



Comparison of the effects of potassium citrate and hydrochlorothiazide on the ureteral stent encrustation in patients with long stent survival; a single-blinded clinical trial

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ABSTRACT

Introduction: The probability of encrustation after embedding ureteral stent is 9.6% in six weeks, 47.5% in 6 to 12 weeks and 76.3% in more than 12 weeks.

Objectives: This study was designed to evaluate the effect of potassium citrate and hydrochlorothiazide on ureteral stent encrustation as a single-blinded clinical trial.

Patients and Methods: After embedding ureteral stent in 130 patients, the individuals were randomly divided into two groups using random allocation software. Convenience sampling method was used in this study. One group was given hydrochlorothiazide and potassium citrate, and the other group did not receive any medication. All stents were the same brand and the maximum time of stents being in situ was six weeks. Four to six weeks after stent implantation, patients were referred for stent removal. Then, ureteral stent encrustation was recorded in the two groups according to the visual appearance and the difficulty in stent removing due to stent encrustation.

Results: The mean age of the patients was 42.62±14.86 years. Regarding gender, 78 patients (67.8%) were male and 37 patients (32.2%) were female. In this study, 15 patients (13%) had ureteral stent encrustation, of which 13 patients (20%) were in the group without medication and two patients (4%) were in the group who received hydrochlorothiazide and potassium citrate ($P = 0.012$).

Conclusion: The rate of ureteral stent encrustation in the patients who received hydrochlorothiazide and potassium citrate was significantly lower than the patients in the control group. This can be justified by the diuretic properties of hydrochlorothiazide and the reduction of urinary calcium levels. Additionally, high urinary citrate level and induction of urinary alkalization after the administration of potassium citrate. Are the ameliorating factors

Trial Registration: Registration of trial protocol has been approved by Iranian Registry of Clinical Trials (identifier: IRCT20180625040232N3, <https://en.irct.ir/trial/46227>, ethical code# IR.UMSU.REC.1396.130).

Implication for health policy/practice/research/medical education:

In a single-blinded clinical trial in 130 patients, we found that administrations of hydrochlorothiazide and potassium citrate significantly reduce the rate of ureteral stent encrustation.

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Introduction

The ureteral stent, or double J (DJ), as a narrow and flexible catheter, is inserted into the ureter during urological surgeries such as TUL (transureteral lithotripsy), PCNL (percutaneous nephrolithotomy), pyeloplasty,

pyelolithotomy. It usually remains inside the ureter for about three weeks and then should be removed by a urologist during outpatient surgery. It is usually removed by urologists in outpatients procedures. However in some cases in which ureteral stent is attached to Foley catheter,

the ureteral stent is also removed during surgery through removing Foley catheter (1). Ureteral stent is usually inserted in these conditions; 1) severe ureteral stenosis, thereby it is impossible for the ureteroscopy device to pass through the ureter, 2) facilitating the passage of the stone fragments after surgery such as TUL and PCNL (2,3).

Numerous problems have been reported related to ureteral stents including stent malfunction, hematuria, stent displacement, twisting of stent, infection, sometimes spontaneous down migration of DJ and stent fragmentation (4-7).

In some cases intrarenal encrusted stent needs extra-procedures such as extracorporeal shock wave lithotripsy (ESWL), ureteroscopy with lithotripsy for stent extraction (8, 9). Ureteral stent encrustation is more common in patients with history of recurrent kidney stone formation (10). For any reason, if the ureteral stent remains in the long-run, renal dysfunction and urinary tract infection (UTI) will be considered as possible complications (11-12). According to the study by El-Fagih et al, the rate of ureteral stent encrustation has direct relation with the duration of ureteral stent being in situ inside the urinary system. The probability of stent encrustation is 9.6% in six weeks, 47.5% in 6 to 12 weeks and 76.3% in more than 12 weeks after stent insertion (5).

Objectives

Considering the high prevalence of stent encrustation

after stent insertion, which may be associated with complications such as renal malfunction and UTIs, we designed a study to evaluate the effect of potassium citrate and hydrochlorothiazide on ureteral stent encrustation.

Patients and Methods

Study patients

This study was a single-blinded clinical trial carried out on 130 patients underwent urological surgeries needing ureteral stents being in situ for at least 4-6 weeks. The patients were randomly divided into two groups using Random Allocation software (Figure 1). Convenience sampling method was applied in this study. One group was given 50 mg hydrochlorothiazide daily and 20 mEq daily potassium citrate powder which was administered in the form of a solution with 100 mL water in three doses after each meal, and the other group did not receive any medication. The researcher was not aware of the type of groups assigned to the patients. All stents were made by the same company and the maximum time of stent being in situ was six weeks.

