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Original Article

Potassium Citrate as a Preventive Treatment for Double-J Stent Encrustation: A Randomized Clinical Trial

Ali Tavoosian[1], Amirhossein Rahimnia[2], Elham Tehranipour[1], Alireza Khajavi[3], Seyed Saeed Tamehri Zadeh[1], Vahid Abedi Yarandi[1*]

[1]*Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran*

[2]*School of Medicine, Tehran University of Medical Sciences, Tehran, Iran*

[3]*Student Research Committee, Faculty of Paramedical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

HIGHLIGHTS

- Potassium citrate can significantly reduce double-J stent encrustation in patients with urolithiasis.
- It is recommended that urologists consider citrate potassium as a preventive treatment for encrustation.

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***Corresponding Author**:
Vahid Abedi Yarandi
Email: drvahidabedi@gmail.com
Address:Sina Hospital, Hassan Abad Sq., Imam Khomeini Ave., Tehran, Iran.

ABSTRACT

Introduction
This research was conducted to assess whether prophylactic citrate potassium can reduce double-J stent encrustation in patients with urolithiasis.

Methods
In the present study, 70 patients with urolithiasis were randomly assigned to two groups of control [22 men; mean age 43 (33-55)] and intervention [25 men; mean age, 41 (37-56)] after meeting inclusion criteria. Potassium citrate (10 mEq Alithoral tablet) was administered three times a day from double-J stent insertion until removal in the intervention group. For the control group, no treatment was given. It was examined after removing the stent, and laboratory tests were performed in encrustation. Moreover, blood and urine were collected for assessing creatinine, crystalluria, and pyuria. Information concerning the duration of double-J stent placement, the composition of urinary stone (calcium oxalate or other), number of attack episodes, type of double-J stent (one way or other), and smoking habit were collected.

Results
Three control group participants were excluded from the study due to missing follow-up. Patients of the two groups were matched for age, sex, duration of the double-J stent placement, and the number of attack episodes. There were significant differences regarding crystalluria and creatinine dosage between the two groups. Furthermore, double-J stent encrustation occurred in 3 (8.8%) and 11 (34.4%) patients of the intervention and control group, respectively, which showed a significant difference (P-value=0.012). Comparison between intervention and control group revealed an odds ratio of 18% (P-value=0.017) and 15% (P-value=0.023) in the crude and adjusted model, respectively.

Conclusions
Potassium citrate can significantly reduce double-J stent encrustation in patients with urolithiasis. Therefore, it is recommended that urologists consider citrate potassium as a preventive treatment for encrustation.

Keywords: Double-J; Potassium Citrate; Stent Encrustation; Transurethral Lithotripsy

Introduction

Nowadays, ureteral stents have become inseparable from urologists' routine practices (1). The ureteral stent has been employed as adjuvant therapy in the treatment

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of renal stones and urinary obstruction, identification of ureter during surgery, and handling urinary leakage (2). Although a broad spectrum of ureteral stents is used in urological settings, they may be associated with various complications, including, but not limited to, stent discomfort, infection, encrustation, and stone formation (2, 3).

Stent encrustation over Double J (DJ) stent is a prevalent complication of ureteral stenting (2, 4). The incidence of encrustation has a positive association with the DJ stent indwelling time (5). Stent encrustation can cause urinary infection (6), reconstruction (7), and even renal failure (8); therefore, it has the potential to be detrimental to patients' health (9, 10).

The applicability of potassium nitrate to reduce urolithiasis recurrence has been investigated in several studies, and virtually all of them have emphasized a significant reduction in renal stones through this approach (11-13). Moreover, high clearance rates of stones can be expected using potassium citrate through several mechanisms, including modulating the concentrations of urine electrolytes and saturation of calcium oxalate (14). Encrustation and resultant urine stones are common following stent insertion. Because potassium citrate is of proven value in reducing the rate of renal stones formation, we designed a randomized clinical trial to assess whether potassium citrate can decrease stent encrustation in patients with ureteral stents.

