9 – ORIGINAL ARTICLE
CLINICAL INVESTIGATION

Influence of clinical therapy and nutritional counseling on the recurrence of urolithiasis[1]

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ABSTRACT

PURPOSE: To evaluate the influence of combined clinical therapy and nutritional guidance on the recurrence of urolithiasis.

METHODS: From our registry of patients with recurrent urolithiasis we selected 57 who had at least 5-years of follow-up. We collected 24h urine samples in order to analyze Ca, Na, uric acid, citrate, oxalate, and Mg concentrations and to assess urine volume. Patients filled out a clinical questionnaire before treatment, and abdominal radiographs and/or ultrasound were performed both before treatment and during the follow-up period. During follow-up, specific and individualized dietary advice was given based on the individual's metabolic disorders. Patients also received specific pharmacological treatment for their metabolic alterations. Outcome measures were metabolites in urine and the urolith recurrence rate. Pre- and post- intervention values were compared using tests as appropriate.

RESULTS: Fifty six of the patients were male and the majority of patients were overweight. The mean BMI was 27 kg/m^2. Urinary excretion of calcium, uric acid and sodium decreased significantly over the five year follow-up period. The number of uroliths that formed during the 5-year follow-up also decreased significantly compared to pre-treatment values.

CONCLUSION: Individualized dietary advice combined with pharmacological treatment significantly reduces long-term urolithiasis recurrence.

Key words: Urolithiasis. Drug Therapy. Feeding Behavior. Recurrence.

Introduction

Urinary lithiasis is a condition that has been recognized for centuries, and is the third most common cause of urinary tract disease. Its prevalence ranges from 2 to 20% in the population[1], with a 40 to 50% recurrence rate within five years[2]. The resulting work absenteeism and increased costs to the health system due to treatment of recurrent episodes of renal colic has major economic impact[1]. The annual cost to the U.S. of urolithiasis, including medical costs and lost work days, is about US$ 2.1 billion[3]. It is estimated that preventing urolith recurrence could result in an average savings of $2,158 ± $500 per patient/year[4].

Metabolic changes frequently occur in patients with urolithiasis[5], and metabolic evaluation should be part of the treatment protocol to allow diagnosis, and specific treatment, of possible metabolic disorders. Both dietary changes and specific drug treatments are important in urolith recurrence[6,7]. Certain nutrients may promote or inhibit urolith formation[8,9]. Drinking more liquids influences lithogenesis by increasing urinary volume and decreasing the concentration of lithogenic components[10]. There is evidence that changes in lifestyle, when combined with appropriate medication, reduce the complications and recurrence rate associated with urolithiasis[6].

In this study we evaluate the influence of combined drug therapy and nutritional guidance on urolith recurrence.

Methods

This study was approved by the Research Ethics Committee of the School of Medicine of Botucatu, UNESP (Protocol CEP 3331-2009) and all patients gave their informed consent. The medical records of 400 patients with urolithiasis were reviewed. Fifty-seven patients met the inclusion criteria (age ≥18 years, creatinine clearance ≥ 60 ml / min, minimum follow-up period of at least five years). Patients were considered to have had regular outpatient follow-up when they had three follow-up evaluations in the first year, two in the second year, and at least one per year for the remainder of the evaluation period. Pregnant women, patients who underwent any urological procedure within the six months before their first visit or during the follow-up period, and patients with hyperparathyroidism or renal tubular acidosis (RTA) were excluded from the study.

During the follow-up period the patients filled out a clinical questionnaire and underwent metabolic investigation and imaging. Patients also received specific nutrition advice and drug treatment (Figure 1).

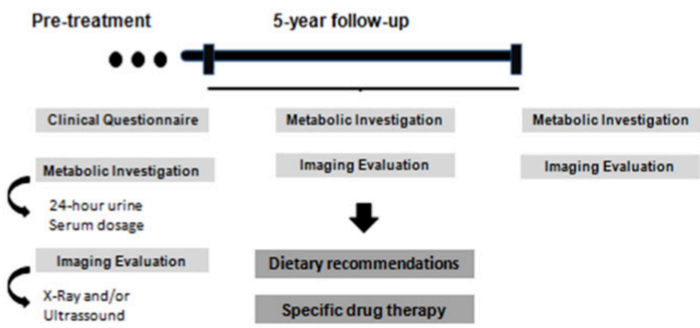

FIGURE 1 – Experimental design.

