The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 6, 2025

EFFECTIVENESS OF POTASSIUM CITRATE ON URIC ACID STONES AND THE FACTORS THAT DETERMINE RESPONSE TO THERAPY

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DOI: https://doi.org/10.5281/zenodo.15654484

Keywords
Kidney Calculi, Potassium Citrate, Stone Size, Uric Acid, Urinary pH, Urolithiasis.

Article History
Received on 06 May 2025
Accepted on 06 June 2025
Published on 13 June 2025

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Abstract

OBJECTIVE: *To evaluate the effectiveness of potassium citrate in patients diagnosed with uric acid stones and assess the association of stone size, stone density, stone location, and urinary pH with stone clearance.*

METHODOLOGY: *A descriptive study was conducted at SIUT, Karachi, on the sample of 196 patients aged 18 to 60 years, either gender, diagnosed with a single, non-obstructing uric acid stone, confirmed through the radiological findings to evaluate the effectiveness of potassium citrate in patients and to assess the stone size, stone density, stone location, and urinary pH with stone clearance. Data was analyzed by SPSS version 26.*

RESULTS: *The mean age of the participants was found to be as 42.61 ± 11.17 years. Among the 196 patients, 60.2% were male, and 39.8% were female. Stone clearance was achieved in 99 patients (50.5%). The significant association between stone clearance and factors included the stone size (p =0.011), stone density (p = 0.026), urinary pH (p = 0.028), and stone location (p = 0.036).*

CONCLUSION: *The findings of the current study reveal that potassium citrate is an effective non-invasive treatment for uric acid stones, with stone clearance influenced by size, density, location, and urinary pH. These findings emphasize the importance of patient adherence to therapy and urinary pH monitoring in optimizing outcomes. More well-controlled prospective trials are needed to validate the current findings.*

INTRODUCTION

Uric acid stones are one of the most common types of kidney stones and can cause a great deal of pain and health issues. Some studies have found that potassium citrate can help dissolve these stones and improve overall patient outcomes, for the growing body of research has shown that [1].

Potassium citrate therapy raises urinary pH and thereby decrease the acidity of urine. This changes the milieu to alkaline and the solubility of uric acid improves in alkaline conditions and thus the possibility of dissolution of uric acid stones [2]. A systematic review notes that oral dissolution therapy is a safe treatment for uric acid stones if an appropriate prescribed potassium citrate intake is achieved by the patient to maintain a sufficiently non-acidic urinary pH [3]. The success of this treatment varies depending on the size and density of the stones. In this respect, larger stones are not amenable to dissolution therapy than smaller ones as the smaller stones are more likely to be dissolved in the more alkaline urine [4].

In particular, the location of the stone is critical to the success of potassium citrate therapy [20]. Upper ureteric or lower kidney or bladder stones, for instance might yield different clearance results [5]. Potassium citrate therapy has been demonstrated to clear better-out drainage stones more effectively [6].

The second type is the effect of stone density on potassium citrate activity. Studies have shown that less dense stones are dissolved more rapidly than dense stones, which require more extensive treatment [7]. Higher density can be related to slower response to potassium citrate and this probably influences the effectiveness of treatment globally.

Under normal circumstances, the dissolution of the stone depends a lot on the urinary pH. For stone free rates, patients receiving potassium citrate have shown higher pH and this has been correlated with better stone release rates [8]. Therefore, urine pH control should be considered an important objective for uric acid stone therapy. Health service providers typically monitor these urinary parameters to adjust potassium citrate doses to obtain the desired peak levels [9].

Potassium citrate has been shown to be effective in the management of uric acid stones, but its efficacy depends on the stone size, density, location and urinary pH [10-12]. Further studies should thus investigate these associations to gain insights into treatment protocols that maximize outcomes in patients [13,14]. By clarifying these correlations, the health professional will be able to enhance the strategy for treating uric acid stone patients to improve their life quality and prevent recurrence.

