Medical treatment of uric acid kidney stones

Michel Normand[1], Jean-Philippe Haymann[2], Michel Daudon[2]
[1]Department of Urology, Clinique Saint-Privat, Boujan sur Libron, France; [2]Department of Physiology, Tenon Hospital, Paris, France

Cite as: Normand M, Haymann JP, Daudon M. Medical treatment of uric acid kidney stones. *Can Urol Assoc J* 2024 June 17; Epub ahead of print. http://dx.doi.org/10.5489/cuaj.8774

Published online June 17, 2024

Corresponding author: Dr. Michel Daudon, Department of Physiology, Tenon Hospital, Paris, France; daudonmichel24@gmail.com

***

ABSTRACT

Introduction: The prevalence of uric acid stones increases regularly due to its high correlation with obesity, hypertension, metabolic syndrome, type 2 diabetes, and aging. Uric acid stone formation is mainly due to an acidic urinary pH secondary to an impaired urinary ammonium availability responsible for uric acid rather than soluble urate excretion. Alkalization of urine is therefore advocated to prevent uric acid crystallization and considered effective therapy.
Methods: We report a large series of 120 patients with uric acid kidney stones who were successfully treated with potassium citrate (K-citrate) for stone dissolution without any urologic intervention to prevent stone recurrence, with a median 3.14 years followup. The K-citrate was diluted in 1.5 L of water, avoiding gastrointestinal disorders.
Results: Among 75 patients having stones in their kidney at initiation of therapy, a complete chemolysis was obtained in 88% of cases. Stone risk factors decreased under treatment, mainly due to increased diuresis, urinary pH, and citrate excretion. Treatment was stopped in only 2% of patients due to side effects, with no hyperkalemia onset despite a median urinary potassium increase of 44 mmol/day.
Conclusions: Contrary to other reports, our data show that medical treatment of uric acid kidney stones is well-tolerated and efficient if regular monitoring of urinary pH is performed.

INTRODUCTION

Urolithiasis is one of the most frequent diseases treated by urologists. The prevalence is 5 to 13% in European countries, 10% in France [1] 13% in the USA [2]. Despite the fact that calcium oxalate is the most frequent component (approximately 70%) of kidney stones [1], uric acid stones account for about 10% and are becoming more and more frequent. This is due to an increase in the prevalence of type 2 diabetes, metabolic syndrome and obesity in the general population since thirty years [1]. The risk of uric acid stones increases with age [1]: 23% versus 6% respectively after or before 55 years of age in our study, especially in men.

The consequences of calculi can be severe. Uric acid stones are highly recurrent [3]. In addition to painful nephritic colic, they can lead to infection, septic shock or renal insufficiency.

Moreover, even though surgery has greatly progressed with extracorporeal shockwave lithotripsy, percutaneous nephrolithotomy, flexible ureteroscopy, nephrolithiasis can lead to complications such as hemorrhage, rupture or stenosis of the ureter and urinary tract infection. The overall cost of urological procedures for stone removal is high, more than two billion dollars each year in the USA [4]. Fortunately, uric acid stones are accessible to medical dissolving treatment [5-8]. However, only very few series of uric acid stones were reported as successfully managed by medical therapy often associated with a significant part of treatment failure [9-11].

Diuresis and hyperuricosuria play a role in the pathogenesis of uric acid stones, but the most important factor is the acidic urinary pH [4, 5].

We report the clinical experience of a single center cohort of 120 patients followed for uric acid nephrolithiasis between 2017 and 2021. We studied the effect of K-citrate for the dissolution of uric acid calculi in the kidney and for the prevention of new calculi.

METHODS

Patients

Among a cohort of 1200 patients followed for urolithiasis, 179 patients had uric acid stones. The diagnosis of uric acid stones was based on CT scan imaging, previous stone analysis by infrared spectroscopy or crystalluria (when no stone available for analysis) and/or acidic urine pH value (<5.4 on morning fasting urine collection). All participants gave their written informed consent. In line with the French legislation on observational studies of routine clinical practice, approval by an institutional review board was not required. Patients were treated with tripotassium citrate (K-citrate) either for dissolving their stone or prevent recurrence. Fifty-nine patients were excluded because they were lost to follow-up. Thus 120 patients (88 men and 32 women) were included (Fig.1).

Methods

Radiologic exams

The diagnosis of uric acid stones is not always obvious, because they are radiolucent with plain abdominal X-rays, similarly to calculi made of 2.8 dihydroxyadenine, drug, or proteins.

