Original Article

# The safety of ureteral stenting with the use of potassium citrate for management of renal uric acid stones

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## Abstract

**Objectives:** The objective is to evaluate the relative risks of ureteric stents application while managing uric acid stones with potassium citrate in terms of stone encrustations and urinary tract infection (UTI).

**Patients and Methods:** We prospectively enrolled patients with renal uric acid stones who received K citrate from 2013 to 2018. Patient's demographics were collected. All patients were evaluated using noncontrast computed tomography (CT) scan to measure the stone size and density. JJ ureteric stent was inserted prior to the initiation of treatment. At follow-up, all patients underwent urine analysis for pH and to detect UTI. CT was repeated at 1 month and those patients who showed incomplete stone resolution underwent another course of treatment for another month. CT was repeated prior to stent removal. The presence of encrustations was inspected and collected.

**Results:** We collected 59 patients with a median age of 36 years (18–73) and median stone burden of 26 $mm^3$ (15–50). The median stone density was 310 HU (175–498). Twenty-one patients (35.6%) received K citrate treatment for 1-month, while the remaining patients had 2 months treatment. Sixteen patients (27.1%) had a complete stone dissolution, 41 patients (69.5%) had more than 50% decrease of stone burden while only 2 patients (3.4%) had stones with poor dissolution. Four patients (6.8%) experienced UTI while 2 patients (3.4%) had visible JJ encrustations. Most of these complications occurred when the treatment was offered for the 2nd month.

**Conclusion:** Short-term use of ureteral stents is safe during the management of uric acid stones with K citrate.

**Keywords:** K citrate, stones, ureteral stents, uric acid

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## INTRODUCTION

Uric acid stones account 5%–10% of urinary tract stones and its prevalence increases in areas with hot climates due to low urine output and presence of acidic urine.[1] Uric acid stones could be managed medically by changing the urine pH to be alkaline. The target urinary pH preferably ranges between 6 and 6.5.[2] Potassium citrate is considered the best alkalinizing agent in uric acid stones management. Medical dissolution showed to be efficient in complete clearance of uric acid stones in 15%–79% of patients.[3-6]

Ureteral stenting is sometimes required during the management of renal stones which could be left for a few

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months or require an exchange. The indications of ureteral stenting include, but not limited to, the violation of urine flow in the upper urinary tract, marked hydronephrosis, and raising serum creatinine. Temporary ureteric stent insertion is not without complications. Urinary tract infection (UTI) and incrustation are considered one of the questionable stent-related problems.[7] We hypothesized that the ureteral stent is safe during the treatment of uric acid stones using potassium citrate with an acceptable complication rate. In the current study, we present our experience in managing uric acid renal stone with potassium citrate after JJ insertion.

## PATIENTS AND METHODS

We prospectively recruited consecutive patients who had renal uric acid stones and underwent JJ insertion. Patients were presented to our clinic from October 2013 to October 2018 were included in our study after obtaining informed consent. We recruited patients with normal serum creatinine, acidic PH on two consecutive urine analyses. JJ stenting was indicated if the patient developed refractory intractable pain or there was ipsilateral moderate or severe hydronephrosis. Moreover, JJ stent was inserted if the patient had rising serum creatine; however, the management using potassium citrate never started before returning to normal condition. We excluded patients who presented initially with febrile UTI (FUTI) to avoid the bias related to the pyogenic biofilm around the JJ. Moreover, patients with stone burden >50 $mm^3$ were excluded from the study.

We collected patients' characteristic including age, gender, the cause of presentation, and side of the stone. All patients were initially assessed by urine analysis to exclude UTI and collect urine pH. All patients with urine pH more than 5.5 were excluded due to the low possibility of uric acid stones formation.[8] Moreover, serum uric acid level was obtained. All patients underwent a preliminary kideny, ureter, and bladder X-ray (KUB) to ensure translucency of stones. Computerized tomography of the urinary tract with no contrast was performed for all included patients. We recorded the stone burden and stone density at presentation. The stone burden was defined as a three-dimensional volume of stone that was calculated automatically during the computed tomography (CT) scan.