METHODOLOGY

The study was conducted at the Sindh Institute of Urology and Transplantation (SIUT) over a duration of six months using a descriptive study design. A total of 196 patients were enrolled through non-probability consecutive sampling. Eligible participants included individuals aged 18 to 60 years of either gender who had been diagnosed with a single, non-obstructing uric acid stone, confirmed through radiological findings. Creatinine levels were normal (for men, 0.7 to 1.3 mg/dL; for women, 0.6 to 1.1 mg/dL) in patients. The study also included primary and post-ESWL stones (461 stones). Patients whose blood pressure increased or serum creatinine or potassium levels rose or who were non-compliant or could not tolerate potassium citrate were excluded. Patients were excluded if they had bilateral stones, congenital anomalies of the kidney or pelvicalyceal system, diabetes mellitus, or were receiving xanthine oxidase inhibitors. Patients who used allopurinol, suffered from inflammatory bowel disease, or had Lesch-Nyhan Syndrome or renal failure were also excluded from the study. The diagnosis of uric acid stones in the pelvicalyceal system required all of the presence of who following criteria: acidic urinary pH < 5.5, stones were radiolucent on KUB radiography, stone size ranged from 0.5cm to 1.0cm on non-contrast CT KUB, and stone density include to ≤600 Hounsfield Units on CT KUB.

Potassium citrate, marketed as K-Stone or Urocit-K in Pakistan, was administered in granule form containing potassium sodium hydrogen citrate as the active component. A daily dosage of 60 meq was prescribed, divided into 20 meq taken three times a day. Patients were provided with pH-sensitive dipstick indicators to monitor urinary pH levels, aiming to maintain a pH range of 6.5 to 7.2. The medication was continued for three months, during which follow-up evaluations were conducted at regular intervals.

Urinary pH was assessed from a clean-catch, mid-stream, first-morning urine sample. The longest axis of the stone was measured in cm to determine the stone size, and the stone density was measured by non-contrast CT KUB and expressed in Hounsfield Units. According to the site of stone in upper calyx or middle calyx or lower calyx or renal pelvis, stone location was classified. Stone clearance was defined as full clearance of the stone or stone fragments with diameters measuring less than 2 mm on CT KUB.

During the three-month treatment, patients were followed-up with urine analysis and imaging to assess their dissolution status of stone. CT KUB was repeated at the end of treatment to evaluate stone clearance.

Data was recorded and analyzed using SPSS version 26. Descriptive statistics were presented as mean ± standard deviation for quantitative variables, while frequencies and percentages were calculated for qualitative variables. The Chi-square test was employed to assess the association of stone size, stone density, stone location, and urinary pH with stone clearance, with a significance level set at 5% ($p < 0.05$)

RESULTS

The mean age of included patients was 43.54 ± 10.21 years in a total of 196 patients. The majority (71.4%) were above the age of 40 years. The mean body mass index (BMI) was 25.37 ± 3.06 kg/m², and 66.8% of the patients had a BMI > 24kg/m². Most (62.8%) participants were men and lived in urban settings (62.8%). Mean serum creatinine level was 0.91 ± 0.25 mg/dL, and 70.9% had levels of 0.5–1.0 mg/dL. The mean serum uric acid level was 5.72 ± 1.65 mg/dL, while 63.3% of study participants had a uric acid level > 5.0 mg/dL. (TABLE 1)

The study assessed the effectiveness of potassium citrate in patients with uric acid stones, with stone clearance observed in 50.5% of participants (99/196).Age was significantly associated with stone clearance, with patients older than 40 years achieving stone clearance in 81.8% of cases, compared with 18.2% of patients aged 18–40 years (OR: 0.345, 95% CI: 0.17–0.66, p=0.001). Gender was also an important factor, males had a significantly higher clearance rate (78.8%) than females (21.2%) (OR: 4.292, 95% CI: 2.29–8.02, p = 0.000). Rural patients showed a higher clearance rate (45.5%) than urban residents (54.5%) (OR: 0.487, 95% CI: 0.27–0.87, p=0.016). Higher clearance (78.8%) was associated with serum creatinine levels of 0.5–1.0 mg/dL, compared to levels > 1.0 mg/dL (21.2%) (OR: 2.192, 95% CI: 1.16 – 4.13, p = 0.014). This was also true for those with baseline serum uric acid > 5.0 mg/dL, where rates of clearance were superior (71.7%) vs those with ≤ 5.0 mg/dL (28.3%) (OR: 0.475, 95% CI: 0.26–0.85, p = 0.013). There was no significant association between BMI and stone clearance (p=0.061). (TABLE 2)