Inclusion criteria were patients over the age of 18 and under 60 years, having American Society of Anesthesiologists Classification (ASA) I and II, elective surgery, and patients without UTIs or metabolic disorder. Exclusion criteria included emergency surgery, sensitivity to hydrochlorothiazide and potassium citrate, and ASA > II. After the preoperative evaluation of the patients by

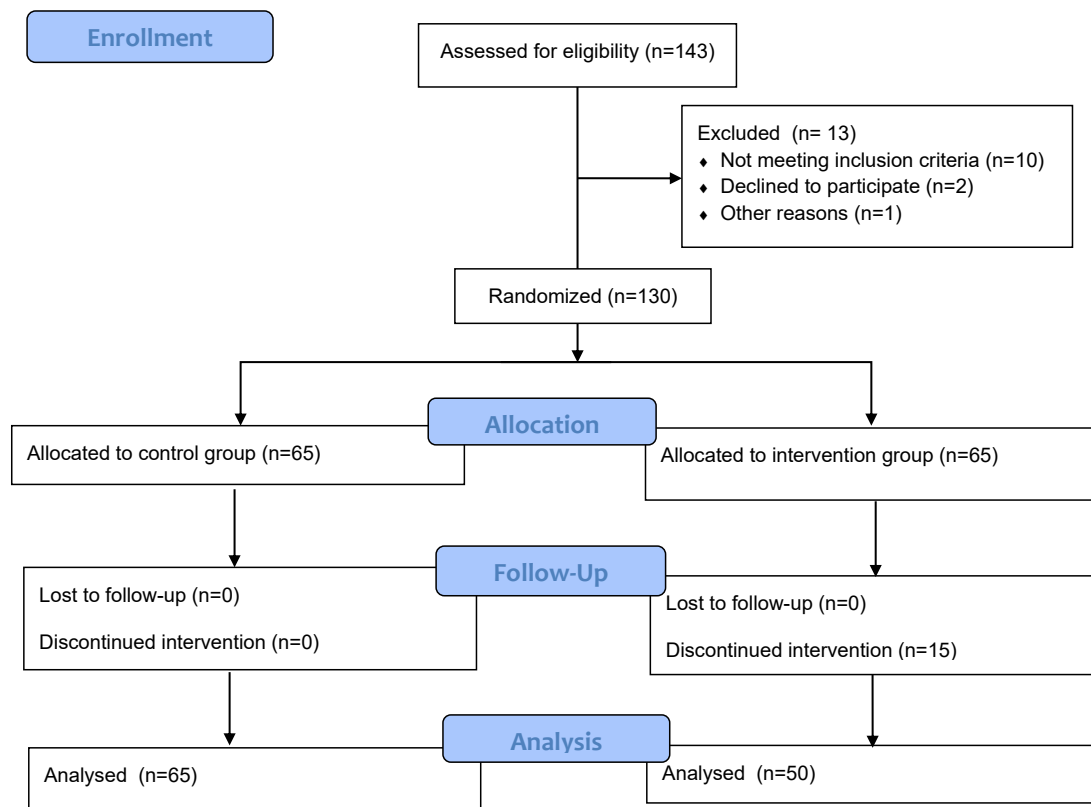


Figure 1. CONSORT (consolidated standard of reporting trial) chart for study.

the project manager, patients were placed in the operating room. After induction of general or spinal anesthesia and performing the surgery, insertion of ureteral stent in the qualified patients was conducted at the end of surgery. A tablet of 50 mg hydrochlorothiazide once a day and 20 mEq potassium citrate powder three times a day were given to the intervention group up to the time of stent removal. No medication was given to the other group. Four weeks after insertion of the ureteral stent, the patients were referred for stent removal. Stent encrustation is defined as the need to anesthesia for the stent removal and the existence of obvious visible encrustation. A pre-prepared list was filled and then the data were analyzed.

Statistical analysis

The data were analyzed by SPSS version 20. Descriptive statistics for variables were expressed in terms of their type, frequency, percentage, mean and standard deviation. In order to compare quantitative variables, independent *t* test and to compare the frequency of ureteral stent encrustation, the chi-square test was used. Accordingly, *P* value less than of 0.05 was considered significant.

Results

Based on the eligibility criteria, 130 patients entered into the study. Fifteen patients in the study group were excluded due to incompliance with the drugs. The mean age of the patients was 42.62 ± 14.86 years. Totally, 78 of the patients (67.8%) were male and 37 (32.2%) were female. In the intervention group, 50 patients (43.5%) completed the treatment course and 65 patients (56.5%) did not receive medication as a control group.

In the study, the mean age of the patients in the intervention group (potassium and hydrochlorothiazide) was 41.40 ± 15.23 years and in the control group (without receiving medication) was 43.56 ± 14.26 years ($P = 0.440$). In the intervention group, 34 patients (68%) were male and 16 patients (32%) were female while in the control group, 44 patients (67.69%) were male and 21 patients (32.31%) were female ($P = 0.927$).