Methods

A total of 70 patients with ureteral stones were enrolled and underwent transurethral lithotripsy at the Urology Department of Sina Hospital during 2020. The study was under the Tehran University of Medical Sciences Ethical Committee after receiving the Iranian Randomized Clinical Trial code (IRCT20190624043991N8). Patients enter the study after signing the written informed consent. All the enrolled patients were indicated for transurethral lithotripsy and randomized to two groups. The exclusion criteria for our study were as follows: 1. Any metabolic abnormality; 2. Digoxin use; 3. History of hyperkalemia; 4. Pregnancy; 5. Calcium supplements usage; 6. Potassium-sparing diuretics; 7. Levodopa prescription; 8. Serum potassium higher than five mmol/l; 9. Glomerular filtration rate lower than 70 ml/min; 10. Patients treated with citrate potassium for any reason.

After confirming the inclusion and exclusion criteria, we explained to the patients that their information would only be used to conduct a research project approved by the ethics committee of Tehran University of Medical Sciences, and their written and informed consent was obtained for this purpose. After transurethral lithotripsy, the patients were randomly divided into intervention (n=35) and control group (n=35) using permuted balanced block randomization method (blocks of 4). The intervention group consisted of those who received double-J stents plus ten mEq Alithoral tablets (potassium citrate) three times a day from insertion until double-J removal (Figure 1). The control group included patients receiving only double-J stents with no potassium citrate. Moreover, we recommended that all the patients continue their routine eating habits, reduce sodium and foods rich in oxalate, consume at least two liters of water per day, and have regular calcium intake. To keep the urine pH in the intervention group between 6.8 and 7.2, we measured it every two weeks. The dosage of Alithoral increased to 40 mEq per day if urine pH was lower than 6.8, and if it was higher than 7.2, we decreased the dose of Alithoral to 20 mEq.

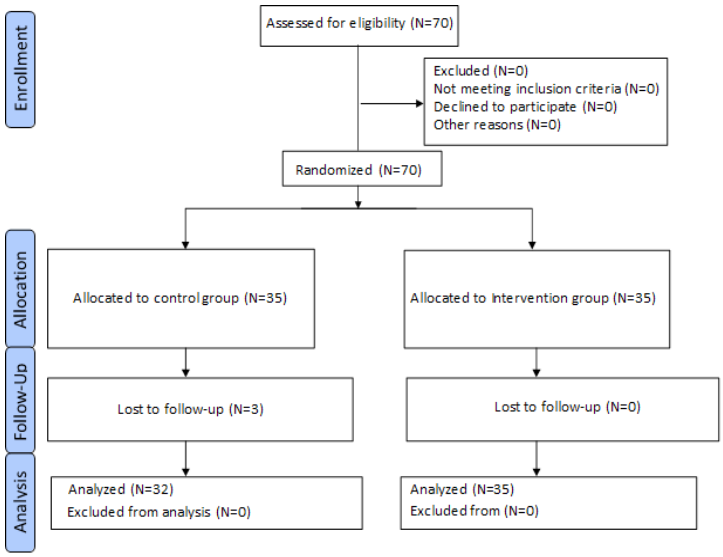

Figure 1. Flow diagram of the progress through the phases of a parallel randomized trial of the two target groups

Table1. Description of measured variables.

Variables	Groups		P-value
	Intervention	Control	
Crystalluria (Yes), N(%)	2 (7.7 %)	8 (25.0 %)	0.082++
Composition of stone (calcium oxalate), N (%)	32 (92.0%)	23(88.5 %)	0.610++
Creatinine dosage, median (IQR)	1.3 (1.2-1.6)	1.1 (1.0-1.3)	0.022+
Smoking (Yes), num. (%)	11 (32.4 %)	7 (21.9 %)	0.339++
Pyuria (No), num. (%)	0 (0.0 %)	6 (18.7 %)	0.013++
Type of Double J (1 way), num. (%)	32 (94.1 %)	29 (90.6 %)	0.471++
A stone found on or inside Double J (Yes), num. (%)	3 (8.8 %)	11 (34.4 %)	0.012++

+: Nonparametric test of comparing two medians; ++: Chi-squared test; IQR: Interquartile range ; num:number