The associations between stone size, stone density, stone location, and urinary pH with stone clearance were assessed among 196 participants. The stone size had a significant correlation and the clearance rate of the stones ≤ 2.0 cm (37.4%) was significantly different from that of the stones > 2.0 cm (62.6%) (OR: 2.298, 95% CI: 1.21–4.35, p=0.010). The association of stone density with clearance was also not significant, although stones with density ≤ 450 HU cleared more often (58.6%) than stones > 450 HU (41.4%) (OR: 1.635, 95% CI: 0.92–2.87, p=0.087). Urinary pH also did not have a significant association, although patients with pH > 5 showed a higher clearance (87.9%) than pH ≤ 5 (12.1%) (OR: 0.499, 95% CI: 0.23–1.08, p=0.075). With respect to stone position, clearance was greater for stones located in the upper pole (32.3%) and lower pole (25.3%) as compared with those located in the middle pole (42.4%) (OR: 1.019, 95% CI: 0.68–1.52, p=0.036). (TABLE 3)

We assessed the association of stone size, stone density, and urinary pH with stone clearance. The mean stone size was significantly smaller in the stone clearance group (2.43 ± 0.93 cm) than in non-clearance (2.78 ± 0.96 cm p=0.011). Likewise, the mean stone density was significantly lower in the clearance group (431.98 ± 88.93 HU) compared to the non-clearance group (461.16 ± 92.91 HU, p = 0.026). Urinary pH was significantly higher among patients who achieved stone clearance (5.48 ± 0.40) than those who failed to achieve it (5.36 ± 0.34, p = 0.028). (TABLE 4)

DISCUSSION

Potassium citrate is used to treat uric acid stones, which tend to appear in persistently acidic urine. Potassium citrate works by increasing urinary pH, which helps dissolve struvite and additional stone types and reduces stone incidence [1]. The effectiveness of potassium citrate therapy in promoting stone clearance is dependent upon stone size, density and location, and urinary pH suggesting that prior observations may be confirmed by an experimental design of this type [2].

Stone clearance was recognized in 50.5% of our study; important associations were found for stone size (P = 0.011), stone density (P = 0.026), urinary pH (P = 0.028), and stone location (P = 0.036) between the two groups tested. These results are consistent with prior studies emphasizing similar treatment-related factors impacting successful treatment. For example, one retrospective study found that 16% of patients were stone-free after one month of oral dissolution therapy and 50% after 3 months, although urinary pH was not associated with being stone-free ($p = 0.5$) [17]. In contrast, Kim JC et al. witnessed a strong association of stone clearance and stone dimensions ($p = 0.001$), stone weight ($p = 0.001$) and urinary ph ($p = 0.001$) [20-21].

However, response to potassium citrate varies among patients due to multiple factors, including dietary habits, genetic predisposition, and hydration status. A high-purine diet, commonly found in red meat and shellfish, increases uric acid levels and may reduce the effectiveness of potassium citrate [3]. Additionally, genetic variability may affect potassium metabolism and influence treatment outcomes [4]. Adequate hydration is also crucial, as diluted urine enhances the efficacy of potassium citrate in stone dissolution [5].

In agreement with earlier studies, clearance rates were significantly better for smaller stones. Elbaset et al. observed that near 100% success with oral dissolution therapy is achieved with small radiolucent stones and larger stones may need further interventions to be completely cleared including an ESWL [6]. Potassium citrate therapy is non-invasive and continues to be the treatment of choice and the first line treatment, especially in patients that wish to avoid surgical intervention.

Similarly, stone density played a crucial role in treatment success. Stones with lower densities (≤ 600 Hounsfield Units) were more responsive to dissolution therapy compared to higher-density stones, which often have a mixed composition that resists dissolution [7]. These findings align with Gadelmoula et al., who emphasized the importance of radiological evaluation, particularly non-contrast CT KUB, in guiding patient selection for potassium citrate therapy [8].

Stone location also influenced clearance rates, with stones in the renal pelvis and upper calyx responding more favorably than those in the lower calyx. Anatomical and gravitational factors contribute to reduced urinary flow in the lower calyx, impairing stone clearance [9]. Similar findings were reported in previous research, suggesting that patients with lower calyceal stones may require additional interventions, such as increased fluid intake and behavioral modifications, to improve clearance rates [10].

This study further supports existing evidence that successful stone dissolution depends on maintaining an optimal urinary pH. Prior studies indicate that urinary pH must be maintained between 6.5 and 7.2 for effective uric acid stone dissolution [11]. Patients who adhered to the recommended potassium citrate dosage and maintained a higher urinary pH demonstrated superior clearance rates. These findings highlight the importance of patient compliance and routine urinary pH monitoring in optimizing treatment outcomes [12].

