

Does potassium citrate administration change the type and composition of encrusted material on Double-J stent compared to primary stone?

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Abstract

Purpose To evaluate the effect of potassium citrate administration on the composition of encrusted material on the ureteral stent after Double-J insertion.

Methods We designed a randomized clinical trial for our study; 65 patients that underwent transurethral lithotripsy and Double-J stent insertion were included in the study after informed consent and divided into two groups. In the first group (33 patients) potassium citrate was prescribed after surgery till stent removal and the second group (32 patients) followed without prescribing this medication. After stent removal, encrusted materials on removed stents were analyzed then the type and composition of encrusted material compared with the primary stone that was removed.

Results Our results revealed that the type and composition of primary stone and encrusted stone were similar in patients that do not receive potassium citrate (*p*-value of 0.073, 0.251 and 0.944 for calcium oxalate, uric acid, and calcium phosphate respectively). In patients that taking potassium citrate rate of calcium oxalate (*p*-value < 0.001) and uric acid (*p*-value < 0.001) material on encrusted stent significantly decreased compared with the non-intervention group.

Conclusion Results of this study revealed that taking of potassium citrate after ureteral stent insertion significantly decreases the formation of calcium oxalate and uric acid encrusted material on Double-J stent so it could be recommended for prevention of stent encrustation in patients that primary stone analysis are calcium oxalate and uric acid stone.

Keywords Urolithiasis · Double- J stent · Potassium citrate · Stent encrustation

Abbreviations

BMI	Body mass index
UVJ	Ureterovesical junction
Ca. ox	Calcium oxalate
Ca.H.po4	Calcium hydrogen phosphate
Fr	French
DJ	Double-J
SWL	Shock wave lithotripsy
COVID-19	Coronavirus disease 2019

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Introduction

With the advance in endourologic procedure need to stent placement is increasing. The consensus for ureteral stent insertion is compromised renal function, mucosal ureteral wall injuries or perforation, and significant residual stone. Placement of ureteral stent is not free of morbidity, and is associated with Irritative urinary symptoms, urinary tract infection, stent encrustation, and sometimes rare situations like stent migration, fragmentation, and retained/forgotten stent [1–3].

Among these morbidities, encrustation is sometimes problematic as could prevent easy removal of the stent [4-6]. The most important factor related to stent encrustation is the duration of stent placement as this time increase by more than 3 months, the rate of encrustation will have increased [7-11]. The other risk factors are urinary tract infections and pregnancy [12]. Using of potassium citrate in urolithiasis is well-established especially in hypocitraturic

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patients and recurrent calcium stone formers. The potential mechanisms are inhibition of the nucleation, aggregation of calcium and oxalate crystals, and alkalinization of urine [13]. Also, the effect of potassium citrate on the dissolution of uric acid confirmed as strongly recommended in these stones [14–16]. With these well-known effects of potassium citrate, we designed a study if it could change the type and composition of encrusted material on the stent in patients that underwent transurethral lithotripsy and Double-J stent insertion.

Materials and methods

In a randomized clinical trial study from January 2020 to April 2020, seventy patients that undergone transurethral lithotripsy and Double-J stent insertion for ureteral stone were enrolled in our study after obtaining written informed consent. This study was approved by the ethics committee of Tehran University of Medical Sciences (IRCT20190624043991N6). The exclusion criteria were patients that taking drugs such as digoxin and potassium sparing-diuretics, pregnancy, chronic kidney disease, and history of hyperkalemia. Patients were divided randomly to separate groups; the first group (35 patients) received the extended-release oral tablet of potassium citrate; 10 meq three times a day till stent removal, and the second group (35 patients) do not receive this medication. The same dietary recommendation was given to the control and intervention groups in written instruction. To kept the urine pH of the intervention groups between 6.8 and 7.2, we measured their urine pH every 2 weeks. The dosage of potassium citrate 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 dosage of potassium citrate to 20 meg per day. Also, to prevent hyperkalemia, we controlled the electrolytes of the patients of the intervention group every two weeks. If patients had severe urinary symptoms or fever that suggestive of urinary tract infection, a urine sample was sent for culture. We used Double-J 4.8 Fr stent for all patients (Gohar Shafa, Polyurethane type, 4.8 Fr Double-J stent). Our indications for stent insertion were significant bolus edema, ureteral stricture, ureteral perforation, and significant hydronephrosis. After removal of the Double-J stent, we evaluated the proximal tail of double-j stent (4-5 cm) for any difference of stent encrustation in two groups (due to more problematic stent removal if encrustation formed in the proximal tail), also we had analyzed stents in our laboratory for the difference in type and composition of encrusted material on stent from primary stone in two groups. The primary stone analysis was performed in our laboratory by an expert biologist with a qualitative infrared spectroscopy method. After stent removal, the encrusted material on the stent was removed mechanically and analyzed in the same way as primary stone analysis by the infrared spectroscopy method. Demographic data, location of ureteral stones, type of primary stone, the composition of encrusted materials, stent-related symptoms evaluated in two intervention and control groups. All statistical analysis was performed by independent *t*-test, Chi-Square test, Fisher-exact test, paired *t*-test, and by using SPSS 22.0 software for windows. A flowchart of our study is depicted in "Appendix".

