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ORIGINAL ARTICLE

Effects of dietary interventions on 24-hour urine parameters in patients with idiopathic recurrent calcium oxalate stones

Mustafa Kıraç [a,*], Bora Küpeli [b], Lokman İrkilata [c], Özlem Gülbahar [d], Nur Aksakal [e], Üstünol Karaoğlan [b], İbrahim Bozkırlı [b]

[a] *Department of Urology, Koru Hospital, Ankara, Turkey*
[b] *Department of Urology, Gazi University, Ankara, Turkey*
[c] *Department of Urology, Samsun Education and Research Hospital, Samsun, Turkey*
[d] *Department of Biochemistry, Gazi University, Ankara, Turkey*
[e] *Department of Public Health, Gazi University, Ankara, Turkey*

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Abstract The aim of this study is to investigate the effects of dietary factors on 24-hour urine parameters in patients with idiopathic recurrent calcium oxalate stones. A total of 108 of idiopathic recurrent calcium oxalate stones were included in the study. A 24-hour urinalysis was performed and metabolic abnormalities were measured for all of the patients. All of the patients were given specialized diets for their 24-hour urine abnormalities. At the end of first month, the same parameters were examined in another 24-hour urinalysis. Hyperoxaluria, hypernatruria, and hypercalciuria were found in 84 (77%), 43 (39.8%), and 38 (35.5%) of the patients, respectively. The differences between the oxalate, sodium, volume, uric acid, and citrate parameters before and after the dietary intervention were significant ($p < 0.05$). The calcium parameters were not significantly different before and after the intervention. We found that oxalate, sodium, volume, uric acid, and citrate—but not calcium—abnormalities in patients with recurrent calcium oxalate stones can be corrected by diet. The metabolic profiles of idiopathic calcium oxalate stone patients should be evaluated and the appropriate dietary interventions should be implemented to decrease stone recurrence.

Introduction

Urolithiasis affects a large proportion of the population in many regions of the world and has several etiologic factors.

* Corresponding author. Meksika Street, Yeni Çağın Buildings A Block, No 38, 06530 Ankara, Turkey.
E-mail address: mkirac@gmail.com (M. Kıraç).

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Its prevalence is approximately 5—12% [1—3], and it is an increasingly serious health problem in industrialized societies. The disease has a high incidence and recurrence rate; the recurrence rate is approximately 50% within 3 years of the initial diagnosis. In addition, surgical procedures are required for more than half of the patients with symptomatic stones [4,5]. Therefore, preventing stone disease is a more reasonable approach than treatment.

Medical therapies for recurrent urinary stones should aim to prevent recurrences by the reducing new stone formation [6]. The basic rules for medical therapies include the following: (1) decreasing the activators (oxalate, sodium, calcium, and uric acid) and increasing the inhibitors (citrate and magnesium) in the urine; (2) providing adequate urine volume to prevent urinary crystallization; and (3) ensuring effective dietary regulation.

Because calcium oxalate stones are the most common recurrent stones, treatment should be particularly considered for these patients [7,8]. The risk factors for calcium oxalate stones include environmental, metabolic, genetic, and dietary factors. In the patients at high risk for stones, detecting and correcting these factors could prevent recurrences.

In this study, we evaluated the effectiveness of dietary interventions for correcting 24-hour urine parameters and decreasing stone recurrences in patients with idiopathic recurrent calcium oxalate stones.

Materials and methods

Patients

In this prospective study, 108 patients with idiopathic recurrent calcium oxalate stones were admitted to the urology department at Gazi University between November 2003 and July 2006 and were evaluated. The patients with calcium oxalate stones, as determined by a stone analysis, were included this study. The following inclusion criteria were used: (1) a stone analysis confirming calcium oxalate stone components; (2) recurrent stone disease (at least two occurrences or progression of stones); (3) age older than 18 years; and (4) at least one risk factor, such as a family history positive for the disease, a history of low fluid intake, or recurrent urinary infections. The stones were analyzed using x-ray diffraction analysis and scanning electron microscopy. Urine parameters, including analysis and culture, and serum parameters, including calcium, phosphate, chloride, urea, creatinine, uric acid, and parathormone, were measured for all of the patients. The patients who had no risk factors, were at low risk for stones, did not have recurrent stones, or were diagnosed with hyperparathyroidism were excluded. A 24-hour urinalysis, including volume, pH, sodium, calcium, magnesium, oxalate, citrate, uric acid, and phosphate parameters, was performed for all of the 108 recurrent calcium oxalate stone patients. All of the patients were given a dietary intervention for their particular 24-hour urine abnormality. At the end of the first month, the 24-hour urinalysis was repeated, and the values obtained before and after the dietary intervention were compared.

A consent form that included the urine and blood analyses, dietary information, and study design was given to all of the patients.