A low dose non-contrast enhanced computed tomography (NCCT) or CT SCAN was performed in all patients. It allows seeing the location, the number and the density of calculi, which was low, less than 400 Hounsfield units for pure uric acid stones [6]. In our series, the median density was 431 ± 74 UH (range: 319-560 UH). However, as for plain abdominal X-rays, CT-SCAN does not allow distinguishing between uric acid, dihydroxyadenine, drug and protein stones and thus was completed by stone analysis and/or crystalluria.

Stone analysis
Stone analysis was performed by Fourier transform infrared spectroscopy [12]. In case of patient relapses, if stone was collected, a new analysis was performed for assessing the potential presence of calcium or urate salts due to an excessive alkaline therapy.

Crystalluria
If no stone was available for analysis, a study of crystalluria on the first morning urine with a measure of urinary pH was performed for seeking one of the four types of uric acid crystals known in urine, i.e. amorphous UA, UA anhydrous, UA monohydrate and UA dihydrate [13].

Urinary pH
Urinary pH was performed in all cases as it is a cornerstone for diagnosis and treatment of uric acid lithiasis. Indeed, urinary pH is expected acidic (<5.4), and in some cases less than 5.0. It has to be checked in the first morning urine in a fasting patient. Patients were advised to use a pH meter with a precision of 0.1 unit which was preferred to colored strips, precise only to 0.5 unit. One pH meter device mostly used was the Checker portable pH meter HI98103 with a HI 1270 electrode accurate to 0.1 pH unit (Hanna Instruments, Lingo Tanneries, France). Urine pH was determined three times a day before meals for at least two days before and after the beginning of treatment.
Urinary pH measurement and crystalluria were performed regularly during follow up in order to check alkalization therapy efficiency. Indeed, crystalluria is expected to disappear under treatment.

Patient medication management
Seventy-five patients with *in situ* kidney stones at the beginning of the study underwent a medical therapy in order to dissolve uric acid stones.
In order to alkalize patients' urine, K-citrate was used because it was reported as efficient for both dissolving existing calculi and preventing the formation of new uric acid stones [14].

Because no pharmacological specialty was available in France, K-citrate was prescribed as pharmaceutical preparation containing 4 to 9 grams (mean= 7.2 ± 1.8 grams, i.e. 23.5 ± 5.9 mmoles) or 39 to 87 mEq per day (mean=70.5 ± 17.7 mEq), diluted in 1.5 liter of water and taken throughout all the day.

The main objective was to permanently obtain a urine pH greater than 6.0 but not higher than 7.0 in order to avoid crystallization of urate salts or calcium phosphates. In patients with *in situ* uric acid stones, the target of urine pH under K-citrate was within the range 6.5-7.0.

Patient's monitoring was relying upon a close self-follow up as patients, at the initiation of treatment, were sending by email UpH data, checked 3 times a day, during 2 days to the medical team in order to adjust the treatment.
Adjustment of K-citrate posology was prescribed according to the urine pH value as summarized in Table 1.

When K-citrate was prescribed for preventing stone recurrence in free stone patients, the target of urine pH was 6.0-6.5. Recurrence rate was defined as the formation of new stone/patient/year.
Hyperuricemia (> 460 µmol/l in men, > 400 µmol/l in women) and/or hyperuricosuria (>4.2 mmol/d in men, or 3.6 mmol/d in women), were found in 49% of patients. In case of hyperuricemia or hyperuricosuria, allopurinol was administered (100 mg tapered up to 300 mg per day according to uricemia target). Among our population, forty-five per cent of patients received both K-citrate and allopurinol. No case of hyperkaliemia was noticed in our population (all patients had a GFR > 30 ml/mm).

In addition, because stone formation is favored by inappropriate dietary habits, advices were given to all patients to reduce proteins intake (0.8-1g/kg/d), purine-rich foods and sodium chloride intake (less than 9g/d) in agreement with the 2022 recommendations of the AFU Lithiasis Committee [15]. Proteins and sodium chloride intake was assessed from 24h-urine excretion of urea and sodium.

Statistical analysis
Categorical variables were described as numbers and percentage and continuous variables as mean ± SD. Comparison of biological data before therapy and under therapy were performed using paired t test and the chi 2 test, for quantitative and qualitative variables, respectively.

RESULTS
Patient average age was 63 ± 12 years with a sex-ratio M/F of 2.7. Table 2 shows patient's clinical and biological characteristics at baseline with obesity, hypertension and diabetes present in 40%, 38% and 25% of cases respectively. Hyperuricemia was noticed in 42% of cases and hyperuricosuria in 43% of cases.
Table 2. Demographic, clinical and biological data at baseline.

