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Safety of Omitting Preoperative Antibiotic Prophylaxis in Patients Undergoing Transurethral Ureterolithotripsy

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Abstract

Background: Transurethral ureterolithotripsy (TUL) is a common and highly efficient procedure for treating ureteral stones. The need for preoperative antibiotic prophylaxis to prevent post-TUL infections remains controversial.

Objectives: This study aimed to investigate whether the removal of preoperative antibiotic prophylaxis affects the rate of postoperative complications in patients undergoing TUL.

Methods: A total of 62 patients (aged 15-65 years) undergoing TUL between November 2021 and March 2022 were included in this controlled clinical trial. Patients were divided into two groups by the available gradual and sequential sampling methods: 33 had positive preoperative urine culture (UC), and 29 had negative preoperative UC. None of the patients in the two groups received preoperative antibiotic prophylaxis. Perioperative and postoperative outcomes, such as the operative time, stone-free rate, postoperative analgesic use, fever, urinary tract infection (UTI), and hospital stay, were reviewed in both groups.

Results: Patients with positive UC were significantly older than those with negative UC (P=0.018), and had a higher BMI (P=0.016). No significant differences were observed between the two groups in most perioperative variables or postoperative outcomes (P>0.05). In addition, patients in the positive UC group had significantly more underlying diseases than the other group (P=0.022). Postoperative symptomatic UTI was found in neither of the two groups. Fever was reported in 3 (9.1%) and 1 (3.4%) patients in the positive and negative UC groups, respectively, with no statistically significant differences between the two groups (P=0.616). In the matched logistic regression model, the effect of preoperative UC on postoperative fever was not significant (P=0.40).

Conclusion: The results of our study showed that prophylactic antibiotics can be eliminated at the discretion of the surgeon in patients without symptomatic positive UC.

Keywords: Antibiotic prophylaxis, Fever, Transurethral ureterolithotripsy, Urinary tract infection

1. Background

Transurethral ureterolithotripsy (TUL) is a minimally invasive procedure for the treatment of ureteral stones. In addition to its low cost, this technique is highly efficient and is one of the most common methods for the lithotripsy of urological stones (1-2). Despite the development of urethroscopic devices, equipment, and lithotripsers, the potential complications after TUL are still noticeable (2-3). The most common intra- and postoperative complications include the migration of fragmented stones, especially in upper ureteral stones, the perforation of the ureter, the stenosis of the urethra discomfort in the urethra, and fever associated with sepsis or urinary tract infection (UTI) (1-6). Bacterial infection, which usually follows fever, can lead to urosepsis and, in some cases, even death (3, 7-9).

One of the challenges in these patients is the side effects of antibiotics that can cause hypersensitivity, such as allergic reactions, secondary infections due to saprophytic flora destruction, or even anaphylactic shocks. Antibiotic resistance can often result from the overuse or misuse of antibiotics (1, 8, 10).

According to the EAU and AUA recommendations, the patient should have a negative urine analysis or urine culture (UC) test before any ureteroscopy procedure. In the case of positive UC, the procedure should be held for three days to receive antibiotic treatment (11, 12).

Although it is essential to treat symptomatic UTI before any kind of urological procedure, there is still uncertainty about treating asymptomatic UTI (2, 3). Some studies do not agree on the effectiveness of preoperative antibiotic prophylaxis on the outcome of TUL (1-2). In other words, some researchers have recently shown that a single oral dose of preoperative antibiotics is sufficiently effective in preventing postoperative UTI with less economic burden and side effects (1, 13, 14).

2. Objectives

Given that the results of recent studies are inconsistent with guideline recommendations on

whether preoperative antibiotic therapy is necessary or can be eliminated before TUL, this study aimed to evaluate the outcome of TUL in patients with and without preoperative positive UC with and without eliminating prophylactic antibiotics before surgery.