The mean body mass index in the intervention group was 23.82 ± 4.38 kg/m² and in the control group was 24.96 ± 4.46 kg/m². The two groups had no significant difference in this regard ($P = 0.192$). In this study, 15 patients (13%) had stent encrustation, of which 13 patients (20%) were in the control group and two patients (4%) were in the intervention group ($P = 0.012$). One of the patients in the encrustation group was a 35-week pregnant woman (Table 1).

In the group with ureteral stent encrustation, the mean age was 41.46 ± 13.93 years and in the group without ureteral stent encrustation, the mean age was 50.40 ± 18.77 years. The two groups differed in terms of mean age, which was statistically significant ($P = 0.029$).

The mean BMI in the patients without stent encrustation

was 23.97 ± 4.50 kg/m², and in the patients with ureteral stent encrustation was 27.46 ± 4.89 kg/m², this difference was statistically significant ($P = 0.003$; Table 2, Figure 2). The rate of ureteral stent encrustation in groups based on gender was investigated. The results of this study showed that in the group with ureteral stent encrustation, 8 patients were male and 7 patients were female, and in the group without ureteral stent encrustation, 70 patients were male and 30 patients were female; this difference was not significant ($P = 0.239$, Figure 3). Stent encrustation was significantly higher in the control group ($n = 13$) compared to the intervention group ($n = 2$) ($P = 0.012$; Table 3).

Discussion

Over the past two decades, the introduction of less invasive methods such as ESWL and laser ureteroscopy has led to less attention being paid to drug prophylaxis treatments and their reduction in the treatment of kidney stones. Studies show that approximately 90% of patients seek to determine the cause of kidney stones and follow a diet and take medication to prevent them in the future. Theoretically, alkaline citrate is a preventative treatment to prevent the re-formation of calcium oxalate stones. In addition, citrate limits the activity of calcium ions (2-5). Therefore, the present study aimed to determine the effect of hydrochlorothiazide and potassium citrate in the formation of ureteral stent encrustation in patients with long stents in Urmia, Iran. As mentioned, in our study, 15 patients (23%) were excluded from the study (control group due to drug intolerance. In a study by Parks et al (13), the exclusion rate was 38% higher than in our study. The reason why patients refuse to take the drug can be due to the low-motivation of the patients, the lack of symptoms and the taste of the drugs, and the possible side effects of the drug. Studies have shown that thiazides are

Table 1. Demographic characteristics of the studied patients

Variable	Intervention group	Control group	P value
Age (y) (Mean±SD)	41.40 ± 15.23	43.56 ± 14.62	0.440
BMI (kg/m ²) (Mean±SD)	23.82 ± 4.38	24.91 ± 4.46	0.192
Gender	Male	34 (68%)	44 (67.69%)
	Female	16 (32%)	21 (32.31%)

Table 2. Comparison of BMI in the patients by ureteral stent encrustation

Variable	Group	Mean	SD	P value
BMI (kg/m ²)	Without stent encrustation	23.97	4.50	0.003
	With stent encrustation	27.56	4.89	
Age (year)	Without stent encrustation	50.40	18.77	0.029
	With stent encrustation	41.46	13.93	

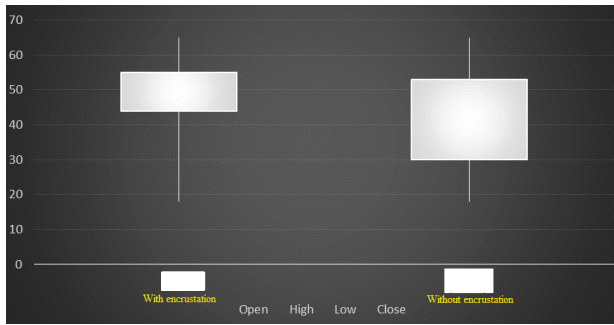


Figure 2. Evaluation of age distribution of patients based on ureteral stent encrustation.

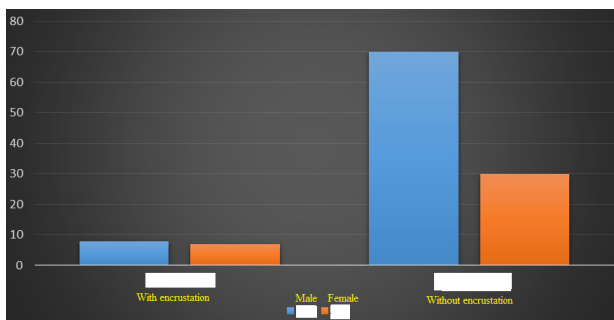


Figure 3. Evaluation of gender distribution of patients based on ureteral stent encrustation.