Results

At the end of the study, three patients of the control group and two patients of the intervention group lost the follow-up so excluded from the study ("Appendix"). The control group (32 patients) and intervention group (33 patients) matched for the location of ureteral stone and duration of the indwelling double-j stent. There were no significant differences between the 2 groups in terms of demographic characteristics such as age, sex, and body mass index (Table 1). The hospital stay time and duration of stent-related symptoms were not significantly different between the two groups. There was no significant difference between groups regard to primary stone composition. As mentioned earlier our indications for stent insertion were significant bolus edema, ureteral stricture, ureteral perforation, and significant hydronephrosis; in these conditions, we routinely remove DJ stent after 4-6 weeks but due to the beginning of COVID-19 pandemic and fear of hospital admission many of them had several days delay in returning for DJ removal. There were not any significant differences between the two groups regarding the indications for stent placement.

In patients that had not received potassium citrate, type of primary stone and encrusted material on stent was not significantly different (*p*-value of 0.073, 0.251, and 0.944 for calcium oxalate, uric acid, and calcium phosphate respectively) but in patients taking potassium citrate by comparing the pre-stenting primary stone composition and poststenting encrustation materials; results revealed a decrease in calcium oxalate and uric acid encrustation on stent surface (*p*-value < 0.001). An image of the effect of potassium citrate on decreasing encrustation represents in Fig. 1. The results are mentioned in detail in Table 2.

The mean duration of double-j stent placement in the control group and intervention group was 50.59 ± 17.01 and 50.03 ± 15.07 days respectively (due to the beginning of COVID-19 pandemic and fear of hospital admission many of them had several days delay in returning for DJ removal), in this period stent-related complication including hematuria, Irritative symptoms, urinary tract infection, and rare complications such as stent migration and fracture compared between two groups (Table 3). There were no significant

	Citrate: $N=33$ (mean \pm SD)	No citrate: $N=32$ (mean \pm SD)	<i>p</i> -value
Age (years)	47.76 ± 14.125	46.25 ± 13.63	.663*
Weight (kg)	78.03 ± 10.48	74.81 ± 12.77	.270*
Height (cm)	170.85 ± 6.47	170.41 ± 6.74	.788*
BMI	26.65 ± 2.65	25.62 ± 3.27	.169*
Pain duration (days)	9.42 ± 5.25	10.16 ± 5.51	.585*
Hospitalization (days)	2.79 ± 1.36	2.28 ± 1.11	.107*
Primary DJ (days)	50.03 ± 15.07	50.59 ± 17.01	.888*
	Number (%)	Number (%)	_
Sex			
Female	10 (30.3%)	11 (34.4%)	.726**
Male	23 (69.7%)	21 (65.6%)	
Location of primary stone			
UVJ	18 (54.5%)	18 (56.3%)	.879 ^I
Mid ureter	10 (30.3%)	11 (34.4%)	
Upper ureter	5 (15.2%)	3 (9.4%)	
Type of primary stone (% Ca.ox)			
0–30	13 (39.4%)	8 (25.0%)	.352**
31–70	9 (27.3%)	14 (43.8%)	
>70	11 (33.3%)	10 (31.3%)	
Type of primary stone (% uric acid)			
0–30	16 (48.5%)	23 (71.9%)	.106 ^I
31–70	13 (39.4%)	5 (15.6%)	
>70	4 (12.1%)	4 (12.5%)	
Type of primary stone (%Ca.H.ph)			
0-30	31 (93.9%)	30 (93.8%)	1.000^{H}
31–70	1 (3.0%)	2 (6.3%)	
>70	1 (3.0%)	0 (0.0%)	

*Independent T-test

**Chi-Square test

¹Fisher-exact

differences between mentioned items in the two groups especially the rate of urinary tract infection. We didn't have Clavien-Dindo complication of grade 3 or 4, and most complications were categorized as grade 2 complications.