3. Methods

3.1. Study Design

A total of 73 consecutive patients underwent TUL for ureteral stones from November 2021 to March 2022 in Razi Hospital, Rasht, Guilan, Iran, of whom patients aged 15-65 years were included in this controlled clinical trial. On the other hand, those with upper UTI based on symptoms of fever, shivering, flank pain, and leukocytosis, as well as those with a history of drug abuse, preoperative antibiotic use, a single kidney, primary or secondary immunodeficiency, and uncontrolled systemic diseases, were excluded from the study. Finally, 62 patients were eligible to join the study.

Patients were divided into two groups of positive or negative preoperative UC based on the results of their UC. Intraoperative prophylactic antibiotics were prescribed for all patients, which included one intravenous (IV) dose of gentamicin 80 mg plus cefazoline 1 g.

Written informed consent was obtained from each participant before participation. All procedures were carried out under general or regional anesthesia. Age, gender, BMI, underlying disease, stone operation history, hydronephrosis, stone size, stone number, operative time, post-TUL UTI, fever, complication, analgesic use, success rate, and hospital stay were reviewed.

All patients received postoperative antibiotic treatment, including gentamicin (80 mg) every 8 h and cefazolin (1 g) every 6 h during the first 24 h after surgery. Post-TUL fever was defined as at least one episode of body temperature over 38°C on postoperative days of hospitalization. UC retesting was requested 48 h after the operation to check for postoperative infections. Patients were followed up until discharge, and all complications were recorded at discharge.

3.2. Statistical Analysis

All statistical analyses were conducted by the IBM SPSS Statistics software (version 26.0, IBM Corp, Armonk, NY, USA). The level of significance was set at $P<0.05$. According to the normality of the data (by Kolmogorov-Smirnov test), comparisons of variables between patients of the two groups were performed using the independent samples t-test for continuous data and the Chi-squared or Fisher's exact test for categorical data. Backward multivariate logistic regression was also used to assess the risk factors for postoperative fever.

4. Results

Patients' age ranged from 16 to 63 years with a mean age of 46.35±15.76. Out of 62 patients, 33 had preoperative positive UC, and 29 had negative UC. Table 1 shows the baseline characteristics of the patients. No significant differences were observed between the groups in the demographic, as well as pre- and peri-operative variables, including gender, stone operation history, hydronephrosis, stone size, stone number, and the operative time. Among the preoperative factors, age, body mass index (BMI), and underlying diseases were significantly different between the two groups ($P<0.05$).

Patients with positive UC were significantly older than those with negative UC (59.39±12.32 vs. 43.62±15.53, respectively; P=0.018). The mean BMI showed higher obesity problems in the positive UC group than the negative one (27.14±3.27 kg/m^2 vs. 25.06±3.29 kg/m^2, respectively; P=0.016)

Background examination showed that patients in the positive UC group had significantly more underlying diseases than the other group (63.6% vs. 34.5%, respectively; P=0.022).

There were 9 (27.3%) patients in the positive UC group with a history of diabetes mellitus versus 5 (17.2%) patients in the negative UC group. In addition, 8 (24.2%) patients in the positive UC group and 2 (6.9%) in the negative UC group had dyslipidemia. Heart disease was reported in just 1 (3.4%) patient in the negative UC group.

The comparison of postoperative outcomes in the two groups is shown in Table 1. No statistically significant differences were found in these variables between the two groups ($P>0.05$).

There was no significant difference in stone-free rates between the two groups (P=0.488). Although the mean hospital stay in the positive UC group was slightly longer than the negative UC group (3.24±1.41 vs. 2.65±1.04, respectively), the difference was not statistically significant (P= 0.066).

Postoperative symptomatic UTI was found in neither of the two groups. There was one episode of fever in one patient in the negative UC group (3.4%) and three patients in the positive UC group (9.1%), none of which had evidence of UTI (P=0.616). No serious complications were found in any of the four patients with postoperative fever, and it resolved within 24 h after the incidence of fever.

