Original Article

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Effect of Potassium Citrate on Prevention of Recurrence and Expulsion of Residual Fragments of Calcium Oxalate renal Stones

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Abstract

Considering potassium citrate ability to induce urine alkalization, it might be useful in the treatment and prevention of renal stones formation. This study aimed to evaluate the preventative effect of potassium citrate on expulsion of residual fragments and recurrence of calcium oxalate renal stones. The study was conducted on 96 adult patients who were referred to Shahid Faghihi hospital, an affiliate of Shiraz University of Medical Sciences, who underwent surgical intervention with detected and cleared calcium oxalate renal stones (more than 60% of stones component). The patients did not have urinary tract infections or urogenital anomalies. Four weeks following the treatment of urolithiasis, patients cleared from the renal stones (n=58) and patients with urinary residual stones (n=38) were divided into two age- and sex-matched groups. Each group was divided into two subgroups. One subgroup received 40 mEq of oral potassium citrate daily for one year while the other was observed. All 4 subgroups were encouraged to high fluid intake with low salt, low oxalate diet. A significant difference in recurrence rate of renal stone was seen in the untreated subgroup (25.86%) compared with the treated subgroup (1.72%) in the stone-cleared group. In the patients with residual urinary fragments, a significant decrease in stone fragments was reported in the treated subgroup (72.22%) in comparison with the untreated subgroup (33.33%). The findings demonstrated that the administration of potassium citrate has a beneficial expulsive effect on residual stone fragments. Also, it causes a significant decline in the recurrence rate of calcium oxalate renal stones.

Keywords: Potassium citrate, Renal stone, Calcium Oxalate, Stone Expulsion.

1. Introduction

Renal stones are of major clinical and health concerns, which can cause a large burden of the disease (1-3). Calcium oxalate (CaOx) stones constitutes more than 60% of kidney stones. It comes with various underlying risk factors such as hypercalciuria, hypocitraturia, hyperoxaluria, low urine volume, and abnormalities in urine pH (4, 5).

Although there are various methods for the treatment of renal stones, recurrence of renal calculi reduces the success rate of most therapeutic methods (6, 7). However, there are treatment protocols for avoiding the recurrence of renal calculi and prevention of the formation of stones in stone cleared individuals such as changing urine pH (8-10).

Recently, the administration of potassium citrate has been considered as an alternative therapeutic and preventive method for such cases, especially for the treatment of calcium oxalate nephrolithiasis (11, 12). There are some advantages for alkali citrate in clearing calcium-based renal stones; it elevates the levels of urinary citrate and provides alkalization of the urine, which is ben-

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eficial for patients with uric acid stones (13, 14). Such advantages of alkali citrate suggest its application for treatments of a wide range of urinary stones. This study aimed to assess the effects of potassium citrate on residual fragments of calcium oxalate renal stones and the recurrence rate.

2. Material and method

2.1. Study Population

The current study was carried out from December 2017 to January 2019 on 137 patients with a documented history of calcium oxalate renal stone who were referred to Shahid Faghihi Hospital, an affiliate of Shiraz University of Medical Sciences. Calcium oxalate was the main component of their stones (more than 60% of stones) according to stone analysis. All patients were given enough information about the medication, and informed written consent was obtained. The study was conducted after obtaining Research Ethics Committee approval and was registered by IR.SUMS.REC 1398.1394 code.

2.2. Study Protocol

Patients aged 18 to 70 years old who underwent urolithiasis surgery were recruited. Patients with residual stone fragments (less than 5 mm stone diameter) and those who were stone-cleared post-operation were included in this study. All patients were consented to be involved in the study.

Patients with 1) urinary tract infection (n=9), 2) other anatomical, metabolic, or structural urogenital abnormalities (n=3), 3) those who were out of the age range (n=5) were excluded from the study, and 4) patients who did not tolerate the medication (n=24) were not included in this study.