24-hour urinalysis

Before the dietary interventions, a 24-hour urinalysis was performed for all of the patients who had recurrent calcium oxalate stones and were not having an acute stone episode. A 24-hour urine sample was collected to measure the pH, citrate, calcium, uric acid, oxalate, phosphorus, sodium, magnesium, and total volume. The calcium, phosphorus, sodium and uric acid were measured by an auto-analyzer using a special kit for these parameters (Abbott-Architect C4000, Santa Clara, California, USA). The oxalate was manually measured by the oxalate oxidase and peroxidase assay (Abbott-Hitachi Axsym Plus, Bohemia, New York, USA). The citrate was manually measured by the citrate lyase assay (Abbott-Hitachi Axsym Plus). The urine pH was measured by standard clinical chemistry procedures.

Diet

Under the supervision of a dietician, a specialized diet program was administered for each particular 24-hour urine abnormalities. The same dietician conducted and recorded each patient's dietary intervention. For most of the patients, a diet that addressed multiple abnormalities was required; however, a dietary intervention designed for only one abnormality was used in a small number of patients. If the urine volume was less than 2 L/day, then the patients were advised to increase their daily water intake [1,8,9]. If the urinary sodium was greater than 200 mg/day, then the maximum daily NaCl was restricted to 5 mg. [10]. If the urinary uric acid was greater than 700 mg/day, then meat and meat products were restricted [11]. If the urinary oxalate was greater than 40 mg/day, then high-oxalate foods, such as tea, coffee, spinach, nuts, and chocolate, were restricted [10]. If the urinary calcium was greater than 250 mg/day, then calcium intake was restricted to 400—600 mg daily [12,13]. If the urinary citrate was $<$400 mg/day and the urinary pH was low, then increased dietary intake of orange juice and other foods containing citrate, such as grapefruit, was advised [14,15]. Dietary modifications were not performed for magnesium and phosphate.

All of the patients who were assigned a dietary intervention were informed of its identity and nutritional contents. These patients recorded their daily diets. At the end of the first month, all of the patients returned to our clinic for re-evaluation and a repeat 24-hour urinalysis.

Statistical analysis

SPSS for Windows, version 11.5 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. The results of the descriptive analyses are given as means $\pm$ standard deviations. The statistical analyses for the patient groups were performed using parametric and nonparametric tests. The parametric tests, which were used when the number of patients was greater than 30, were the paired-sample and simple *t*-tests. The nonparametric tests, which were used when the number of patients was less than 30, were the Chi-square test, Wilcoxon and Kruskal-Wallis tests. P-values less than 0.05 were considered to be statistically significant.

Results

A male predominance was noted in the 108 patients included in the study; 72 patients were male (66.7%), and 36 were female (33.3%). The mean age was 40.3 ± 10.3 for the males and 45.4 ± 13.3 for the females. Table 1 gives the general characteristics of the patients. Of the 108 patients, 15 (13.8%) had a single metabolic abnormality and 93 (86.2%) had mixed metabolic abnormalities (two or more abnormalities). The most common metabolic abnormality was hyperoxaluria (77.0%). Table 2 gives the metabolic abnormalities of the patients.

Dietary interventions for two or more abnormalities were recommended for 69 (63.9%) of the patients. A dietary intervention for a single abnormality was implemented for 39 (36.1%) of the patients. Fifteen patients received the oxalate diet only, 15 patients the fluid diet only, five patients the sodium diet only, two patients the calcium diet only, one patient the citrate diet only, and one patient the uric acid diet only.

Among the patients who received a diet, the difference between the oxalate values before and after the diet was statistically significant ($p < 0.05$). In addition, the differences between the citrate, uric acid, sodium, and volume values before and after the diet were also statistically significant ($p < 0.05$). The calcium values before and after the diet ($p = 0.136$) were not significantly different. In the patients who received the calcium diet, by contrast, the mean urinary oxalate value was 90.6 ± 57.7 mg/day before the diet and 55.6 ± 45.4 mg/day after the diet, which was statistically significant. Table 3 shows the analysis of the 24-hour urine parameters in the patients that received a dietary intervention.

In the 58 male patients who received the oxalate diet, the difference between the before and after oxalate values was statistically significant; however, this difference was not statistically significant for the 26 female patients ($p = 0.1$). In the 52 patients with no family history, the difference between the before and after oxalate values was significant, but it was not significant in the 32 patients with such a family history ($p < 0.01$ and $p = 0.4$, respectively). Table 4 shows the 24-hour parameters in the patients who received the oxalate diet.

Table 1 General patient characteristics.