Table 2 shows the effect of the study group (positive or negative UC) on the most important outcome of the study, namely fever, in a matched logistic regression model. By adjusting the confounding variables, such as age, gender, BMI, and underlying diseases, similar to univariate analysis, the effect of preoperative UC on postoperative fever was not significant (P=0.40).

Table 1. Demographic, pre-, peri-, and postoperative data

	Positive UC (n=33)	Negative UC (n=29)	P-value
Age (years)	59.39±12.32 (34-63)	43.62±15.53 (16-65)	0.018*
Gender			
Male	24 (72.7)	25 (86.2)	0.193**
Female	9 (27.3)	4 (13.8)	
BMI (kg/m^2)	27.14±3.27	25.06±3.29	0.016*
Underlying diseases			
Yes	21 (63.6)	10 (34.5)	0.022**
No	12 (36.4)	19 (65.5)	
Stone operation history			
Yes	16 (48.5)	8 (27.6)	0.092**
No	17 (51.5)	21 (72.4)	
Hydronephrosis			
Mild	11 (33.3)	13 (44.8)	0.172**
Moderate	14 (42.4)	14 (48.3)	
Severe	8 (24.2)	2 (6.9)	
Stone size (mm)	11.5±4.00 (7-23)	10.7±3.3 (5.1-18)	0.375*
Stone number			
Single	23 (69.7)	23 (79.3)	0.388**
Multiple	10 (30.3)	6 (20.7)	
Operation time (min)	44.91±16.42	40.14±11.73	0.199*
Analgesic Use			
Yes	19 (57.6)	11 (37.9)	0.122**
No	14 (42.4)	18 (62.1)	
Hospital stay (day)	3.24±1.41	2.65±1.04	0.066**
Stone free			
Yes	29 (87.9)	27 (93.1)	0.488**
No	4 (12.1)	2 (6.9)	
Pyuria			
Positive	7 (21.2)	4 (13.8)	0.519**
Negative	26 (78.8)	25 (86.2)	
Complication			
Fever	1 (3.4)	3 (9.1)	0.486**
Gross hematuria	1 (3.4)	0 (0.0)	
Pain	1 (3.4)	3 (9.1)	
Stone migration	2 (6.9)	4 (12.1)	

Data presented as N (%) or mean±standard deviation
BMI: Body mass index, UC: Urine culture
*Independent-samples t-test, **Chi-squared or Fisher's exact test

Table 2. Multivariate logistic model

	B	S.E.	Sig.	Odds Ratio	95% CI for OR	
					Lower	Upper
Sex	-0.100	1.347	0.941	0.905	0.065	12.693
Age	-0.032	0.055	0.559	0.968	0.870	1.078
BMI	-0.104	0.169	0.539	0.901	0.647	1.256
Underlying disease	1.514	1.577	0.337	4.546	0.206	100.089
Group (UC+/UC-)	1.119	1.331	0.400	3.062	0.226	41.571
Constant	-1.046	5.024	0.835	0.351		

BMI: Body mass index, UC: Urine culture

5. Discussion

The effect of antibiotic prophylaxis on postoperative bacteriuria in patients undergoing urological surgery is still controversial. Our results showed that the outcome of TUL was not different in patients with and without preoperative bacteriuria without receiving prophylactic antibiotics.

Although the patients in the two groups were not the same in terms of age, BMI, and underlying diseases, these variables did not affect postoperative outcomes and complications in multiple regression analyses.

In 2005, Lopez et al. analyzed the data of 449 cases undergoing endourologic procedures and showed that less than 25% of postoperative bacteriuria is due to preoperative bacteriuria. In this study, the operative time was considered the main cause of urosepsis (15). However, in another study, there was no statistically significant difference in the operative time between three groups of patients who received IV cefazolin, oral cefuroxime, and those with no prophylaxis (16).