All patients underwent a detailed urinalysis investigation. Abdominal plain x-ray radiography and ultrasound scans were performed, and patients were divided into two age- and sex-matched groups. They were grouped as stone-cleared (n=58) and residual stone fragments (n=38). Then, the patients of each group were divided into two subgroups. In each group, one subgroup was given potassium citrate 40 mEq per day orally (2 tablets of 5meq Urocitra® four times daily), and the other subgroup was considered as the control group.

All patients were recommended to high fluid intake, low salt diet, and also reduce oxalate-rich foods. Patients were examined 6 and 12 months later, and abdominal X-ray and ultrasonography were done for each patient to determine the presence of renal stones. Urinalysis investigation was done for all patients, and it was reviewed in terms of volume, calcium, citrate, uric acid, and creatinine level. Hypercalciuria was defined if early morning calcium to creatinine ratio was >0.8. Uric acid to creatinine ratio more >1 was considered as hyperuricosuria, and Hypocitraturia was reported in cases with citrate to creatinine ratio of less than 0.51.

2.3. Statistical Analysis

Obtained data was analysed using SPSS software version 19.0, and reported as descriptive reports, including Mean±Standard deviation. Non-parametric data was compared using the Chi-square test. P-values less than 0.05 were considered as statistically significant.

3. Results

Ninety-six patients were enrolled in this study, including 50 men and 46 women. The mean age of the patients was 47.62±27.95 years ranged from 18 to 68 years. The mean age of stone-cleared patients treated with potassium citrate (n=29) was 40.01±21.31, while it was 39.31±32.01 in the control subgroup. In residual fragment group, the mean age of treated patients (n=19) was 38.12±13.88, and it was 39.74±29.33 for the control subgroup. The frequency of hypocitraturia in treated and control subgroups of stone-cleared group was 7 (12.06%) and 8 (13.79%), respectively. In the residual fragment group, hypocitraturia frequency was 7 (18.42%) in the treated subgroup and 9 (23.68%) in the control subgroup.

The frequency of hypercalciuria in treated and control subgroups of the stone-cleared group individuals was 3 (4.36%) and 4 (6.89%), respectively. Hypercalciuria frequency was 3 (7.89%) in the treated subgroup and 5 (13.15%) in the control subgroup of the residual fragment group.

In the stone-cleared group, hyperuricosuria was seen in 2 (3.44%) patients of the treated subgroup, while it was seen in 1 (1.72%) patient

Table 1. Para-clinical findings of the patients with stone-cleared and residual fragment groups treated and non- treated by potassium citrate.

Variables	Stone-cleared group(n=58)			Residual fragment group(n=38)		
	Treated with Potassium Citrate(n=29)	Control Group(n=29)	p	Treated with Potassium Citrate(n=19)	Control Group(n=19)	p
Male	16 (55.2%)	18 (62.1%)	0.790	9(47.4%)	7 (36.8%)	0.743
Female	13 (44.8%)	11(37.9%)		10(52.6%)	12(63.2%)	
Age (Mean±SD), years	40.01±21.31	39.31±32.01		38.12±13.88	39.74±29.33	
Normocitraturia	25(43.10%)	21(36.20%)	0.659	12(31.57%)	10(26.31%)	0.832
Hypocitraturia	7(12.06%)	8(13.79%)	1.00	7(18.42%)	9(23.68%)	0.804
Normocalciuria	29(50.00%)	25(43.10%)	0.683	16(42.10%)	14(36.84%)	0.856
Hypercalciuria	3(4.36%)	4(6.89%)	1.00	3(7.89%)	5(13.15%)	0.727
Normouricosuria	30(51.72%)	28(48.27%)	0.896	18(47.36%)	17(44.73%)	1.00
Hyperuricosuria	2(3.44%)	1(1.72%)	1.00	1(2.63%)	2(5.26%)	1.00

of the control subgroup. In the residual fragment group, hyperuricosuria was seen in 1 (2.63%) patient of the treated subgroup and 2 (5.26%) patients of the control subgroup.