Discussion

With increasing the routine use of ureteral stent in the endourologic procedure, stent-related complications will be more common. One of the complex problems of Double-J stent insertion is stent encrustation [17]. Stent encrustation could result in difficulty in stent removal and occasionally due to obstruction of ureteral lumen result in renal failure in case of forgotten stents [18]. The most significant factor related to stent encrustation is the time of stent placement [11, 19, 20]. In an interesting study by Sighinolfi et al., they analyzed variables that related to stent encrustation and found encrustation in the proximal tail of double-j stentrelated to the metabolic factors such as hypercalciuria and calcium oxalate was the most common composition on proximal tail whereas encrustation at the distal tail related to the urinary tract infection and age of patients; maybe aging could predispose to urinary tract infection [21]. In the study by Kawahara et al., they mentioned that stent encrustation is not related to the duration of stent placement, but interestingly caliber of stent-related to stent encrustation as larger caliber stent (> 7 Fr) demonstrated a lower rate

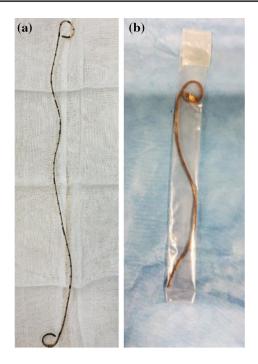


Fig. 1 a Citrate administration and b control group

of encrustation compared with smaller stents (<6 Fr) [22]. The stent encrustation is a complex phenomenon and several theories are suggested in this regard; as stent encrustation increased by duration of stent placement, the role of urinary tract infection could not be ignored, especially urease-producing bacteria can predispose to stone formation by increasing urinary pH (especially in urine pH more than 7.2). Also, bacteria could have formed a biofilm that accelerates the aggregation of crystals on biofilm [23–26]. In recent years many inventions in stent material have been made to reduce the chance of stent encrustation such as using silicone stents instead of conventional polyurethane stents; in the study by Bouzidi et al. rate of stent encrustation and biofilm formation were lower in silicone stents compared with polyurethane stents [27]. The other novelty in ureteral

stent design to reduce stent encrustation were drug-eluting stents(antibiotic-eluting) and heparin-coated stents (antiadhesive effect) that both of which had incongruous results [28–30].

In the study by Scarneciu et al., they evaluated 138 removed ureteral stents for the composition of encrustation material on the Double-J stent in a different part of the stent and found the most common composition is calcium oxalate; they concluded that the mechanism of stent encrustation and urolithiasis is similar [31]. Ilie et al. [32]cited encrustation mainly occurred in renal and bladder end of the stent and ureteric segment of the stent is less prone to encrustation due to peristaltic movement of the ureter, but on the contrary study by Baltitude et al. [33]mentioned only proximal tail of double-j stent predispose to encrustation because peristalsis has an inhibitory effect on encrustation on the body and distal end of the double-j stent with the washing of debris. Several studies confirmed that encrustation in the proximal tail of double-j stent is more problematic for stent removal and predict the need for multiple sessions of surgery for stent removal [19, 34]. The role of potassium citrate as an inhibitor of calcium oxalate stones is well known for the inhibition of nucleation and aggregation of crystals. Also since the most frequent composition of encrusted material is calcium oxalate it is the rationale that encrustation and stone formation have the same pathophysiology. A study by Pak et al. evaluated 1392 patients with urolithiasis and mentioned hypocitraturia as the most common metabolic finding in their report (44.3%) [35]. In a retrospective study by Idweini they compared two group of patients that underwent Shock Wave Lithotripsy(SWL) and double-j stent insertion;82 patients underwent SWL and double-j stent insertion without potassium citrate administration and 132 patients underwent SWL and stent insertion and taking potassium citrate due to metabolic reasons, stent encrustation reduced significantly in patients used potassium citrate (7 vs 33% *p*-value < 0.05) [36] Concerning these known effects of potassium citrate and prevalence of hypocitraturia in stone formers, we have conducted a randomized trial study to evaluate its impact