All patients underwent JJ insertion under spinal anesthesia. All inserted JJ stents were made from polyurethane. Patients were discharged on the same day of surgery. Prior to JJ insertion, an interview was held with the patient to teach him the way to use potassium citrate. One day after JJ insertion, all patients started the potassium citrate therapy. Granules of potassium citrate were administrated as a solution in a glass of water. We started the daily dose as; one spoonful in the morning, another one in the afternoon and 2 at night. Immediately before taking any dose, the urine pH was tested using a strip of indicator paper which was wetted with a mid-stream urine sample. Thereafter, the color of the wet strip was compared to the color chart enclosed in the package. Each color represented a specific range of pH. In this study, the optimum pH range was between 5.5 and 6.5. If the urine pH was <5.5 the dose was increased by half spoon and decreased by half spoon if the pH was higher than 6.5. All patients were instructed to keep drinking plenty of water during treatment (at least 3 L/d). The duration of treatment was 1 month. All patients were interviewed at 5, 14, and 30 days after treatment start. If the treatment was extended for another month, the additional follow-up was scheduled at 6 and 8 weeks. The aim of these interviews was to ensure that the patient was taking his treatment probably and detect the occurrence of UTI. A urine sample was obtained at each visit to measure the pH and to evaluate the presence of pus cells.

After 1 month of treatment, all patients underwent another noncontrast CT to measure the stone burden after treatment. Those with significant residual stone underwent another month of treatment with K citrate. After 2 months, if the stone was not completely responded to treatment, the JJ was either exchanged or the patient underwent another line of treatment according to our discussion with the patient.

To determine the response to treatment, we reassessed the stone size using noncontrast CT after 1-month of K citrate administration and those who had significant residual underwent another course of treatment for another month. For those who had 2 months' K citrate, another noncontrast CT was ordered before JJ stent removal.

The stent was removed after treatment (maximum 2 months). All removed JJ were inspected for the presence of encrustation. In order to classify the encrustation, we used the modified encrustation score. Encrustation scoring, modified from Keane *et al*., included: Score (0) when there is no visible stent biofilm, score (1) if there was a visible stent biofilm, score (2) when a bladder coil encrustation is detected, score (3) if <50% of entire stent is encrusted, and score (4) if >50% of stent was encrusted.[9]

UTI was classified as simple (nonfebrile) cystitis and FUTI. Simple cystitis was defined as the presence of predominant irritative lower urinary tract symptoms associated with pyuria (pus cells >10 leukocytes/μL) which

was then confirmed by the presence of single bacterial species >$10^3$ CFU/mL. FUTI was defined as acute flank pain, fever >37.7° and pyuria.

Patients who did not respond to treatment were candidates for percutaneous nephrolithotomy or ultrasound-guided Extracorporeal Shock Wave Lithotripsy (according to the size of the remaining stone).

Our primary outcome was to evaluate the safety of using potassium citrate in a stented patient to manage uric acid stones.

SPSS version 20, (IBM corporation, Armonk, New York, USA) was used to collect data and thereafter for statistical analysis. Continuous data were presented in the form of medians and ranges, while categorical data were described in numbers and percentages. The Chi-square test was used to compare categorical data while the Mann–Whitney U-test was used to evaluate continuous data. $P \leq 0.05$ was considered statistically significant.

## RESULTS

Over a period of 5 years, 138 patients were diagnosed with renal uric acid stones. We excluded 12 patients who presented with positive bacterial culture, 3 patients refused to participate, the remaining patients (64 patients) were not indicated for JJ insertion. Finally, 59 patients met our inclusion criteria then were recruited in the study 30 patients presented with renal colic, 8 patients presented with high serum creatinine, and the rest of the patients had marked hydronephrosis.

Patients' characteristics are presented in Table 1. The median age at presentation was 36 years old (18–73). JJ insertion was indicated due to intractable loin pain in 34 patients, rising serum creatinine in 7 patients, and moderate-to-severe hydronephrosis in 18 patients. Sixty-four percent of patients (28 patients) had pelvic renal stones with calyceal extension, while the remaining patients (21 patients) had no calyceal stones. The median initial serum creatinine was 0.9 mg/dl (0.6–3.8). All patients who had initial high serum creatinine commenced the K citrate when the creatinine was <2 mg/dl. These groups of patients started the treatment in a median period of 4 days (3–7).

Using the CT software (General Electric Company, Milwaukee, Wisconsin State, USA), the pretreatment stone burden was 26 $mm^3$ (15–56). Thirty-nine percent (23 patients) had a stone burden <25 $mm^3$ while the remaining patients had a stone burden more than 25 $mm^3$.

