} = (\lambda+1)\times m_{repeated}$$

λ: The ratio of the sample volume in group 2 to group 1 = 1

v: The number of measurements before intervention = 1

w: The number of measurements after intervention = 3

ρ: correlation coefficient between repetition of measurements = 0.1

plan: standardized expected impact size = 1.463

m: Sample size in group 1

n: Sample size in group 2

N: Total sample size of the study

The sample size per group was calculated as 16. Accounting for 20% loss, the final sample size in each group was considered as 20, thus, the total sample size was 40. Among the inclusion criteria were having 30–70 years of age, diagnosed with T2D for at least 3 months, proteinuria (urinary protein secretion >500 mg/24 h), and a plasma hydroxyvitamin D level >20. Exclusion criteria included hypercalcemia (>10 mg/dl), high phosphorus serum levels (>5.5 mg/dl), uncontrolled hypertension (>90.140 mmHg), hyperparathyroidism, kidney stones, CKD, heart failure, metabolic disorders of calcium and phosphorus such as osteoporosis and bone metastases, parathyroid hormone (PTH) suppression based on laboratory expression, pregnancy, or lactation.

Methodology

In this 12-week study, DN patients treated with standard medicines (oral medicines for controlling glucose or insulin, and valsartan) for diabetes and proteinuria who had relatively stable conditions were included and randomly assigned into two groups of control (no active vitamin D intake) and intervention [daily intake of 0.25 mg of active vitamin D (calcitriol)]. In this study, the doses of glucose or insulin controlling drugs were chosen according to the physician's opinion and the dose of valsartan drugs remained unchanged during the study and maintained as before the intervention. In cases where the dose of valsartan needed to be increased, blood pressure could not be controlled, and the type or dose of diabetes medication needed to be changed, the patient was excluded from the study. The patient should be treated with valsartan at least three months before the study's inception. Patients were evaluated at the beginning of the study, the end of the first month, the end of the second month, and the end of the third month. Antihypertensive drugs were used to maintain standard blood pressure (systolic: −30 mmHg, diastolic: 80 mmHg). Patients' information including their age, sex, height, weight, and diabetes duration were collected before starting the intervention. Patients' data were collected based on their last visit and using the information registration form. Blood pressure, the levels of PTH, calcium, phosphorus, and hemoglobin, glycosylated hemoglobin (HbA1C) and FBS, 25 hydroxyvitamin D and creatinine, 24-h urine proteinuria, and GFR were measured based on creatinine clearance and modification of diet in renal disease (MDRD) method. The levels of FBS, calcium, phosphorus, creatinine, GFR, and 24-h urinary proteinuria were measured at the end of the first, second, and third months. Systolic/diastolic blood pressure was measured at each visit using a mercury sphygmomanometer and checked twice at 20-min intervals if the limit was exceeded. HbA1C was measured at the beginning and end of the intervention. Proteinuria is defined as the urinary protein excretion greater than 150 mg/m^2 per day.

Statistical analysis

Since the primary and secondary variables were quantitative, analysis of covariance was used to compare post-intervention measurements with the controls at the baseline values. Moreover, repeated measures analysis and generalized estimating equation were used for general comparison between the intervention and control groups.

Results

The demographic characteristics of the patients participating in the present study are shown in Table 1. The results showed that of the participants in this study, 21 (52.5%) were male and 19 (47.5%) were female. The results of Chi-square test showed the two groups of control and intervention were not significantly different in terms of gender ($P = 0.264$). The mean age of the patients in the present study was 55.52 ± 6.58 years. Other statistical differences in demographic characteristics of the patients in the control and intervention groups are presented in Table 1.

The results [Table2] the difference in calcium levels was not statistically significant between the control and intervention groups at the beginning of the study ($P = 0.542$) and at the end of the first month ($P = 0.530$). However, based on the results of t-test, there was a significant difference in the mean calcium levels between patients in the control and intervention groups at the end of the second ($P = 0.015$) and the third month ($P = 0.033$). Calcium levels at the end of the second and third months were higher in patients in the intervention group than in controls. Figure 1 shows the changes in calcium levels in the control and intervention groups.