In the present study, although the time of operation was longer in the negative UC group, there was no statistically significant difference between the

two groups in the operative time (P=0.199). Indeed, we believe that asymptomatic bacteriuria does not prolong the operative time, and there is no compelling reason to treat asymptomatic bacteriuria before surgery.

Postoperative bacteriuria is of unknown importance, and the use of pre-TUL antibiotic prophylaxis to prevent postoperative infection is still controversial (1, 2, 17).

One study conducted in Columbia in 2019 found no relationship between asymptomatic bacteriuria and postoperative infections (18). Another study showed that postoperative complications of TUL did not increase in patients with negative UC without antibiotic prophylaxis (2). The results of the study by Li et al. demonstrated that antibiotic prophylaxis could not reduce the incidence of postoperative febrile UTI and pyuria in ureterorenoscopic lithotripsy (16).

In our study, there was no significant difference between the two groups regarding complications such as stone migration, resistant pain, gross hematuria, fever, and pyuria. No ureteral perforation or post-operation symptomatic UTI was found in the two groups.

The most concerning complication after ureteroscopy is fever, which usually indicates an infection in the patient. In the present study, the incidence of postoperative fever was 9.1% (3/33) in the positive UC group and 3.4% (1/29) in the negative UC group, with no significant differences between the two groups and without any evidence of UTI. The duration of postoperative fever was short in all patients and did not last more than a day.

In another study by Aghamir et al., the rates of postoperative fever were 0.0% and 3.3% in patients with and without pre-TUL antibiotic prophylaxis, respectively, but the difference was not statistically significant (2). In another study performed on patients undergoing ureterorenoscopic lithotripsy with preoperative sterile urine, there was no significant difference in the incidence of postoperative fever between patients who did not receive any antibiotic prophylaxis and those who received one of the three antibiotics: cefazolin (1 g), ceftriaxone (1 g), or oral levofloxacin (500 mg) (19). Similarly, a study in Taiwan found no significant difference between patients without pyuria undergoing ureterorenoscopic surgery who received a single dose of IV cefazolin (1 g) and those with no prophylactic antibiotics (16).

The incidence of post-TUL fever was 8.8% in a study conducted by Takahashi et al. These incidences were 4.5% and 11.6% in the single and two-day antimicrobial prophylaxis groups, respectively, with no significant differences (12).

While in most studies, the incidence of fever after ureteroscopic stone removal procedures was not significantly different between two groups of patients with and without prophylactic antibiotics, Pricop et al. found significantly higher rates of fever in patients who received antibiotic prophylaxis than those with no antibiotic prophylaxis (32.65% vs. 22.83%, respectively; P=0.0009) (5).

Subsequently, a meta-analysis showed that patients who received antibiotics before ureteroscopic lithotripsy had a higher incidence of postoperative fever than those who did not (1).

According to the available evidence, we do not expect to see more serious complications after TUL in patients with asymptomatic bacteriuria.

It is believed that preoperative infection can affect the success rate of TUL and even the duration of postoperative hospitalization, whereas in our study, despite the longer hospital stay in the positive UC group, there were no other significant differences between the two groups. Moreover, the stone-free rate was similar in the two groups.

Similar results were also found in a study by Aghamir et al. (2). In another study, Hsieh et al. showed that there was no significant difference in the success of the operation between groups with a single dose of three different antibiotics and the control group (no treatment) (19). Likewise, Li et al. reported similar stone-free rates between groups of patients who received antibiotics (oral or IV) and the control group with no prophylactic antibiotics (16).

Therefore, it has been shown that asymptomatic UTI cannot alter the success of TUL, so antibiotic therapy of asymptomatic UTI prior to TUL is not recommended as it cannot increase the success rate of the operation or reduce the length of hospitalization.