Table 3. Comparison of cases with or without stent encrustation by gender and group

Variable	Stent encrustation		P value
	Yes	No	
Gender	Male	7	0.239
	Female	30	
Group	Intervention	63	0.012
	Control	52	

rate of ureteral stent encrustation in their study compared to our study could be due to the long-duration of the study and longer stent survival with follow-up of one year, while the follow-up was four weeks in our study.

The overall purpose of our study emphasized the role of potassium citrate in ureteral stent encrustation. The effects of potassium citrate were confirmed in the study by Idweini and Soygür et al (16,17) which were consistent with our study. In a study by Soygür et al (17), 90 patients following ESWL with stones less than 5 mm were randomly treated with potassium citrate in three doses and received placebo in the other group.

Azm and Higazy (18) evaluated the effects of thiazide on stones after ESWL in the stent encrustation. In this study, patients received 40 mg of normal saline and 40 mg of furosemide serum when receiving ESWL. The results of this study showed that ureteral distal stones significantly lower in the case group than in the control group, which were standardized by ESWL. Although the method of this study is different from our study, the overall results of this study emphasize that diuresis is a useful and important principle for stone excretion in patients and the reduction of urinary calcium and high excretion of oxalate and alkalization of urine by citrate should be justified. Rebl et al developed an in vitro encrustation system for provoking encrustation on polymer samples during five days. They showed that materials with a slight hydrophilicity and a strong negative surface charge are not suitable to be used as stent material. They suggested developing new ureteral stents to minimize encrustation, indicating that the materials used in the stents can be facilitated the encrustation process (19).

In a study by Torrecilla et al (20), ureteral stent encrustation reduced after modulating the urine PH. The duration of the study was 3 to 8 weeks. All patients check the PH of urine every morning in the home. Approximately, encrustation rate was 8 times greater in the placebo group (8%) compare to the intervention group (1%). Besides, the mean encrustation score in the placebo and intervention groups were 85.12 and 18.91, respectively.

Conclusion

The rate of ureteral stent encrustation in the patients who received hydrochlorothiazide and potassium citrate was significantly lower than that of the patients who did not

associated with side effects such as hypotension, fatigue, and hypercalcemia, increased urinary and blood urea. Potassium citrate can also cause anxiety as well as an increase in urine volume in patients (14,15).

In this study, 15 patients (13%) had ureteral stent encrustation, of which 13 patients (20%) were in the control group and two patients (4%) were in the group who received hydrochlorothiazide and potassium citrate powder. The difference was statistically significant. The duration of treatment in our study was four weeks and the patients were evaluated after 4 weeks regarding ureteral stent encrustation. A study by El-Faqih et al (5) reported ureteral stent encrustation (9.2% before 6 weeks, 47.5% at 6 to 12 weeks, and 76.3% after 12 weeks). In their study, patients did not receive drugs while the aim of the study was only to evaluate the degree of ureteral stent encrustation in those patients.

In a recent study by Idweini (16) on the effect of potassium citrate to prevent ureteral stent encrustation, 82 patients in the control group and 130 patients in the intervention group were included in the study. The two groups were homogenized regarding demographic characteristics. In their study, the mean ureteral stent encrustation time for the control group was 6.2 months, which included 33% of patients, however this rate was 7% in the intervention group and the mean ureteral stent encrustation time was 8.6 months. The reason for the high

receive any prophylactic medication of stone formation. This can be justified by the diuretic properties of hydrochlorothiazide and the reduction of urinary calcium levels and high urinary citrate level and induction of urinary alkalization. Citrate and hydrochlorothiazide can be used as a prophylactic treatment for stent encrustation in patients with a history of recurrent stone formation.

Suggestion

It is suggested that in future studies, the effects of hydrochlorothiazide and potassium citrate be divided into two groups to be assessed separately, thereby the effective role of each drug in different groups can be evaluated.

Study limitations

Problems such as the combined effect of the two drugs (hydrochlorothiazide and potassium citrate) can affect the results. The ureteral stent's company can affect the rate of stent encrustation as well.

Authors' contribution

RV, SF and AT designed the study. HR and SF performed the experiments. HR collected data from patients and helped in performance of experiments. HR, SF and RV prepared the primary draft after analysis. Final draft was checked by MRR, RV and SF. All authors read and signed the final paper before publication.

Conflicts of interest

There are no conflicts of interest.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. This study is a randomized controlled trial, registered in the Iranian Registry of Clinical Trials (IRCT20180625040232N3, <https://en.irct.ir/trial/46227>). The study was reviewed and approved by the ethical committee of Urmia University of Medical Sciences (IR.UMSU.REC.1396.130). Accordingly, written informed consent was taken from all participants before any intervention. This study was extracted from medical thesis of Hadi Ranjbar, at the urology department of Urmia University of Medical Sciences (Thesis# 27820). Besides, ethical issues (including plagiarism, double publication) have been completely considered by the authors.

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