Characteristics	Sex		General ($n = 108$), %
	Male ($n = 72$), %	Female ($n = 36$), %	
Age, yr	40.3 ± 10.3	45.4 ± 13.3	42.33 ± 11.8
Family history	40 (55.6)	23 (63.8)	63 (41.0)
Fluid intake			
Low: (<1 L/d)	25 (34.7)	12 (33.3)	37 (34.3)
Moderate: (1–2 L/d)	29 (40.2)	18 (50.0)	47 (43.5)
High: (>2 L/d)	18 (25.0)	6 (16.7)	24 (22.2)
History of RUTI	4 (5.6)	4 (11.1)	8 (7.4)

RUTI = recurrent urinary tract infection.

Table 2 Range of metabolic abnormalities in the 24-hour urine samples.

Metabolic abnormality	Patients (%)
Hyperoxaluria	84 (77.0)
Hypernatriuria	43 (39.8)
Low urinary volume (<2000 cc)	43 (39.8)
Hypercalciuria	38 (35.0)
Hyperuricosuria	21 (19.4)
Hypocitraturia	16 (14.0)
Hypomagnesiuria	13 (12.0)

Discussion

The prevalence of urolithiasis in the general population has increased; unbalanced diets, sedentary lifestyles and obesity have induced have led to more cases of recurrent stone formation [16]. Stone recurrence has decreased patient quality of life and requires repeated surgical treatment in some patients. In the literature, many studies have introduced various dietary interventions designed to reduce stone recurrence [10,17]. In our study of patients with recurrent idiopathic calcium oxalate stones, we detected metabolic abnormalities through a comprehensive metabolic evaluation and evaluated the efficacy of dietary interventions for reducing stone recurrence.

The belief that diet plays an important role in reducing stone recurrence is common. Siener et al. [10] have suggested that the major risk factors for calcium oxalate stores are environmental and dietary. Many researchers have also suggested that irregular dietary habits (such as high protein intake and inadequate fluid intake), alcohol, a sedentary life style, obesity, and diabetes mellitus are related to urolithiasis [3,9,18]. In our study, certain risk factors, such as family history and dietary factors, were found to be similar to those reported in the literature.

Most studies have demonstrated that stone recurrence can be reduced by correcting risk factors and other preventive medical measures. Borghi et al. [19] have examined the effects of several dietary compositions on stone recurrence. Recurrence within the 5-year follow-up period was observed in 12 of the 60 patients who received a low-animal protein, low-salt and normal-calcium diets, whereas recurrence was observed in 23 of the 60 calcium oxalate stone patients who received a normal-animal protein and low-calcium diet. Moreover, Siener et al. [3] have demonstrated that crystallization can be changed by several dietary compositions, such as normal, vegetarian, and Western-type diets. In our study, we found that the 24-hour parameters, except for calcium, could be corrected by dietary interventions.

It is well known that the urinary oxalate excretion is controlled by several mechanisms. Many studies have shown that the urinary oxalate excretion rate (as measured by a 24-hour urine value) was high in the normal population [20,21]. In a study by Hesse et al. [22], it has been shown that there is greater intestinal oxalate absorption in calcium oxalate stone patients. In addition, it is known that the presence of intestinal calcium can affect oxalate absorption. In another study, Robertson et al. [23]

Table 3 Comparison of the 24-hour urine parameters before and after the dietary interventions.

	Number of patients	Before diet	After diet	*p* value
Dietary intervention				
Oxalate (mg/d)	84	92.8 ± 45.4	68.6 ± 73.6	0.04
Urine volume (cc)	43	1472.3 ± 434.7	2406.2 ± 752.8	0.001
Sodium (mmol/d)	43	257.8 ± 61.8	219.3 ± 97.7	0.045
Calcium (mg/d)	28	399.4 ± 190.6	319.0 ± 170.1	0.136
Uric acid (mg/d)	21	804.28 ± 250.3	632.85 ± 323.1	0.035
Citrate (mg/d)	16	173.8 ± 172.8	450.8 ± 333.1	0.001
No intervention				
pH	108	5.706 ± 0.7	5.88 ± 0.5	0.012
Phosphorus (g/d)	108	0.84 ± 0.4	0.91 ± 0.8	0.406
Magnesium (mg/d)	108	8.27 ± 6.4	8.0 ± 4.4	0.741

$p < 0.05$ = statistically significant results.

demonstrated that urinary oxalate excretion does not differ between patients with recurrent calcium oxalate stones and the normal population. A high rate of hyperoxaluria was identified in our study, but it responded to a dietary intervention; these results show that dietary interventions are important for urinary oxalate excretion in our population. Several studies have revealed that hyperoxaluria causes an increased risk of stone formation in calcium oxalate stone patients, and the dietary intake of oxalate must be restricted in such patients [23,24]. In our study, dietary interventions for calcium oxalate patients were similarly effective, which is consistent with the results of other studies. However, the oxalate diet was not effective in the 26 female hyperoxaluria patients (in contrast to its effects in the male patients). We think that this result is related to the low number of female patients in our study. We found that the 32 patients with a family history positive for oxalate stones who received the oxalate diet did not benefit from it. We propose that urinary oxalate excretion may not depend on diet in such patients. Persistent hyperoxaluria may be present in patients with a positive family history, and dietary hyperoxaluria interventions may be less effective.