**Table 1: Patients' characteristics**

| Parameter | Findings |
|---|---|
| Number of patients | 59 |
| Age at presentation, median (range) | 36 years old (18-73) |
| Gender, *n* (%) | |
| Male | 27 (45.8) |
| Female | 22 (54.2) |
| Side of stone, *n* (%) | |
| Right | 25 (42.4) |
| Left | 34 (57.6) |
| Site, *n* (%) | |
| Pelvic only | 21 patients (35.6) |
| Pelvic and calyceal | 28 patients (64.4) |
| Stone burden before treatment, median (range) | 26 $mm^3$ (15-50) |
| Stone density, median (range) | 310 HU (175-498) |
| Cause of stenting, *n* (%) | |
| Intractable pain | 34 (57.6) |
| Marked hydronephrosis | 18 (30.5) |
| Rising serum creatinine | 7 (11.9) |

**Table 2: Post-K citrate management outcomes**

| Parameter | Findings |
|---|---|
| Stone burden after treatment, median (range) | 6 $mm^3$ (0-32) |
| Duration of treatment, *n* (%) | |
| 1 month | 21 patients (35.6) |
| 2 months | 38 patients (64.4) |
| Percentage decrease of stone burden, median (range) | 77.4 (25.6-100) |
| Response to treatment, *n* (%) | |
| 100% | 16 (27.1) |
| 50-99% | 41 (69.5) |
| <50% | 2 (3.4) |
| Incrustation, *n* (%) | 2 (3.4) |
| UTI, *n* (%) | 4 (6.8) |

UTI: Urinary tract infection

**Table 3: Outcome of K citrate management according to the stone size**

| Parameter | Stone <25 $mm^3$ | Stone ≥25 $mm^3$ | *P* |
|---|---|---|---|
| Number of patients, *n* (%) | 23 (39) | 36 (61) | |
| Stone density before treatment, median (range) | 320 HU (175-498) | 307 HU (198-480) | 0.74 |
| Duration of treatment, *n* (%) | | | |
| 1 month | 17 patients (73.9) | 4 patients (11.1) | <0.001 |
| 2 months | 6 patients (26.1) | 32 patients (88.9) | |
| Percentage decrease of stone burden, median (range) | 100 (50-100) | 74.2 (25.6-100) | <0.001 |
| Response to treatment, *n* (%) | | | |
| 100% | 15 (65.2) | 1 (2.8) | <0.001 |
| 50%-99% | 8 (34.8) | 33 (91.6) | <0.001 |
| <50% | 0 | 2 (5.6) | 0.25 |
| Incrustation, *n* (%) | 0 | 2 (5.6) | 0.25 |
| UTI, *n* (%) | 0 | 4 (11.1) | 0.09 |

UTI: Urinary tract infection

The median pretreatment stone burden was 6 $mm^3$ (0–32) [Table 2]. Twenty-one patients (35.4%) had K citrate treatment for 1 month while 38 patients (64.4%) received the treatment for 2 months. K citrate was able to diminish the stone burden by 77.4% (25.6–100) ($P < 0.001$). Sixteen

patients (27.1%) had dissolved stone after K citrate administration, 41 patients (69.5%) had more than 50% decrease of the stone burden while only 2 patients (3.4%) had stones with modest dissolution (<50% decrease of the stone burden). Those who had completely dissolved stones had a median pretreatment stone size of 18 $mm^3$ (15–26) while those showed 50%–99% dissolution had a median pretreatment size of 29 (21–50) ($P < 0.001$). The two patients who had <50% decrease of stone size had a pretreatment stone size of 25 and 34 $mm^3$ and percentage of stone dissolution of 34.4% and 25.6%, respectively.

Four patients (6.8%) experienced UTI while 2 patients (3.4%) had visible JJ encrustations [Table 3]. Of those who had UTI, two had simple UTI (cystitis) and two patients developed FUTI. According to encrustation score system, one patient had encrustations at the bladder coil, and the other one had stent biofilm. When JJ was removed at 1 month, only one patient (4.8%) developed UTI While of those had their JJ stents removed at 2 months, 3 patients experienced UTI (7.9%) in the form of acute cystitis ($P = 0.6$). No patients had encrustations on their stents when the stents were removed at 1 month in comparison to 2 patients (5.3%) who had their JJ removed at 2 months ($P = 0.3$). Regarding the complications related to the administration of K citrate, three patients complained of gastrointestinal upset. However, all of them continued their treatment.

Renal stones <25 $mm^3$, had median 100% (50–100) stone dissolution while those with stone burden ≥25 $mm^3$ had median stone dissolution percentage of 74.2% (25.6–100) ($P < 0.001$). Most renal stones <25 $mm^3$ were completely dissolved while 91.6% of stones with size ≥25 $mm^3$ showed 50%–99% decrease of stone burden ($P < 0.001$). No patients with stone size <25 $mm^3$ had dissolution percentage <50% while two stones with stone burden ≥25 $mm^3$ had stone dissolution <50%.