Comparison at baseline between diabetic patients (n=33) who are well known to be prone for uric acid urolithiasis [16-18] and non diabetic patients (n=87) only show a small increase of urinary sodium (216 ± 64 mmol/d vs 187 ± 57 mmol/d, $p < 0.05$) and potassium (75 ± 21 mmol/d vs 64 ± 22 mmol/d), $p < 0.05$) excretion and a significant increase of oxalate excretion: 0.36 ± 0.14 vs 0.29 ± 0.11 mmol/ 24 h ($p < 0.01$) in the diabetic group. No significant difference was found for other urine parameters and diuresis was similar in both groups (1.8 ± 0.47 in diabetics vs 1.7 ± 0.46 L/d in non-diabetics, p=NS).

Uric acid stones outcome
The average number of stones before treatment was 6.11 ± 5.37 per patient.
At the beginning of the treatment, 75 patients (63%) had one or several calculi in their kidneys and 45 patients were stone free and received K-citrate to prevent stone recurrence.

Stone analysis showed that 48% of stones were pure uric acid anhydrous, 43% contain uric acid anhydrous mixed with uric acid dihydrate, and 9% contain uric acid anhydrous mixed with less than 10% of calcium oxalate monohydrate.
All patients received K-citrate at a dosage required to reach urinary pH targets. Among them, 66 patients received only K-citrate while 54 patients received K-citrate + allopurinol because of hyperuricemia or hyperuricosuria. Mixed stones with a calcium oxalate shell found in only two patients were accessible to alkaline dissolving therapy after treatment with extracorporeal lithotripsy.

K-citrate was well tolerated in 91% and moderately tolerated in only 9 % of cases. In case of gastro-intestinal disorders, K-citrate posology was decreased and when possible further increased up in order to reach the target urinary pH.

Mean follow-up under K-citrate was 3.14 ± 2.73 years. Stone recurrence was assessed from either the spontaneous passage of new stones or through the presence of new stones on a new low dose CT scan performed each year. The recurrence rate dropped from 1.29 ± 1.07 at baseline to 0.03 ± 0.02 calculus/patient/year under K-citrate. Three relapses were observed during follow-up due to K-citrate withdrawal.

There was no difference between patient's group receiving K-citrate alone or combined with allopurinol: the recurrent rate was 0.032 ± 0.199 calculus/patient/year with K-citrate alone and 0.028 ± 0.210 calculus/patient/year with K-citrate and allopurinol.
Among the 75 patients with a renal stone at baseline, stone number within patients ranged from n= 1 to 10 (m= 2.20 ± 0.20). Staghorn calculi were present in 11 patients, 7 of whom were treated with K-citrate alone and the other four with K-citrate and allopurinol.
A complete dissolution was obtained in 88 % of the patients (Figure 2). Partial dissolution was obtained in 12 % of patients of whom stone density was more than 500 units Hounsfield (corresponding to presence of another component in the calculus, most often calcium oxalate monohydrate) in 60 % of cases.

For monitoring, in order to be sure that the patient took K-citrate, urinary potassium, easy to measure, was checked, as 24-hour citraturia measurement was less reliable and less precise.

Biological followup
Before the treatment with K-citrate, hypocitraturia (less than 1.6 mmol/d) was found in 27 % of patients, without any difference for the number of calculi per year (1.19 ± 0.95 stone/year vs 1.32 ± 1.16/year in patients with citrate > 1.6 mmol/d, p=NS). Protein intake, checked by the dosage of urea was increased in 73 % of cases. Of notice, acidic fasting urine pH <5.4 was present in all cases.

Under treatment, citraturia increased in all cases. As shown in table 3, no change was observed for 24-hour urine sodium and urea. As expected, urinary potassium was increased in all patients.

In some cases we observed an improvement of the GFR, probably due to the dissolution of calculi, noteworthy in patients with staghorn stones. No case of hyperkalemia was observed during follow up.

Tables 4 and 5 show the biological follow up according to treatments, i.e. K-citrate group alone (table 4) or K-citrate plus allopurinol group (table 5). We observe a significant increase of 24-hour diuresis, potassium, citrate and urine pH and a significant decrease of urate in both groups, whereas a decrease of urea and sodium excretion was noticed only in K-citrate alone group, suggesting no significant changes in dietary habits in patients receiving both K-citrate and allopurinol.

DISCUSSION

It is well known for a long time that factors promoting uric acid crystallization are too acidic urinary pH (UpH), hyperuricosuria and insufficient diuresis [8-10]. In clinical practice, it was shown for more than forty years than the main factor for uric acid stone formation is the overweight responsible for metabolic syndrome inducing insulin resistance, default in ammonia availability and low urine pH [14, 19, 20].