Table 2. The logistic regression model containing the mere effect of groups

Variables	OR (95 % CI)	P-value
Group effect (Reference: control)	0.20 (0.04,1.04)	0.056
Crystalluria (Reference: No)	1.29 (0.25,6.62)	0.757
Group effect (Reference: control)	0.15 (0.03,0.77)	0.023
Cr dosage	1.00 (0.32,3.16)	0.996
Group effect (Reference: control)	0.27 (0.05,1.55)	0.140
Pyuria (Reference: No)	0.31 (0.05,2.07)	0.228

Moreover, we controlled patients' electrolytes in the intervention group every two weeks to prevent hyperkalemia. All patients were evaluated visually for the formation of stones and crusts on double-J stent at the time of double-J stent removal. Also, double-J stents were sent to the laboratory to assess stones and crust formation. For patients with encrustation, the composition of double-J stent encrustation was analyzed. Moreover, blood and urine samples were taken to evaluate crystalluria, creatinine, and pyuria. Patients' demographic information, including age, gender, smoking habits, recurrent formation of urinary stones, the stone composition (calcium oxalate), and type of double-J (one-way or two-way), were recorded. We also compared the patients of both groups for easy removal of the DJ stent, which was defined as DJ stent extraction without any resistance.

Statistical analysis

Continuous variables were reported using the median (interquartile range) and the discrete ones (percent). Moreover, to compare these two types of variables between intervention and control groups, nonparametric tests of comparing medians and Chi-squared test were used, respectively. Because a binary variable is designated as the response variable, logistic regression was used to assess the impact of covariates on this dependent variable, and then the odds ratios (ORs) produced by this model and reported in the results.

Results

Due to missing follow-up, three control group participants were excluded from our study. The control and intervention groups were matched for age and sex, duration of the double-J placement, and the number of attack episodes. The median ages of intervention and control groups were 41 (37-56) and 43 (33-55) years, respectively. Nearly 71.5% of the intervention group and 65.5% of the control group were men.

There were no differences concerning crystalluria, renal stone composition, smoking, and type of double-J between the two groups. Although the removal of the double-J stent was easier in patients of the intervention group than the control group (91.2% and 87.5%, respectively), there were no significant differences between the two groups in this regard (P-value=0.465). There were substantial differences in creatinine, pyuria, and encrustation (Table 1).

The logistic regression model was firstly fitted by considering the mere effect of groups and taking the control group as the reference. Then, the three variables showing significant differences between the two groups were added to this logistic model (Table 2). The crude model produced an OR of 0.18 (95% CI: 0.05, 0.74, p-value=0.017), which means that for a person in the intervention group, the average chance of encrustation is 82% lower than that in the control group. Moreover, the adjusted model generated an OR of 0.15 (95%CI: 0.030,

0.77, P-value=0.023), meaning that in the presence of Cr, the chance of encrustation in the intervention group is 85% lower in comparison with the control group.

Four and three patients of the control and intervention group with encrustation had a history of attack episodes, respectively. Moreover, the duration of double-J stent placement for the intervention and control groups was 28 (26-30) and 29 (27-31), which was not statistically significant.

The composition of the double-J stent in all patients of the intervention group was calcium oxalate. In patients of the control group, 73% had encrustation with calcium oxalate stones and the rest (27%) with calcium phosphate. Double-J extraction was performed quickly in 91.2% and 87.5% of the intervention and control groups, respectively, but there was no significant difference between the two groups in this respect (P-value=0.465).

Discussion

Although various methods have been proposed for managing double-J stent encrustation, there is an ongoing debate concerning the management of double-J stent encrustation because several deleterious complications may arise following double-J stent encrustation; therefore, the best option is to prevent encrustation from occurring. Up to now, there is no available information concerning the prevention of double-J stent encrustation. To the best of our knowledge, this randomized control trial is the first study assessing potassium citrate's efficacy in-stent encrustation or stent stone formation in patients with double-J stents insertion following transurethral lithotripsy. It has been demonstrated that the administration of citrate potassium in patients experiencing transurethral lithotripsy significantly decreases the chance of stent encrustation.