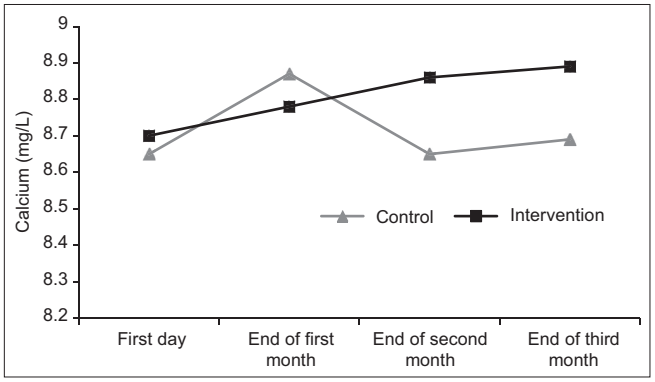

Figure 1: Changes in calcium levels in the control and intervention groups during the experiments

Table 1: Demographic characteristics of the study participants

Variable	Group	Control		Intervention		*P*
		Frequency	Percent	Frequency	Percent	
Gender	Male	12	60	9	45	0.264
	Female	8	40	11	55	
		Mean	SD	Mean	SD	*P*
Age (years)		54.55	7.40	56.50	6.39	0.362
Weight (kg)		74.9	14.09	77.1	12.70	0.607
Height (cm)		164.55	11.34	162.05	10.80	0.480
BMI		27.59	3.79	29.47	4.97	0.186
Disease duration (months)		85.6	24.08	89.10	28.26	0.684
PTH		49.65	8.11	50.05	7.52	0.872
Vitamin D		36.45	5.59	35.60	5.16	0.621

Based on the results of the t-test statistical analysis, the difference in phosphorus levels was not statically significant between the control and intervention groups at the beginning of the study ($P = 0.940$), the end of the first month ($P = 0.112$), the end of the second month ($P = 0.238$), and the end of the third month ($P = 0.437$). Moreover, the results of the repeated measures analysis test showed that the changes in phosphorus levels during the experiment stages (at the beginning of the study, end of the first month, second, and third month) were not statistically significant between the two groups of control ($P = 0.187$) and intervention ($P = 0.694$). The results also showed that the difference in FBS levels was not statistically significant between the patients in the control and intervention groups at the beginning of the study ($P = 0.639$), the end of the first month ($P = 0.511$), the end of the second month ($P = 0.173$), and the end of the third month ($P = 0.162$). According to the results of repeated measures analysis, the changes in FBS levels during the experimental stages (at the beginning of the study, end of the first, second, and third month) were not statistically significant between the two groups of control ($P = 0.949$) and intervention ($P = 0.235$). As shown in Table 3, the results of t-test statistical analysis showed that the difference in HbA1C1 levels was not statistically significant between the control and intervention groups at either the beginning of the study ($P = 0.204$) or the end of the third month ($P = 0.130$). The results of t-test statistical analysis also showed that there was no significant difference in HbA1C1 levels on the first day of the study and at the end of the third month between the two groups of control ($P = 0.567$) and intervention ($P = 0.499$).

According to the results of t-test statistical analysis, there was no statistically significant difference in creatinine levels at the beginning of the study ($P = 0.271$) and at the end of the first month ($P = 0.493$) between the patients in the control and intervention groups. However, the results of the t-test statistical analysis showed a significant difference in the mean creatinine level between the control and intervention patients at the end of the second month (at the level of 5%; $P = 0.011$) and at the end of the third month (at the level of 1%; $P = 0.009$). Creatinine levels at the end of the second and third months were higher in the control group patients than in the intervention group patients. Based on the repeated measures analysis test, it was found that the changes in creatinine levels during the experimental stages (at the beginning of the study, end of the first, second, and third month) were not statistically significant between the two groups of control ($P = 0.057$) and intervention ($P = 0.232$). The difference in the GFR, systolic blood pressure (SBP), diastolic blood pressure (DBP), and proteinuria levels between the control and intervention groups in the experimental stages are presented in Table 4. In addition, the changes in proteinuria levels in the control and intervention groups during the experimental stages are shown in Figure 2.