From an epidemiological point of view, uric acid calculi are increasing in most countries due to changes in dietary habits and the progressive increase in BMI of the general population. In our series, 40% of our uric acid stone formers were obese. In such conditions; the most important factor for the lithogenesis of uric acid stones is the acidic urinary pH, less than 5.4 [7, 17, 20] with a loss of the circadian rhythm of the UpH and a disappearance of the postprandial alkaline tide [21, 22].

Because acid urine is the main factor for uric acid formation, alkalizing treatment was successfully proposed for medical stone dissolution [7, 23]. Bicarbonate or citrate salts were used with variable results [5, 8].

In our study, investigating the risk of renal stone recurrence under K-citrate therapy and the success rate of chemolysis in 75 patients with *in situ* renal uric acid stones, a complete dissolution was obtained in 88 % and it was partial in 12 %. All the staghorn calculi were dissolved. The reported success rates of oral dissolution therapy in the literature range from 15 to 87% of stones [10, 11, 24-30]. In the recent review by Ong et al. including 1075 patients, a complete or partial dissolution rate was respectively 61.7% and 19.8%, while 15.7% of patients required surgical intervention [30]. Of note, as clearly shown by Nevo et al., medical treatment of uric acid stone is more cost-effective than urological treatment [31]. Regarding the biological exams, we had no case of hyperkalemia [32] even in the case of moderate renal insufficiency, and no case of metabolic alkalosis under K citrate treatment. On the contrary, we observed in some cases an improvement of the GFR. A durable alkalization and citraturic response was shown to be achieved with long-term studies with K-citrate [33]. The posology of K-citrate at the initiation of the treatment was depending on three factors: the weight of the patient, the acidity of the urine (dosage was different if basal urine pH was 4.8 or 5.4) and stone disease status (number of calculi per year, the presence or not of stones in the kidney, with or without staghorn).

Currently a urinary pH of 6.5 to 7.2 is recommended for the treatment of uric acid stones [11, 34] and pH levels between 7.0 and 7.2 for dissolution [25]. To avoid the risk of calcium phosphate precipitation, we recommended a UpH ranged from 6.5 to 7.0 which was sufficient for a successful dissolution of the stones and from 6.0 to 6.5 for the prevention of a new calculus. As reported by Cameron et al, the monitoring of the response to alkali therapy

with only one 24-hour urinary pH measurement during follow up is not enough because excessive nocturnal and early morning acidity can persist despite apparent alkalization of pooled 24-hour urines [22].

A low dose CT-scan and 24-hour urine collection were performed every 6 months after the start of treatment in order to ensure that calculi were dissolved, and that there was no recurrence; but also to check treatment compliance assessed by an increased kaliuresis with a special emphasis on patient's information about diet counseling and the high risk of recurrence in the event of stopping treatment. Following this procedure, compliance was excellent with a mean diuresis close to two liters per day, a urine density less than 1012, and the recommendation to drink in the evening and at bedtime; and in case of urine voiding during the night to drink again 250 ml. The tolerance was good in 91%, which is better than in other studies [10, 35]. In only 2% of patients, K-citrate was stopped due to gastrointestinal side-effects. A review by Mattle and Hess [10] reported that up to 48 % of patients taking alkali citrate left the treatment prematurely because of adverse gastrointestinal effects. The fact that K-citrate was dissolved in 1.5 liter of water in our study and taken throughout the day probably explains this good tolerance.

Limitation of the study. This retrospective observational study performed in a single center with a dedicated medical team does not provide by nature the power of a randomized double blind study. Nevertheless, it shows that using the K citrate protocol mentioned above, with the strong commitment of a medical team and a close monitoring, patient's compliance is excellent and uric acid stones may be successfully controlled by a medical treatment relying on patient information, self-urine pH measurement sent to the medical team to adjust daily posology and a six month check up including a low dose CT scan until stone free status.

CONCLUSIONS

Our data suggest that treatment using K-citrate is very efficient both for dissolution of calculi, and for prevention of new stones. However, several conditions must be filled. The first is to be sure that the calculus is made of uric acid, usually confirmed by infrared analysis of a former stone, or by a uric acid crystalluria with an acidic UpH, and low stone density by CT-scan. The second is to explain to patient the need of drinking K-citrate diluted in 1.5 liter of water all throughout the day, for better tolerance, to avoid gastroenterological problems. The third is for the patient to check their UpH several times a day with a pH-meter, and send the results to the medical team by email. The last condition is to inform patient that they will take this treatment life-time to avoid new stones, as UA stone formers are more likely to have a recurrence in comparison to calcium oxalate stones-formers. If all these conditions are fulfilled, the patients are unlikely to experience new renal colic.