Clinical questionnaire

The patients completed a clinical questionnaire, which included questions about their age, sex, weight, height, and history of uroliths (year of disease onset and number of stones passed). Body Mass Index (BMI) was calculated using the formula described by Garrow[11] and classified according to the World Health Organization (WHO) guidelines[12].

Metabolic investigation protocol

Metabolic investigation was conducted on initial presentation and during the follow-up period. Two non-consecutive 24h urine samples were collected in order to determine concentrations of calcium (Ca), phosphorus (P), uric acid (UA), sodium (Na), potassium (K), creatinine (Cr), magnesium (Mg), chlorine (Cl), citrate (Ci), oxalate (Ox), cystine, uric acid (UA), and fasting serum glucose.

Imaging evaluation

All patients underwent ultrasound and/or abdominal radiographs at initial presentation. During follow-up examinations, these tests were repeated as needed to assess stone recurrence.

Dietary recommendations

As an initial recommendation, all patients were advised to increase their fluid intake to an amount sufficient to result in a urine volume greater than or equal to 2 liters/day. All patients were also instructed to maintain a protein intake of 0.8 to 1 g/kg body weight/ day and an adequate calcium intake (800 to 1000 mg/ day)[8]. Salt restriction (less than 5 g/ day) was recommended if appropriate based on their 24h urine sodium excretion[9]. During the five year follow-up after the initial intervention, all patients received individualized and specific nutritional guidance appropriate to their specific metabolic changes.

Drug therapy

All patients received specific pharmacological treatment according to their individual metabolic alterations (Table 1). During the five years of follow-up, drug treatments were individually modified to suit changes in metabolic profiles.

TABLE 1 - Drug therapy for diagnosed metabolic disorders.

Metabolic alteration	Medication	Dosage
Idiopathic hypercalciuria	Hydrochlorothiazide	25 to 50 mg/day
	Indapamide	2.5 mg/day
	Potassium citrate	1 to 6 g/day
Hyperuricosuria	Allopurinol	100 to 300 mg/day
	Potassium citrate	1 to 6 g/day
Secondary hyperoxaluria	Magnesium oxide	100 to 800 mg/day
Hypocitricuria	Potassium citrate	1 to 6 g/day

Evaluation of urolith recurrence

The pre-treatment urolith recurrence rate (Rp) was considered to be the average yearly number of uroliths eliminated from the time of disease onset until treatment as reported by clinical questionnaire. At the initial consultation, the number of uroliths present (NI) was determined by imaging. During follow-up, the number of uroliths spontaneously eliminated (NE) was assessed, and imaging tests were repeated to allow diagnosis of possible new urolith formation.

The urolith recurrence rate during the intervention period (R_I) was calculated by summing NE with those observed at the end of the five year follow-up (NEnd) and then subtracting NI. This result was divided by five to obtain the average number of uroliths formed per year (Figure 2).

$$RI = \frac{NE + NE_{nd} - NI}{5}$$

Abbreviations: **RI**, Recurrence during the intervention period; **NE**, number of stones eliminated in the period of 5 years; **NEnd**, number of stones at the end of 5 years; **NI**, number of stones in the initial evaluation.

FIGURE 2 - Formula for calculating the yearly urolithiasis recurrence rate.

Statistical analysis

Data were analyzed using SPSS. The periods before and during the intervention were compared using exploratory inferential analysis. In the presence of Gaussian distribution the paired t test was used and, when the data were not normally distributed, the nonparametric Wilcoxon test was used. Differences were considered statistically significant when $p<0.05$.

Results

The patients had a mean age of 45.7 years (ranging from 20 to 55 years), 56% were male, and their mean initial BMI was 27.8 kg/m². There was a positive correlation between BMI and the Rp (p=0.012). On average, 11.28 appointments per patient were conducted during the 5-year follow-up period. The main metabolic abnormalities during at initial presentation were hypercalciuria in 56%, hypocitraturia in 44%, hyperoxaluria in 36% and hyperuricosuria in 33% of patients. Urinary calcium and sodium concentrations were positively correlated during the pre-treatment period (p=0.048).