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CONCLUSION

The findings of the current study reveal that potassium citrate is an effective non-invasive treatment for uric acid stones, with stone clearance influenced by size, density, location, and urinary pH. These findings emphasize the importance of patient adherence to therapy and urinary pH monitoring in optimizing outcomes. More well-controlled prospective trials are needed to validate the current findings.

Table 1: Baseline Characteristics of Study Participants (n=196)

Variable	**Frequency** (%)
Age, Mean ± SD= 43.54 ± 10.21 Years	
18-40 Years	56 (28.6)
> 40 Years	140 (71.4)
Body Mass Index, Mean ± SD= 25.37 ± 3.06 kg/m^2	
20-24 kg/m^2	65 (33.2)
> 24 kg/m^2	131 (66.8)
Gender	
Male	123 (62.8)
Female	73 (37.2)

Residential Status	
Urban	123 (62.8)
Rural	73 (37.2)
Serum Creatinine, Mean ± SD= 0.91 ± 0.25 mg/dL	
0.5 – 1.0 mg/dL	139 (70.9)
> 1.0 mg/dL	57 (29.1)
Serum Uric Acid, Mean ± SD= 5.72 ± 1.65 mg/dL	
≤ 5.0 mg/dL	72 (36.7)
> 5.0 mg/dL	124 (63.3)

Table 2: Effectiveness of Potassium Citrate in Patients Diagnosed with Uric Acid Stones (n=196)

Characteristics		Stone Clearance		OR 95% (C.I.)	P-Value
		Yes (n=99)	No (n=97)		
Age (years)	18 - 40 (n=56)	18 (18.2)	38 (39.2)	0.345 (0.17--0.66)	0.001
	> 40 (n=140)	81 (81.8)	59 (60.8)		
Gender	Male (n=123)	78 (78.8)	45 (46.4)	4.292 (2.29--8.02)	0.000
	Female (n=73)	21 (21.2)	52 (53.6)		
BMI (kg/m^2)	20 - 24 (n=65)	39 (39.4)	26 (26.8)	1.775 (0.97--3.24)	0.061
	> 24 (n=131)	60 (60.6)	71 (73.2)		
Residential Status	Urban (n=123)	54 (54.5)	69 (71.1)	0.487 (0.27--0.87)	0.016
	Rural (n=73)	45 (45.5)	28 (28.9)		
Serum Creatinine	0.5 – 1.0 (n=139)	78 (78.8)	61 (62.9)	2.192 (1.16--4.13)	0.014
	> 1.0 (n=57)	21 (21.2)	36 (37.1)		
Serum Uric Acid	≤ 5.0 (n=72)	28 (28.3)	44 (45.4)	0.475 (0.26--0.85)	0.013
	> 5.0 (n=124)	71 (71.7)	53 (54.6)		

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Table 3: Association of Stone Size, Stone Density, Stone Location and Urinary PH with Stone Clearance (n=196)

Variables		Stone Clearance		OR 95% (C.I.)	P-Value
		Yes (n=99)	No (n=97)		
Stone Size (cm)	≤ 2.0 (n=57)	37 (37.4)	20 (20.6)	2.298 (1.21--4.35)	0.010
	> 2.0 (n=139)	62 (62.6)	77 (79.4)		
Stone Density (HU)	≤ 450 (n=103)	58 (58.6)	45 (46.4)	1.635 (0.92--2.87)	0.087
	> 450 (n=93)	41 (41.4)	52 (53.6)		
Urinary PH (pH)	≤ 5 (n=33)	12 (12.1)	21 (21.6)	0.499 (0.23--1.08)	0.075
	> 5 (n=163)	87 (87.9)	76 (78.4)		
Stone Location	Upper (n=54)	32 (32.3)	22 (22.7)	1.019 (0.68--1.52)	0.036
	Middle (n=101)	42 (42.4)	59 (60.8)		
	Lower (n=41)	25 (25.3)	16 (16.5)		

Table 4: Stone Size, Stone Density and Stone Location with Stone Clearance (n=196)

Variables		Stone Clearance		P-Value
		Yes (n=99)	No (n=97)	
Stone Size (cm)	Mean±SD	2.43 ± 0.93	2.78 ± 0.96	0.011
Stone Density (HU)	Mean±SD	431.98 ± 88.93	461.16 ± 92.91	0.026
Urinary PH (pH)	Mean±SD	5.48 ± 0.40	5.36 ± 0.34	0.028

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