REFERENCES

1. Daudon M. Épidémiologie actuelle de la lithiase rénale en France. *Ann Urol* 2005;39:209-31. https://doi.org/10.1016/j.anuro.2005.09.007
2. Sakhaee K, Maalouf NM. Kidney stones 2012: Pathogenesis, diagnosis and management. *J Clin Endocrin Metab* 2012;97:1847-60. https://doi.org/10.1210/jc.2011-3492
3. Daudon M, Jungers P, Bazin D, et al. Recurrence rates of urinary calculi according to stone composition and morphology. *Urolithiasi*s 2018;46:459-70. https://doi.org/10.1007/s00240-018-1043-0
4. Straub M, Hautmann RE. Developments in stone prevention. *Curr Opin Urol* 2005;15:119-26. https://doi.org/10.1097/01.mou.0000160627.36236.6b
5. Trinchieri A, Esposito N, Castelnuovo C. Dissolution of radio- lucent renal stones by oral alkalinization with potassium citrate/potassium bicarbonate. *Arch Ital Androl* 2009;81:188-91.
6. Pearle MS, Goldfarb DS Assimos DG et al. Medical management of kidney stones: AUA guideline. *J Urol* 2014;192:316-24. https://doi.org/10.1016/j.juro.2014.05.006
7. Heilberg I. Treatment of patients with uric acid stones. *Urolithiasis* 2016;44:57-63. https://doi.org/10.1007/s00240-015-0843-8
8. Sakhaee K, Nicar M, Hill K, et al. Contrasting effects of potassium citrate and sodium citrate therapies on urinary chemistries and crystallization of stone-forming salts. *Kidney Int* 1983;24:348-52. https://doi.org/10.1038/ki.1983.165
9. Chugtai MN, Khan FA, Kaleem M, et al. Management of uric acid stone. *J Pak Med Assoc* 1992;42:153-5.
10. Mattle D, Hess B. Preventive treatment of nephrolithiasis with alkali citrate - a critical review. *Urolithiasis* 2005;33:73-9. https://doi.org/10.1007/s00240-005-0464-8
11. Tsaturyan A. Bokova E, Bosshard P, et al. Oral chemolysis is an effective, non-invasive therapy for urinary stones suspected of uric acid content. *Urolithiasis* 2020;48:501-7. https://doi.org/10.1007/s00240-020-01204-8
12. Daudon M, Bader CA, Jungers P. Urinary calculi: Review and classification methods and correlations with etiology. *Scanning Microsc* 1993;7:1081-104.
13. Daudon M, Frochot V, Bazin D, et al. Crystalluria analysis improves significantly etiologic diagnosis and therapeutic monitoring of nephrolithiasis. *Comptes Rendus Chimie* 2016;19:1514-26. https://doi.org/10.1016/j.crci.2016.04.010
14. Sakhaee K, Adams-Huet B, Moe OW, et al. Pathophysiologic basis for normouricosuric uric acid nephrolithiasis. *Kidney Int* 2002;62:971-9. https://doi.org/10.1046/j.1523-1755.2002.00508.x
15. Lemoine S, Dahan P, Haymann JP, et al. Lithiasis Committee of the French Association of Urology (CLAFU). 2022 Recommendations of the AFU Lithiasis Committee: Medical management - from diagnosis to treatment. *Prog Urol* 2023;33:911-53. https://doi.org/10.1016/j.purol.2023.08.004
16. Pak CY, Sakhaee K, Moe O, et al. Biochemical profile of stone-forming patients with diabetes mellitus. *Urology* 2003;61:523-7. https://doi.org/10.1016/S0090-