Table 2: Comparison of Ca levels in control and intervention groups

Variable	Control		Intervention		*P*
	Mean	SD	Mean	SD	
Ca level on the first day	8.65	0.16	8.70	0.28	0.542
Ca level at the end of the first month	8.87	0.45	8.78	0.39	0.530
Ca level at the end of the second month	8.65	0.15	8.86	0.32	0.015
Ca level at the end of the third month	8.69	0.21	8.89	0.34	0.033
Repeated measures (RM) analysis	0.393		0.157		

Ca: Calcium

Table 3: Comparison of HbA1C1 levels in control and intervention groups

Variable	Control		Intervention		*P*
	Mean	SD	Mean	SD	
Ca level on the first day	7.34	0.12	7.28	0.17	0.204
Ca level at the end of the third month	7.31	0.15	7.24	0.15	0.130
P	0.499		0.567		

Ca: Calcium

According to the results of t-test statistical analysis shown in Table 4, the difference in proteinuria levels was not statistically significant between patients in the control and intervention groups at the beginning of the study ($P = 0.728$) and the end of the first month ($P = 0.185$). However, the results of t-test statistical analysis showed a significant difference (at the level of 1%) in the mean levels of proteinuria between the patients in the control and intervention groups at the end of the second month ($P = 0.001$) and the third month ($P = 0.000$). The level of proteinuria followed a decreasing trend in the intervention group patients. At the end of the second and third months, the level of proteinuria in patients in the intervention group was significantly lower than this rate in controls. The changes in proteinuria levels in the control and intervention groups are shown in Figure 2. According to the repeated measures analysis test, there was a significant decrease in creatinine level in the intervention group ($P = 0.057$) during the experimental stages (at the beginning of the study, end of the first, second, and third month). However, this decrease was not significant in the control group ($P = 0.232$).

Discussion

In recent years, it has been hypothesized that active vitamin D may reduce proteinuria in DN patients. In this regard,

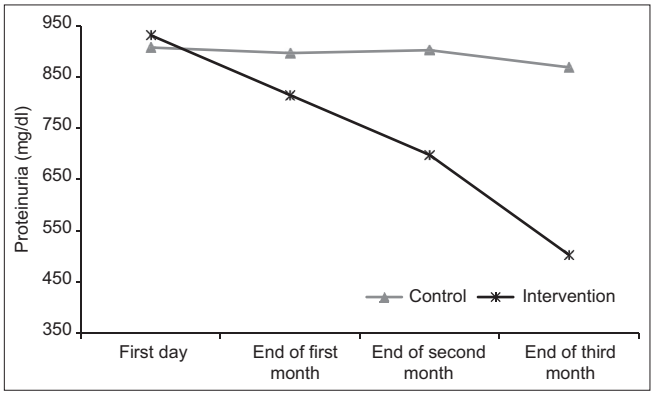

Figure 2: Changes in proteinuria levels in the control and intervention groups during the experiments

Table 4: Comparison of creatinine, GFR, SBP, DBP, and proteinuria levels in control and intervention groups

Variable	Control		Intervention		*P*
	Mean	SD	Mean	SD	
Creatinine levels					
Ca level on the first day	0.97	0.17	1.03	0.18	0.271
Ca level at the end of the first month	1.03	0.16	0.99	0.15	0.493
Ca level at the end of the second month	1.09	0.13	0.97	0.15	0.011
Ca level at the end of the third month	1.06	0.14	0.94	0.14	0.009
RM analysis	0.057		0.232		
GFR levels					
Ca level on the first day	90.70	7.13	92.05	8.95	0.601
Ca level at the end of the first month	91.15	6.82	93.60	10.63	0.391
Ca level at the end of the second month	91.35	9.63	94.35	10.78	0.359
Ca level at the end of the third month	91.60	12.48	95.15	9.81	0.324
RM analysis	0.780		0.347		
SBP levels					
Ca level on the first day	124.15	5.42	123.00	5.07	0.493
Ca level at the end of the first month	125.25	5.00	122.70	6.13	0.157
Ca level at the end of the second month	126.25	4.45	121.70	4.68	0.003
Ca level at the end of the third month	126.45	3.95	123.50	4.70	0.038
RM analysis	0.415		0.615		
DBP levels					
Ca level on the first day	74.70	2.53	75.40	3.33	0.459
Ca level at the end of the first month	75.10	3.30	74.75	3.43	0.744
Ca level at the end of the second month	75.85	3.36	73.45	2.64	0.016
Ca level at the end of the third month	76.25	2.12	73.55	3.17	0.003
RM analysis	0.286		0.115		
Proteinuria levels					
Ca level on the first day	907.55	220.52	931.60	231.76	0.728
Ca level at the end of the first month	896.40	198.70	814.40	185.30	0.185
Ca level at the end of the second month	902.35	176.41	697.55	171.98	0.001
Ca level at the end of the third month	868.75	180.68	502.95	118.40	0.000
RM analysis	0.319		0.000		