Among the patients with a history of calcium oxalate renal stones, who were stone-cleared and received potassium citrate, one patient developed calcium oxalate urolithiasis. However, among patients who did not receive potassium citrate, 15 had renal stones.

So, the stone recurrence rate for the treatment subgroup was 1.72%, while it was 25.86% in the control sub-group after 12 months. This difference was statistically significant (p=0.015) (Table 2).

In the present study, most of the patients had normal levels of urine uric acid, citrate, and urine calcium, and there was no significant correlation between stone formation and hypocitraturia, hypercalciuria, nor hyperuricosuria.

In patients with residual urinary fragments, among those who were treated with potassium citrate, five patients had calcium oxalate renal calculi (27.77%), which means 72.22% decline in stone fragments. Renal stones were detected in 12 patients in the residual fragment control subgroup (66.66%), indicating 33.33% decline in renal stone formation. The difference between the two subgroups was also statistically significant. (p=0.032).

The effects of potassium citrate on renal stones formation are summarized in table 2.

4. Discussion

Although there are several treatment methods for removing renal stones, the risk of renal stone recurrences seems to be one the main subjects in urology (1). In a study, the overall stone-free rate for lower pole calculi was 53.3% (2). Recently, studies have focused on the efficacy

Table 2. The effects of potassium citrate on renal stones formation in stone-cleared group and Residual fragment group.

Variables	Subgroups	12-months stone recurrence	Stone formation
Stone free group	Treated with Potassium Citrate	1 (1.72%)	-
	Control Group	15 (25.86%)	-
Residual fragment group	Treated with Potassium Citrate	-	5 (27.77%)
	Control Group	-	12 (66.66%)

of the chemical methods such as changing urine pH for treatment of urolithiasis (3). For example, oral citrate medication has been considered in patients with calcium oxalate stones (4, 5). Citrate inhibits the aggregation of calcium oxalate crystals and exhibits prophylactic medical properties for new stone formation (6).

Citrate is a natural substance that inhibits urinary calcium stone formation due to change in urine pH (6, 7). Also, studies have revealed that treatment of hypocitraturia, can largely decrease stone formation especially in renal stones with calcium basis (8, 9).

In the present study, we assessed the effect of potassium citrate on recurrence and residual fragments of calcium oxalate renal stones. In one study, the formation of stones were substantially reduced (91%) in individuals treated by citrate orally (5). Similarly in the present study, we found that administration of potassium citrate for patients with residual urinary stones declined the stone frequency by as much as 72.23%, while in control patients with other curative methods it was about 33.33%.

In addition, the present study indicated that potassium citrate has the capability to inhibit calcium oxalate formation. The 12-month recurrence rate of calcium oxalate stone formation in our patients treated by oral citrate was 1.72%, while in the un-treated individuals, it was 25.86%. This constituted a near 25 times greater difference ($p<0.05$).

In the present study, the experimental subgroups received potassium citrate 40 mEq per day orally (2 tablet of 5meq Urocitra® 4 times daily), and the other subgroups were considered as control. Our findings revealed effects of the administration of potassium citrate on prevention of stone formation.

In this study, we evaluated the effect of potassium citrate on residual fragment expulsion and recurrence of calcium oxalate renal stones. One of the main strengths of the present study was comparison of the outcome of the administration of potassium citrate on calcium oxalate stones in stone free and stone residual individuals with individual who did not received the medication. However, our findings corroborated the findings in other similar studies. In the present study, 12-months stone recurrence and stone formation were evaluated with or without administration of potassium citrate.

One of the main limitations of the present study was the limited sample size of the study, which could be developed in a complementary study with larger duration and also involving more clinical and para-clinical variables. In addition, there was no definite data about urine pH before and after the administration of potassium citrate to clarify the exact effect of pH on formation of the stones.

5. Conclusion

Our study revealed that administration of potassium citrate led to significantly reduced recurrence rates of calcium oxalate renal stones. Also it has a good expulsive effect on residual fragments. Although, we suggest a larger sample size in a multicenter study.

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Conflict of Interest

None declared.

6. References

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