4295(02)02421-4
17. Daudon M, Traxer O, Conort P, et al. Type 2 diabetes increases the risk for uric acid stones. *J Am Soc Nephrol* 2006;17:20-6. https://doi.org/10.1681/ASN.2006030262
18. Sakhaee K. Epidemiology and clinical pathophysiology of uric acid kidney stones. *J Nephrol*. 2014; 27:241-5. https://doi.org/10.1007/s40620-013-0034-z
19. Maalouf NM, Cameron MA, Moe OW, et al. Novel insights into the pathogenesis of uric acid nephrolithiasis. *Curr Opin Nephrol Hypertens* 2004;13:181-9. https://doi.org/10.1097/00041552-200403000-00006
20. Daudon M, Lacour B, Jungers P. Influence of body size on urinary stone composition in men and women. *Urol Res* 2006;34:193-9. https://doi.org/10.1007/s00240-006-0042-8
21. Cameron MA, Baker LA, Maalouf NM, et al. Circadian variation in urine pH and uric acid nephrolithiasis risk. *Nephrol Dial Transplant* 2007;22:2375-8. https://doi.org/10.1093/ndt/gfm250
22. Cameron M, Maalouf NM, Poindexter J, et al. The diurnal variation in urine acidification differs between normal individuals and uric acid stone formers. *Kidney Int* 2012;81:1123-30. https://doi.org/10.1038/ki.2011.480
23. Kenny JE, Goldfarb DS. Update on the pathophysiology and management of uric acid renal stones. *Curr Rheumatol Rep* 2010;12:125-9. https://doi.org/10.1007/s11926-010-0089-y
24. Sinha M, Prabhu K, Venkatesh P, et al. Results of urinary dissolution therapy for radiolucent calculi. *Int Braz J Urol* 2013; 39:103-7. https://doi.org/10.1590/S1677-5538.IBJU.2013.01.13
25. Gridley CM, Sourial MW, Lehman A, et al. Medical dissolution therapy for the treatment of uric acid nephrolithiasis. *World J Urol* 2019;37:2509-15. https://doi.org/10.1007/s00345-019-02688-9
26. Salem SM, Sultan MF, Badawy A. Oral dissolution therapy for renal radiolucent stones, outcome, and factors affecting response: A prospective study. *Urol Ann* 2019;11:369-73. https://doi.org/10.4103/UA.UA_20_19
27. Elsawy AA, Elshal AM, El-Nahas AR, et al. Can we predict the outcome of oral dissolution therapy for radiolucent renal calculi? A prospective study. *J Urol* 2019;201:350-7. https://doi.org/10.1016/j.juro.2018.09.027
28. Moore J, Nevo A, Salih S, et al. Outcomes and rates of dissolution therapy for uric acid stones. *J Nephrol* 2022;35:665-9. https://doi.org/10.1007/s40620-021-01094-y
29. Frolova EA, Tsarichenko DG, Saenko VS, et al. Dissolution of uric acid stones in the ureter. *Urologiia* 2022;6:56-60. https://doi.org/10.18565/urology.2022.6.56-60
30. Ong A, Brown G, Tokas T, et al. selection and outcomes for dissolution therapy in uric acid stones: A systematic review of literature. *Review Curr Urol Rep* 2023;24:355-63. https://doi.org/10.1007/s11934-023-01164-7
31. Nevo A, Humphreys MR, Callegari M, et al. Is medical dissolution treatment for uric acid stones more cost-effective than surgical treatment? A novel, solo practice, retrospective cost-analysis of medical vs. surgical therapy. *Can Urol Assoc J*

2023;17:E29-34. https://doi.org/10.5489/cuaj.7833
32. Reichard C, Gill BC, Sarkissian C, et al. 100% uric acid stone formers: What makes them different? *Urology* 2015:85:296-8. https://doi.org/10.1016/j.urology.2014.10.029
33. Robinson MR, Leitao VA, Haleblian GE, et al. Impact of long-term potassium citrate therapy on urinary profiles and recurrent stone formation. *J Urol* 2009;181:1145-50. https://doi.org/10.1016/j.juro.2008.11.014
34. Straub M, Hautmann RE. Developments in stone prevention. *Curr Opin Urol* 2005;15:119-26. https://doi.org/10.1097/01.mou.0000160627.36236.6b
35. Ettinger B, Pak CY, Citron JT, et al. Potassium-magnesium citrate is an effective prophylaxis against recurrent calcium oxalate nephrolithiasis. *J Urol* 1997;158:2069-73. https://doi.org/10.1016/S0022-5347(01)68155-2

FIGURES AND TABLES

Figure 1. Study flow chart.