Ca: Calcium

the results published in various studies are contradictory. The results of the present study conclusively showed that the administration of active vitamin D leads to a significant reduction in proteinuria. Similar to the present study, Momeni *et al.*[13] showed that correction of vitamin D deficiency reduced proteinuria in diabetic patients with nephropathy. The results of a cross-sectional study in US adults clearly showed that vitamin D has anti-proteinuria activity.[14] The results of a cross-sectional study by Lee *et al.* (2011)[12] also showed a decrease in proteinuria in kidney transplant patients. In two separate meta-analyzes, Xu *et al.* (2013)[15] and Kandula *et al.*[16] examined the role of vitamin D and its analogs in the management of CKD. The results showed that the administration of vitamin D and its analogs reduced proteinuria without any side effects, which is in line with the findings of the present study. Similar to the results of the present study, Saeedi *et al.*[17] also showed an improvement in proteinuria in the intervention group compared to the control group. The results of the present study showed a significant effect of active vitamin D in improving proteinuria in DN patients, which is in consistent with the results of Krairittichai *et al.* (2012) and De Zeeuw *et al.* (2010) who showed in their study that vitamin D analogs, including paricalcitol and calcitriol, significantly reduced proteinuria.[18,19] In the present study, there was no significant difference in proteinuria levels between the control and intervention groups at the beginning of the study and at the end of the first month. However, the level of proteinuria reduction was significant at the end of the second month and afterward. Indeed, another important finding of the present study was that treatment of proteinuria with vitamin D requires a period of at least two months to take effect. In this regard, the results of our study are consistent with the results of other studies, such as the study of Huang *et al.* (2012) and Momeni *et al.* (2017). In their cross-sectional study, Huang *et al.* (2012)[20] found that normal doses of 25(OH) D3 (800 IU daily) for 6 months had a significant effect on reducing proteinuria in Chinese patients with type 2 DN. Momeni *et al.* (2017)[13] also showed that treating patients with type 2 DN with vitamin D (50,000 IU per week) for 8 weeks significantly reduced proteinuria. The anti-proteinuria effect of vitamin D has also been indicated in type 1 diabetic kidney patients who were deficient in vitamin D after 12 weeks of treatment.[21] In all these studies, as in the present study, vitamin D seems to reduce proteinuria by inhibiting hyperglycemia-induced podocyte apoptosis, on the one hand, and reducing podocyte damage or reducing podocyte hypertrophy, on the other hand.[22,23] Other reasons for the decrease in proteinuria include long-term

suppression of RAAS and subsequent suppression of renin secretion by vitamin D.[9]

The results of the present study showed that there was no significant difference in the GFR of patients between the control and intervention groups. Moreover, the changes in GFR during the experiment (at the beginning of the study, end of the first, second, and third month) were not significant in the control and intervention groups. Overall, the level of GFR was higher in patients in the intervention group than in the controls. These results are consistent with the results of the study by Krairittichai *et al*. (2012) and De Zeeuw *et al*. (2010). Researchers of these studies also showed that vitamin D had no effect on the GFR of treated patients.[18,19,24] The results of the present study on the effect of active vitamin D on calcium levels showed a significant increase in patients in the intervention group compared to patients in the control group at the end of the second and third months. Because this increase did not meet the exclusion criteria (hypercalcemia greater than 10 mg/dl), it did not cause complications such as hypercalcemia that prevent the administration of these drugs. Research has shown that vitamin D can increase insulin receptor gene expression in beta cells, glucose transport in the intestine, and intestinal calcium uptake as a stimulus for insulin release.[25] In the present study, the increase in the calcium level of patients in the intervention group can be attributed to the effect of active vitamin D in increasing intestinal calcium absorption. The results of the present study also showed that the administration of active vitamin D had no effect on changing the trend of calcium levels in patients in the intervention and control groups. These results are consistent with the results of previous studies,[18,20,26,27] all of which showed that vitamin D is not associated with hypercalcemia. These results were also confirmed in the present study. Contrary to the results of the present study, Ibrahim *et al*. (2015)[28] showed that the taking vitamin D supplements for 6 months led to a significant increase in calcium level. One of the reasons for the difference between the results of this study and our results could be due to the differences in the statistical population.