There were no statistically significant differences in mean BMI or urinary volume when the pre- and post-treatment periods were compared. The concentrations of calcium, sodium and uric acid in the 24h urine samples were significantly lower during the post-treatment period. A concomitant increase in citrate in the 24h urine sample post-treatment was also observed (Table 2).

TABLE 2 - BMI and metabolic parameters before intervention and at the end of the five year follow-up period.

Variable	Evaluation period		Statistical Analysis (p)
	Pre-treatment	5 year follow-up	
BMI (kg/m²)	27.83 ± 4.28	28.25 ± 4.3	0.228
Urine Volume (ml/24h)	1752.37 ± 657.68	1730.2 ± 477.86	0.822
Calcium (mg/24h)	344.15 ± 170.88	217.32 ± 124.43	< 0.001
Sodium (mEq/24h)	275.17 ± 117.18	223.92 ± 63.81	< 0.005
Uric acid (mg/24h)*	650.0 (312.0; 2846.0)	543.0 (245.0; 1267.0)	< 0.001
Citrate (mg/24h)*	383.0 (50.0; 1955.0)	466.0 (18.7; 1980.0)	< 0.009

*Median (minimum value, maximum value)

The number of stones during the 5-year follow-up period decreased significantly relative to the pre-treatment period (Table 3).

TABLE 3 - Urolithiasis recurrence rates before and after the 5 year follow-up period.

Evaluation period		Statistical Analysis (p)
Pre-treatment	5 years	
0.60 (0.06; 6.5)	0.00 (0.00; 1.4)	< 0.001

Discussion

Recent epidemiological studies have shown an increasing prevalence of urolithiasis in both sexes[13]. This increase has been greater in women than in men, resulting in a decrease in the male:female ratio (from 1.7:1 to 1.3:1) of affected patients. This change may be related to increased body weights and changes in lifestyle among women[13,14]. In this study we observed a similar trend; the male:female ratio of the patients in this study was 1.3:1.

Many of the patients in this study were overweight and there was a positive relationship between BMI and urolith formation. Some authors[15,16] have shown that being overweight or obese is a risk factor for urolithiasis. Weight gain may also be related to the formation of kidney stones[17] , and weight reduction can decrease the excretion of lithogenic salts in the urine[18]. In this study, significant weight gain was not observed during the follow-up period. The dietary guidance provided to the patients probably prevented weight gain during the 5-year follow-up, which may have contributed to the reduced urolith recurrence rate.

Identification and correction of the metabolic disorders that may cause urolithiasis is critical to preventing its recurrence[19]. In our patients, diet change coupled with specific pharmacological treatments had an important influence on urolith recurrence. The relationship between sodium intake and increased urinary calcium excretion is well established[20]. In another study, dietary salt intake was significantly higher in patients with idiopathic hypercalciuria[9]. We observed a direct relationship between urinary calcium and sodium in the pre-treatment period, demonstrating that salt intake is an important lithogenic factor.

Increasing fluid intake is an important first intervention in the general treatment of urolithiasis[1]. Controlled studies have shown that increasing urine volume to 2 liters/day can reduce urolith recurrence[10]. In this study, there was no difference in the proportion of patients whose urine volume was greater than or equal to 2000 ml during the pre- and post-treatment periods (28% (16/57) *vs*. 33% (16/49), respectively; p>0.05). Although all patients in this study were advised to increase their fluid intake, few complied with this recommendation. This demonstrates the difficulty of using only this increased fluid intake as a strategy for the prevention of urolithiasis.

There was a significant decrease in urolith recurrence, as well as in urinary calcium and uric acid concentrations, over the five years follow-up period. This suggests that our intervention decreased the excretion of these solutes, thus preventing urolith formation and recurrence. Parks and Coe[21] also reported a long-term reduction in urolith recurrence and urine calcium excretion in patients receiving dietary guidance and drug treatment. Other authors also found similar results in a controlled study[22].

Preventing urolith recurrence may decrease the costs associated with urolithiasis and have an important economic impact. However, there are few studies similar to this one available in the literature. This suggests that there is a need for greater involvement of different professionals in the prevention of urolithiasis.

Conclusion

Individual dietary guidance combined with specific drug treatment significantly reduces long-term recurrence of uroliths.

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