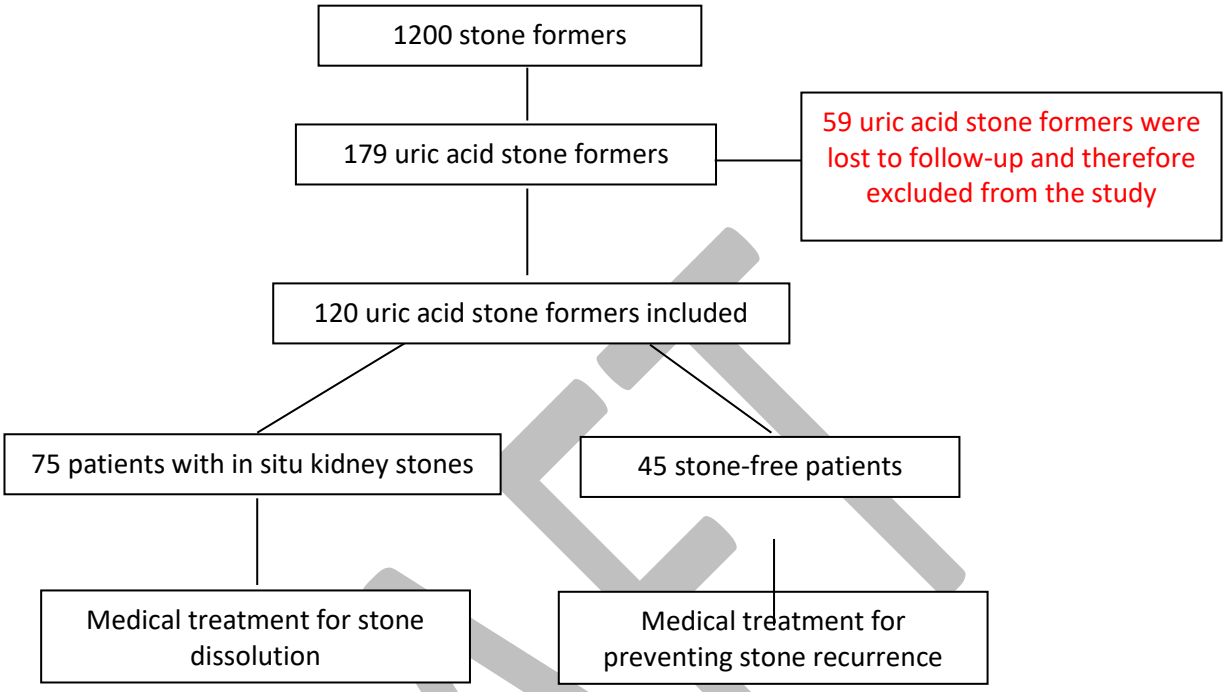
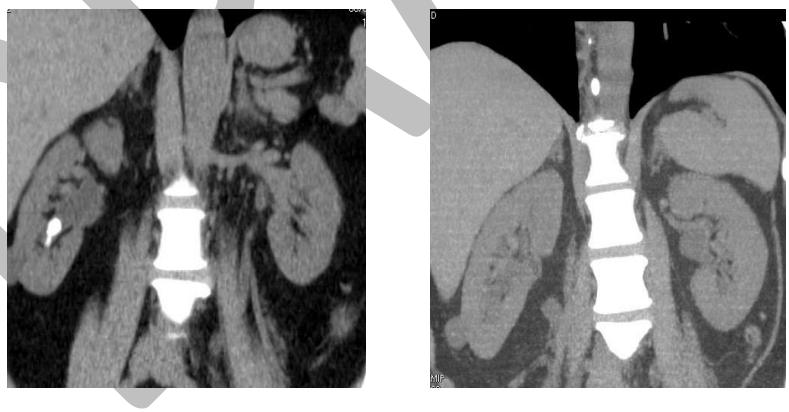
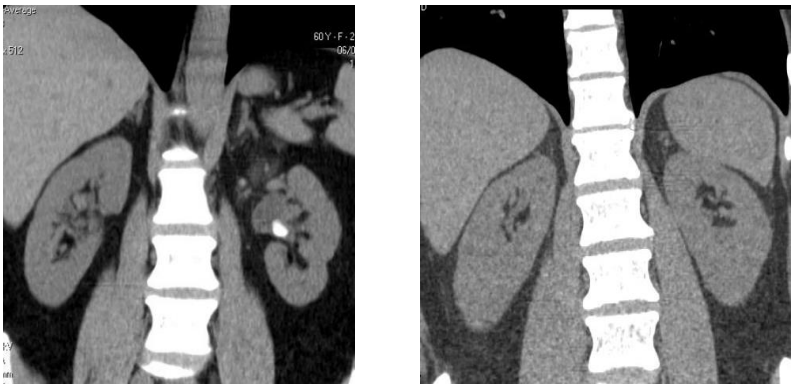


Figure 2. Illustration of two patients' computed tomography scans before (left) and after 3 months of K-citrate treatment (right) showing the dissolution of calculi.



Patient 1



Patient 2

Table 1. Adjustment of K-citrate dose according to urine pH (urine pH was measured three times a day before meals)	
Daily pH readings	**Adjustment**
Three pH <6.5	↗ the dose of K-citrate by 1 to 3 grams more
One pH <6.5	↗ the intake of water with K-citrate for the same period on the next day
Three pH between 6.5 and 7.0	→ the patient goes on drinking water with K-citrate in the same way
One pH > 7.0	↘ the intake of water with K-citrate for the same period on the next day
Three pH >7.0	↘ the dose of K-citrate by 1 to 3 grams less