The progression of nephropathy in diabetic patients may lead to serum phosphate accumulation and subsequent dysfunction of some vital enzymes.[24] There is growing evidence that high serum phosphate levels are an important cardiovascular risk factor in patients with end-stage renal disease (ESRD). Thus, the control of serum phosphate level is an important factor in preventing the progression of cardiovascular calcification in patients with ESRD.[29] In addition to calcium, vitamin D also plays a significant role in phosphate metabolism.[30] When prescribing vitamin D-based drugs, therefore, it is important to consider the effects of the drug on the amount of phosphate accumulation. The results of the present study showed that there was no difference in serum phosphate levels of patients between the control and intervention groups in different stages of sampling. Moreover, the changing trend of phosphate in the intervention group was not significant. These results indicate that the use of active vitamin D in these patients causes no complications including hyperphosphatemia. In line with the results of the present study, Saeedi *et al*. (2016)[17] showed that vitamin D has no effect on phosphate levels. The results of the studies by Lee *et al*. (2012) and Huang *et al*. (2012) are also consistent with our findings (92, 113). Evaluation of FBS in study patients showed no significant difference in FBS between the patients in the control and intervention groups. Moreover, there were no significant changes in FBD levels during the experiment between the control and intervention groups. Similar to our study, Nasri *et al*. (2014),[31] Bonakdaran *et al*. (2012), and Krul-Poel *et al*. (2015)[32] showed that vitamin D had no significant effect on FBS levels of patients with nephropathy. Based on the results of the present study, there was no significant difference in the mean HbA1c level of patients at the beginning of the study and at the end of the third month. Consistent with the results of the present study, Al-Sofiani *et al*. (2015)[33] and Sheth *et al*. (2015)[34] also showed that the effect of vitamin D on HbA1c was insignificant. Contrary to the results of the present study, Nasri *et al*. (2014),[31] Krul-Poel *et al*. (2015)[32], and Tabesh *et al*.[35] showed that vitamin D has a significant effect on HbA1c. This inconsistency could be attributed to the different designs of these studies or potentially unknown mechanisms.

The results of the present study showed that vitamin D had no effect on patients' creatinine levels during treatment. In line with the results of the present study, Bonakdaran *et al*. (2012)[36] also showed that the difference in creatinine level at the beginning and end of the study was not significant between the patients. Krairittichai *et al*. (2012)[19] also showed that oral calcitriol had no effect on the creatinine levels of treated patients. In addition, Esfandiari *et al*. (2019)[37] found similar results to the present study, reporting that vitamin D administration had no effect on creatinine levels in the studied patients. In contrast to the results of the present study, Liyanage *et al*. (2018)[38] stated in their study that vitamin D has a significant effect on reducing creatinine levels in patients with type 2 DN. Among the possible reasons for the difference between the results of this study and the present study are the different duration and methodologies used in the two studies.

Hypertension is one of the most important factors in the development of CKD and cardiovascular diseases (CVD) that can be easily treated, however, the effects of vitamin D on reducing blood pressure is one of the most controversial issues in the literature. The results of the present study showed that the level of SBP and DBP in the intervention group patients at the end of the second and third months was significantly lower than this level in patients in the control group. In their study, Huang *et al*. (2021) stated that T2D patients with vitamin D deficiency have a higher diastolic blood pressure than patients in the control group.[39] In the present study, therefore, reduced blood pressure of patients in the intervention group compared to the controls at the end of the second and third months can be attributed to vitamin D consumption. Overactivity of the renin-angiotensin system is associated with hypertension, kidney disease, and diabetes.[40] Therefore, the effect of vitamin D on reducing

blood pressure may be related to its ability in suppressing renin formation or reducing PTH.[36] Despite the low systolic and diastolic blood pressure of patients in the intervention group of this study, the results showed that the changes in the systolic and diastolic blood pressure were not significant over time (at the beginning of the study, end of the first, second, and third month). This may be due to the fact that the blood pressure of patients in the present study was normal. The findings of our study are consistent with the results of other studies.[41]

Conclusion

The results showed that vitamin D significantly reduced proteinuria in DN patients. On the other hand, vitamin D had no effect on the GFR of these patients.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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