The mechanisms behind the decrease in odds of stone recurrence have been virtually illustrated. The strong binding between calcium ions and citrate leads to soluble complexes, thereby decreasing the supersaturation of calcium salts in urine (14, 15). Moreover, it is essential to note that urinary secretion or citrate reabsorption depends on the body's acid-base status. To modulate extra levels of acid in the blood, an increase in reabsorption of citrate from proximal renal tubule will occur, and in contrast, the decrease in the reabsorption of citrate will be expected in alkalosis; therefore, citrate concentration will be increased when using potassium citrate, but the likelihood of stone formation will decrease (16, 17).

Several studies have been dedicated to assessing the efficacy of potassium citrate in patients with renal stones of different compositions (18, 19). Robinson et al., investigated the effect of potassium citrate on 503 renal stone patients by measuring pre-treatment and post-treatment 24-hour urine values and following patients for 41 months. They claimed that urine pH and citrate of patients significantly increased in short- and long-term treatment with potassium citrate and the annual risk of stone formation also decreases significantly (from 1.89 to 0.46) following potassium citrate treatment.

Encrustation has remained one of the main stent complications causing quite a few troubles for the urologist. Crystallization of urine salts is the primary pathophysiology of encrustation following catheter or stent insertion (20, 21). It has been demonstrated that there are various risk factors for encrustation, including long duration of the indwelling stent, urinary sepsis, chemotherapy, pregnancy, chronic kidney failure, and history of urolithiasis (22, 23). Our patients were matched for the duration of double-J placement and history of urolithiasis and were negative for other risk factors.

Several studies have investigated the composition of encrustation in double-J stents. The main component of the double-J stent was calcium oxalate in the study of Scarneciu et al., which was performed on 134 ureteral stents, of which 57 had encrusted ureteral stents (22). Singh et al., pointed out that calcium oxalate is the main component of encrustation (23). In the present study, the same finding was observed, and calcium oxalate was the main constituent of the double-J stent. Since the main component of double-J stent encrustation was calcium oxalate and because it has been postulated that citrate potassium is beneficial to prevent a renal stone recurrence, it is plausible that citrate potassium is capable of reducing the odds of encrustation occurrence.

No severe side effects for potassium citrate have been reported, and a majority of side effects such as diarrhea, nausea, and abdominal bloating are related to the gastrointestinal system. According to a review conducted by Mattle et al., the rate of side effects among patients treated with potassium citrate and placebo were 33% and 17%, respectively (17). While the tablet form of potassium citrate (Alithoral) is associated with lower complications versus the liquid form, there is a limitation in its usage among patients with chronic diarrhea (24). In our study, there were no complaints of complications.

This study has several strong points. First, in a clinical trial study, we showed for the first time that potassium citrate could safely be used to prevent double-J stent encrustation. Second, to avoid bias in the current study, we matched the patients of both groups for well-known risk factors of double-J stent encrustation, especially duration of double-J placement and history of urolithiasis.

The main limitation of our study is that urine citrate, potassium, and other components were not measured before and after the treatment to assess their changes during the treatment.

Conclusions

The main focus of previous studies has been managing double-J stent encrustation, and no option has been

presented for preventing double-J stent encrustation. Our study provides a novel finding that potassium citrate can decrease the chance of double-J stent encrustation, which is a common complication following double-J stent insertion in patients with urolithiasis. Thus, we suggest urologists consider potassium citrate as a preventive treatment for encrustation.

Authors' contributions
All authors contributed equally.

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Conflict of interest
All authors declare that there is no potential competing or conflict of interest.

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Ethics statement
The study was under the Tehran University of Medical Sciences after receiving the Iranian Randomized Clinical Trial code (IRCT20190624043991N8). Patients enter the study after signing the written informed consent.

Data availability
Data will be provided on request.

Abbreviations
DJ Double J
TUL Transurethral Lithotripsy

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Author (s) biosketches

Tavoosian A, Assistant Professor**,** Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran.

Email: alitavoosian@gmail.com

Rahimnia A, MD, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.

Email: rahimnia.amir@gmail.com

Tehranipour E, MD**,** Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran.

Email: etehranipour80@yahoo.com

Khajavi A, PhD, Student Research Committee, Faculty of Paramedical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Email: alireza.khajavi.student@gmail.com

Tamehri Zadeh SS, MD, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran.

Email: tamehrysaeed@gmail.com

Abedi Yarandi V, MD, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran.

Email: drvahidabedi@gmail.com

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