Table 2. Demographic, clinical, and biological data at baseline	
Patient characteristics	
Number of uric acid stone formers	120
Gender (M/F)	88/32
Frequency of stone recurrence (number/patient/year)	1.29±1.07
Median age	63±12
BMI (kg/m^2)	28.9±6.25
Obesity (≥30 kg/m^2)	40%
Moderate (<40 kg/m^2)	34%
Severe (≥40 kg/m^2)	6%
Hypertension	38%
Diabetes type 2	25%
Occurrence of hyperuricemia	42%
Malformative uropathy (no case of polycystic kidney disease or MSK)	5%
Median density at CT scan (Hounsfield units)	431±74
First diagnosis of uric acid lithiasis performed by: Stone analysis Urinary uric acid crystals (and pH <5.4)	 83% 17%
Number of patients with in situ stones	75
Number of patients free of stones at the beginning of K-citrate	45
Biochemistry at baseline	
Blood	
Creatinine (micromol/l)	92.9±19.5
Uric acid (micromol/l)	368 ±89
Potassium (mmol/l)	4.21±0.30
Bicarbonate (mmol/l)	28±2.5
24h-urine biochemistry	
Urine volume (liters/day)	1.70±0.46
Creatinine (mmol/d)	12.94±3.26
Uric acid (mmol/d)	4.0±1.2
Potassium (mmol/d)	66.7±23.9
Sodium (mmol/d)	195±58
Urea (mmol/d)	425±118
Citrate (mmol/d)	2.46±1.20
Occurrence of high urine sodium excretion (> 150 mmol/d)	77%
Occurrence of hyperuricosuria (>4.2 mmol/d in men, >3.8 mmol/d in women)	43%
Occurrence of hypocitraturia (<1.6 mmol/d)	27%
First morning urine	
Urine pH <5.4	100%

BMI: body mass index; CT: computed tomography; MSK: musculoskeletal.

Table 3. Biological parameters (24h-urine and blood) for the whole series of patients before and under K-citrate			
	Before K-citrate	**Under K-citrate**	**p**
	24h urine		
Diuresis (liter)	1.70±0.46	1.95±0.45	<0.003
Creatinine (mmol)	12.95±3.27	12.86±3.46	NS
UpH	5.19±0.35	6.25±0.50	<0.001
Uric acid crystalluria	47%	0%	<0.001
Potassium (mmol)	67±24	116±29	<0.001
Citrate (mmol)	2.35±1.15	3.92±1.32	<0.001
Uric acid (mmol)	4.01±1.22	3.07±0.92	<0.001
Urea (mmol)	425±118	412±105	NS
Phosphorus (mmol)	28.0±7.55	27.4±7.27	NS
Magnesium (mmol)	3.34±1.39	3.52±1.29	NS
Sodium (mmol)	195±57	192±59	NS
	Blood		p
Creatinine (micromol)	92.9±19.5	91.2±23.0	NS
Potassium (mmol)	4.21±0.30	4.50±0.34	<0.001
Uric acid (mmol)	368±89	302±75	<0.001
Bicarbonate (mmol)	28.0±2.5	28.7±2.0	NS

NS: non-significant.

Table 4. Biological parameters in 24h-urine before and under K-citrate alone (n=66)			
Per 24 hours	**Before K-citrate**	**Under K-citrate**	**p**
Diuresis (liter/d)	1.61±0.48	1.90±0.48	<0.003
Creatinine (mmol/d)	12.78±3.09	12.05±3.04	NS
UpH	5.21±0.36	6.21±0.48	<0.001
Potassium (mmol/d)	66±26	109±25	<0.001
Citrate (mmol/d)	2.20±1.03	3.56±1.20	<0.001
Urate (mmol/d)	3.78±1.21	3.11±0.89	<0.001
Phosphate (mmol/d)	26.7±7.2	24.4±6.1	<0.05
Urea (mmol/d)	408±113	360±107	<0.05
Sodium (mmol/d)	181±57	164±56	<0.003

NS: non-significant.

Table 5. Biological parameters in 24h-urine before and under K-citrate and allopurinol treatment (n=54)

Per 24 hours	**Before K-citrate**	**Under K-citrate**	**p**
Diuresis (liter/d)	1.81±0.42	2.01±0.45	<0.003
Creatinine (mmol/d)	13.14±3.49	13.77±3.70	NS
UpH	5.16±0.34	6.28±0.52	<0.001
Potassium (mmol/d)	69±21	125±29	<0.001
Citrate (mmol/d)	2.52±1.25	3.56±1.20	<0.001
Urate (mmol/d)	4.29±1.19	3.04±0.96	<0.001
Phosphate (mmol/d)	29.4±8.4	30.4±7.7	NS
Urea (mmol/d)	448±123	468±98	NS
Sodium (mmol/d)	212±53	210±54	NS

NS: non-significant.