One of the most important complications of TUL is the migration of stone fragments toward the kidneys. Although in our study, there was a higher migration rate in the negative UC group (3 cases) than the positive UC group (2 cases), the difference was not statistically significant. Our results may have been affected by the small number of our cases. So far, no study has reported the effect of preoperative antibiotic prophylaxis on stone fragment migration. Overall, it can be said that there is no concern about the migration of stone fragments in patients with untreated preoperative asymptomatic UTI.

Analgesic use following an operation is an important factor in evaluating patients' satisfaction. In our study, we have shown there is no significant difference between the two groups based on the use of analgesics. Therefore, there is no substantiated evidence to treat an asymptomatic UTI before TUL to reduce analgesic use.

In our study, postoperative pyuria was higher in the positive UC group, but the difference was not significant. Although postoperative pyuria may be more common in asymptomatic bacteriuric cases, there is no serious complication regarding this issue

that would convince us to treat asymptomatic bacteriuria before TUL.

Based on the findings of the present study, if patients do not have symptomatic UTI, lack of prophylaxis antibiotics treatment does not lead to any noticeable post-operative complications.

The most important limitation of this study was its small sample size, which led to a mismatch of preoperative factors, including age, BMI, and underlying diseases, between the two groups. However, these factors were not able to predict the outcome of TUL by logistic regression.

6. Conclusion

The results of our study showed that prophylactic antibiotics can be eliminated at the discretion of the surgeon in patients without symptomatic UTI. It is rarely possible to consider a standard treatment for all patients, and it should become individualistic.

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Footnotes

Conflicts of Interest: The authors declare no conflicts of interest.

Authors' contributions: Conceptualization and methodology: SF, AA; Data collection: RF, EMA; Data analysis and interpretation: EK; Drafting the article: SF, SE; Revising and final approval of the manuscript: AA, RF, SE.