	Table 2	Changes in	type of	encrustation	after interve	ention
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Stone type	Citrate			No citrate		
	Pre	Post	p-value*	Pre	Post	<i>p</i> -value*
Ca.ox	54.84±37.51 (%)	14.84±35.71 (%)	<.001	65.93 ± 34.06 (%)	49.68±40.28 (%)	.073
Uric acid	30.60±39.60 (%)	6.36±24.21 (%)	<.001	20.93 ± 34.48 (%)	14.68±28.16 (%)	.251
Ca.H.ph	14.54±27.51 (%)	9.09±29.199 (%)	.331	13.12±23.20 (%)	12.81±27.26 (%)	.944

*Paired T-test

Table 3 Comparison of symptoms in two study group

	Citrate	No citrate	<i>p</i> -value
Urinary leakage			
, e	_	_	_
Mild Hematuria	25 (75.8%)	23 (71.9%)	.783*
Urinary obstruction	-	-	-
Antibiotics			
Cefexime	0	1 (3.1%)	.475**
Cephalexin	6 (18.2%)	3 (9.4%)	
Ciprofloxacin	27 (81.8%)	28 (87.5%)	
Fever and chill	-	-	-
Irritative voiding symptoms	22 (66.7%)	26 (81.3%)	.181*
Incontinence	1 (3.0%)	0	.508**
Suprapubic or flank pain	11 (33.3%)	13 (40.6%)	.543*
Vesicorenal reflux	-	-	-
Pyuria	7 (21.2%)	4 (12.5%)	.273*
Urinary tract infection	1 (3.0%)	3 (9.4%)	.355**
Malposition	-	-	-
Migration	-	-	-
Inadequate relief of obstruction	2 (6.1%)	1 (3.1%)	.512**
Ureteral erosion or fistulization	-	-	-
Fracture	-	-	-

*Chi-Square test

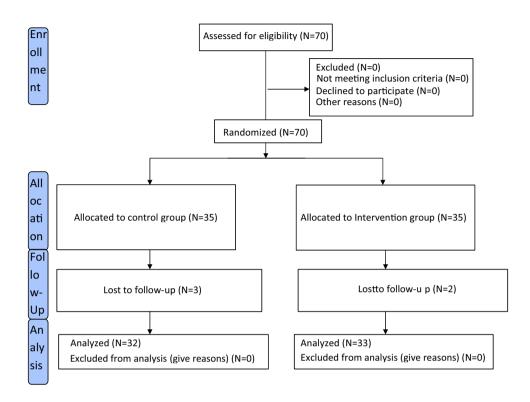
**Fisher-exact test

on changing composition of encrusted material on stent especially proximal tail because removal of double-j with proximal tail encrustation is more difficult than encrustation in body and distal tail of stent. As far as we know, this study is the first clinical trial that evaluated the effect of potassium citrate on the composition of encrusted material on double-j stents. The results revealed that in patients who had a Double-J stent and primary stone analysis is calcium oxalate and uric acid, type and composition of encrusted material on stent significantly change by taking of potassium citrate compared to control group that does not receive this medication, so this may result in easier stent removal in this group. We don't find serious complications with this medication so it could be recommended as a low-cost and feasible way to reduce stent encrustation in daily practice. One of the concerns about potassium citrate administration is that if alkalinization of urine exceeds more than 7.2, the risk of stone formation increased so we measured their urine pH every two weeks to adjust the dose of potassium citrate. Our study had some shortcomings and limitations; the first one is that some patients lost the follow-up, the second one is that some patients had a delay in their DJ removal due to fear of hospital admission during the COVID-19 pandemic but this factor matched in the two groups in the final analysis. The third one is that our study was a single-center study with a limited number of patients so we recommend a similar study by multicenter collaboration with evaluating a large number of patients. Another study that compares recurrent and first stone former for evaluating the impact of potassium citrate on stent encrustation in patients with a metabolic change in 24-h urine analysis could be interesting. This study revealed that in patients who underwent transurethral lithotripsy and double-j stent insertion and primary stone analysis is calcium oxalate and uric acid, potassium citrate administration has a preventive effect on stent encrustation, but this effect is not evident in patients with other types of stones (calcium phosphate and struvite stones).

Conclusion

Results of this study revealed that taking of potassium citrate after ureteral stent insertion significantly decreases the formation of calcium oxalate and uric acid encrusted material on Double-J stent so it could be recommended for prevention of stent encrustation in patients that primary stone analysis are calcium oxalate and uric acid stone.

Appendix



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Declarations

Conflict of interest Nothing to declare.

Ethical approval This study was approved by the ethics committee of Tehran University of Medical Sciences (IRCT20190624043991N6).

Informed consent Informed consent was obtained from all patients included in our study.

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