Only one patient with stone size ≥25 $mm^3$ had his JJ removed after 1 month of treatment in comparison to 73.4% of patients (17 patients) who had stones <25 $mm^3$ ($P < 0.001$). All patients who had JJ removal at 1 month had 100% stone dissolution. No patients with stone size <25 $mm^3$ experienced UTI or had encrustation on their JJ. The median pretreatment stone size of patients who experienced UTI was 43.5 $mm^3$ (29–50). The two patients who had stone encrustations had pretreatment stone size of 42 and 43 $mm^3$.

## DISCUSSION

The formation of uric acid stones requires the presence of multiple factors such as supersaturation of urine with uric acids, urine acidity, and decrease of urine output.[8] In comparison to sodium alkali, K citrate is not associated with increased the urinary sodium load which could promote the formation of calcium oxalate stones.[10]

Temporary ureteral stent insertion is one of the common procedures that are performed extensively in urology. The use of JJ stents has been associated with some morbidities such as infection, and encrustation. Many factors contribute to the occurrence of such morbidities including the stent material, urine composition, and duration of use. The risk of stent encrustation is increased in patients with a history of urolithiasis and with progressively longer indwelling times.[11]

Some urologists worry about the complications of ureteral stenting, especially with the use of K citrate in terms of the occurrence of UTI and encrustations. According to our knowledge, there is a paucity of information about the usefulness and the estimated risks while using K citrate in the presence of ureteral stents. In the current study, we studied the risks, namely UTI and encrustations, of concomitant use JJ while administrating K citrate.

The most commonly used material in the manufacture of modern stents is polyurethane.[12] Encrustation begins by the formation of a biofilm on the ureteral stent which encourages the deposition of mineral salts.[13] Being a foreign body, which is placed in the urinary tract, ureteric stents provide a surface for bacterial colonization.[14]

We thought that the administration of K citrate would not encourage the precipitation of insoluble crystals on the ureteric stent. This could be explained by that the presence of alkaline medium is associated with increased solubility of urate salts (90% of urate salts are soluble at pH of 6.75).[15] Moreover, K citrate is not associated with the formation of calcium oxalate stones which can be formed in alkaline medium.[8]

Encrustation is a well-known complication of retained stents in the urinary tract, and its risk increased when left for longer durations.[16] In their cohort, El-Faqih and colleagues found that the most common complication of polyurethane ureteral stents was the encrustation which accounted 9.2% when the stent was left for <6 weeks and 43.3% for those left up to 12 weeks.[17] In our study, the encrustation rate was 0% for those had their JJ removed after 4 weeks and 3.4% for those had their JJ left for 8 weeks. In their study, El-Faqih *et al*. reported that nearly all patients underwent procedures where the stones were

fragmented. The stone fragments could be easily precipitate on the surface of the stent and cause encrustations or even occluding the lumen. On the other hand, in our study, K citrate causes stone dissolution where the urate minerals are more soluble; hence, the encrustation is less likely to happen.

The incidence of UTI in our study was comparable to El-Faqih *et al*. They found that the incidence of UTI when the stent was retained for <6 weeks was 3%. This percentage was slightly increased to 4.2% when the stent was left for 6–12 weeks ($P$ = 0.7). In our study, the incidence of UTI was 4.8% at 1 month and 7.5% at 2 months ($P$ = 0.6).[17] The slight difference between both studies could be explained by the prospective nature of our study with strict patient's follow- up in comparison with the retrospective results of El-Faqih *et al*.

In our study, the stone size (≥25 $mm^3$) affected the period of JJ stay as most of them required K citrate treatment for 2 months to show significant reduction of stone size. Our cohort showed 27.1% complete clearance of the stone while only 3.4% of patients showed poor response to K citrate. In a recent study, Gridley *et al*. reported 67% of patients had complete dissolution of uric acid stones in a median follow-up of 3 months with a median stone burden of 25 $mm^3$.[6] In comparison to our study, our patients with completely dissolved stones a pretreatment median stone burden of 18 $mm^3$. The median dissolved stone size was less in our cohort when compared to Gridly *et al* their patients received the medical treatement for a longer period.

This study has several limitations. First, the number of patients enrolled in the current study is relatively small. However, the incidence of uric acid stones is 5%–10% of global incidence. Moreover, the indications of JJ insertion during the dissolution of such stones limit the number of patients included in our study. Second, we used only one stent type, which made of polyurethane, was evaluated in this trial. However, polyurethane ureteral stents are the most widely used stents in urology practice. Finally, more prospective studies are warranted to evaluate other types of stents made from materials other than the polyurethane as our results could not be generalized for all types of stents.

## CONCLUSIONS

The concomitant application of ureteric stents with K citrate was safe with an acceptable risk of UTI and encrustation. This option could be a good alternative to surgery in a large number of patients with urate lithiasis.

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### Conflicts of interest
There are no conflicts of interest.

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