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References

1. Deng T, Liu B, Duan X, Cai C, Zhao Z, Zhu W, et al. Antibiotic prophylaxis in ureteroscopic lithotripsy: a systematic review and meta-analysis of comparative studies. *BJU Int.* 2018; **122**(1):29-39. doi: 10.1111/bju.14101. [PubMed: 29232047].
2. Aghamir SM, Hamidi M, Salavati A, Mohammadi A, Farahmand H, Meysamie AP, et al. Is antibiotic prophylaxis necessary in patients undergoing ureterolithotripsy? *Acta Med Iran*. 2011;**49**(8):513-6. [PubMed: 22009806].
3. Knopf HJ, Graff HJ, Schulze H. Perioperative antibiotic prophylaxis in ureteroscopic stone removal. *Eur Urol*. 2003;**44**(1):115-8. doi: 10.1016/s0302-2838(03)00189-1. [PubMed: 12814685].
4. Allameh F, Razzaghi M, Fallah-Karkan M, Hosseini B, Azar AT, Ranjbar A, et al. Comparison of stone retrieval basket, stone cone and holmium laser: which one is better in retropulsion and stone-free status for patients with upper ureteral calculi? *J Lasers Med Sci.* 2019;**10**(3):179-84. doi: 10.15171/jlms.2019.28. [PubMed: 31749942].
5. Takahashi T, Somiya S, Ito K, Haitani T, Higashi Y, Yamada H, et al. Risk factors for febrile urinary tract infection after transurethral ureterolithotripsy: analysis of treatment outcomes of 1,235 patients at a single center. *Hinyokika Kiyo.* 2022;**68**(6):171-8. doi: 10.14989/ActaUrolJap_68_6_171. [PubMed: 35850505].
6. Takahashi S, Takeyama K, Miyamoto S, Tanuma Y, Takagi Y. Surgical antimicrobial prophylaxis in transurethral ureterolithotripsy. *J Infect Chemother*. 2005;**11**(5):239-43. doi: 10.1007/s10156-005-0401-3. [PubMed: 16258820].
7. Scotland KB, Lange D. Prevention and management of urosepsis triggered by ureteroscopy. *Res Rep Urol.* 2018;**10**:43-49. doi: 10.2147/RRU.S128071. [PubMed: 30013956].
8. Pricop C, Dorobăt C, Puia D, Orsolya M. Antibiotic prophylaxis in retrograde ureteroscopy: what strategy should we adopt? *Germs*. 2013;**3**(4):115-21. doi: 10.11599/germs.2013.1045. [PubMed: 24432295].
9. Khusid JA, Hordines JC, Sadiq AS, Atallah WM, Gupta M. Prevention and management of infectious complications of retrograde intrarenal surgery. *Front Surg.* 2021;**8**:718583. doi: 10.3389/fsurg.2021.718583. [PubMed: 34434958].
10. Gopalakrishnan PP, Shukla SK, Tak T. Antibiotic prophylaxis and anaphylaxis. *Clin Med Res.* 2010;**8**(2):80-1. doi: 10.3121/cmr.2010.929. [PubMed: 20660929].
11. Zisman A, Badaan S, Kastin A, Kravtsov A, Amiel GE, Mullerad M. Tailoring antibiotic prophylaxis for ureteroscopic procedures based on local resistance profiles may lead to reduced rates of infections and urosepsis. *Urol Int.* 2020;**104**(1)1:106-12. doi: 10.1159/000503905. [PubMed: 31743924].
12. Lo CW, Yang SS, Hsieh CH, Chang SJ. Effectiveness of prophylactic antibiotics against post-ureteroscopic lithotripsy infections: systematic review and meta-analysis. *Surg Infect.* 2015;**16**(4):415-20. doi: 10.1089/sur.2014.013. [PubMed: 26207401].
13. Chew BH, Flannigan R, Kurtz M, Gershman B, Arsovska O, Paterson RF, et al. A single dose of intraoperative antibiotics is sufficient to prevent urinary tract infection during ureteroscopy. *J Endourol.* 2016;**30**(1):63-8. doi: 10.1089/end.2015.0511. [PubMed: 26413885].
14. Mama RK, Al-bazzaz PH, Al-Ibraheem NP. A comparative study between a single dose pre-induction antibiotic versus continuous antibiotics to prevent urinary tract infection during ureteroscopy. *Trends Med*. 2018;**18**(6):1-4. doi: 10.15761/TiM.1000162.
15. López VM, Llópis JA, López ME, Rubias CC, Serra AC, de Paz Cruz L, et al. Urinary bacteriologic study prior to endoscopic urologic surgery. *Actas Urol Esp.* 2005;**29**(7):667-75. doi: 10.1016/s0210-4806(05)73317-9. [PubMed: 16180317].
16. Li MW, Lee YJ. Comparison of prophylactic antibiotics in patients without pyuria undergoing ureterorenoscopic surgery. *Urol Sci.* 2020;**31**(5):216-20. doi: 10.4103/UROS.UROS_40_20.
17. Bootsma AM, Laguna Pes MP, Geerlings SE, Goossens A. Antibiotic prophylaxis in urologic procedures: a systematic review. *Eur Urol.* 2008;**54**(6):1270-86. doi: 10.1016/j.eururo.2008.03.033. [PubMed: 18423974].
18. Ramos-Castaneda JA, Ruano-Ravina A, Munoz-Price LS, Toro-Bermúdez R, Ruiz-Londoño D, Segura-Cardona AM, et al. Risk of infection in patients undergoing urologic surgery based on the presence of asymptomatic bacteriuria: A prospective study. *Am J Infect Control*. 2019;**47**(12):1474-8. doi: 10.1016/j.ajic.2019.06.024. [PubMed: 31375294].
19. Hsieh CH, Yang SS, Lin CD, Chang SJ. Are prophylactic antibiotics necessary in patients with preoperative sterile urine undergoing ureterorenoscopic lithotripsy? *BJU Int.* 2014;**113**(2):275-80. doi: 10.1111/bju.12502. [PubMed: 24127851].