Citrate is a natural inhibitor of stone formation, and a low urinary citrate increases the risk of stone formation.

Table 4 Results for the patients receiving an oxalate diet.

	Number of patients	Oxalate value (mg/d)		*p* value
		Before diet	After diet	
Sex				
Male	58	93.8 ± 40.7	65.8 ± 75.6	0.006
Female	26	90.5 ± 55.1	74.9 ± 69.6	0.1
Family history				
Positive	32	98.7 ± 55.1	65.6 ± 41.3	0.4
Negative	52	89.2 ± 38.3	70.5 ± 88.1	0.03
Recurrent urinary infection				
Positive	5	105.9 ± 31.5	96.3 ± 73.8	0.5
Negative	79	92.0 ± 46.1	66.9 ± 73.6	0.004
Total	84	92.8 ± 45.4	68.6 ± 73.6	0.04

$p < 0.05$ = statistically significant result.

Many studies have demonstrated that the prevalence of hypocitraturia is between 19% and 63% [14,15]. In our study, the hypocitraturia prevalence was 14%. The urinary citrate changed in the 16 patients who received the citrate diet, and it has been shown that citrate-containing foods should be recommended for idiopathic recurrent calcium oxalate patients.

Hypercalciuria causes increased urinary crystallization and stone formation; however, restricting calcium is controversial. It is commonly believed that calcium should not be restricted in patients with calcium oxalate stones [18,25,26]. A study by Heller et al. [26] has shown that urinary oxalate increases when dietary calcium is restricted. In our study, we found that our dietary intervention was not effective in the 28 patients with hypercalciuria. Moreover, we found that the urinary oxalate levels were reduced by our dietary oxalate intervention. Therefore, calcium may be restricted during severe hypercalciuria. Calcium restriction is not a practical approach because the negative consequences are well known. Therefore, restricting calcium should not be advised in calcium oxalate stone patients.

Dietary sodium may cause hypocitraturia and hypercalciuria [11]. There is increased risk of stone formation when urinary sodium excretion is excessive. Kok et al. [11] showed that increasing dietary sodium by 140 to 310 mmol/day increased urine calcium range by 34%. In our study, hypernatriuria was found in 39.8% of the patients, and the dietary intervention was effective for these patients. The high rate of hypernatriuria in our study was related to the dietary habits of the patients. Hypernatriuria can benefit from dietary interventions, which can help decrease recurrences in patients with recurrent calcium oxalate stones.

Hyperuricosuria is a potential risk factor for urinary stone formation. Many studies have shown that a low-animal protein diet is protective for urolithiasis [18,20,27]. In a study by Amaro et al., the rate of hyperuricosuria was 20.2% [20]. Similarly, the rate of hyperuricosuria was 19.7% in our study. In patients with hyperuricosuria, the urine uric acid level can be reduced by dietary interventions.

Increased oral fluid intake can be readily recommended for all patients with stones. This intervention is the best measure for preventing stone recurrences. In our study, we

encouraged increased oral fluid intake for all of the patients. In our study, increased oral hydration was recommended to maintain a urine volume of more than 2 L/day. It is known that increasing urine volume reduces new stone formation in all patients with stones [18,26,28]. Borghi et al. [12] showed that the 5-year recurrence rate was reduced from 12% to 27% when urine volume was increased to more than 2 L/day. In our study, the 43 patients who received the low urine volume diet increased their fluid intake from 1470 cc/day to 2406 cc/day. Increasing fluid intake to maintain a urine output of 2—3 L/day is the most effective intervention for preventing recurrence in calcium oxalate stone patients. It should be recommended for all patients with calcium oxalate stones.

Specific dietary interventions were not recommended for pH, magnesium, and phosphorus. A significant difference before and after the dietary interventions was found for pH only; the urine pH became more alkaline after the dietary interventions. This finding demonstrates that the urine pH may be positively affected when dietary interventions are properly applied.

In summary, several metabolic abnormalities may exist in patients with recurrent calcium oxalate stones, and these abnormalities can be corrected by dietary interventions. The metabolic profiles of these patients should be evaluated to decrease stone recurrence. Dietary preventive measures should be used to increase fluid intake (sufficient to achieve a mean urinary volume of 2—2.5 L/day,) restrict sodium and oxalate, maintain a normal calcium balance, and ensure a suitable intake of citrate and uric acid. Further studies are needed to investigate the effects of dietary interventions on patients with recurrent calcium oxalate stones.

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