DOI: 10.4081/aiua.2023.11084

ORIGINAL PAPER

Randomized comparison of effect of standard antibiotic prophylaxis versus enhanced prophylactic measures on rate of urinary tract infection after flexible ureteroscopy

El-Sayed I. El-Agamy [1], Mohamed A. Elhelaly [1], Tamer A. Abouelgreed [2], Abdrabuh M. Abdrabuh [3], Mohamed F. Elebiary [3], Adel Elatreisy [3], Osama M. Ghoneimy [3], Basem A. Fathi [3], Mohamed Zamra [4], Khalid Kutub [5]

[1] Department of Urology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt & Department of Urology, Armed Forced Hospital, Alhada, KSA;
[2] Department of Urology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt & Gulf Medical University, UAE;
[3] Department of Urology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt;
[4] Department of Urology, AlQasemi Hospital, Sharjah, UAE;
[5] Department of Urology, Al Aharq Jospital, Fujairah, UAE.

Summary ***Purpose: To compare the rate of post-flexible ureteroscopy urinary tract infection (UTI) in patients subjected to the standard antibiotic prophylaxis alone versus enhanced prophylactic measures.***
Methods: A prospective randomized controlled study included 256 patients subjected to flexible ureteroscopy (FURS) for ureteral or renal stones from March 2018 to July 2022. Treatment groups included the standard antibiotic prophylaxis group (group 1, n=128) and the enhanced prophylaxis group (group 2, n=128). Patients in group 1 were injected with intravenous fluoroquinolone one hour preoperatively, and oral antibiotics were used for 24 h postoperatively. Patients in group 2 had urine culture ten days before the procedure; antibiotic-culture based was given for positive asymptomatic cases, while the procedure was deferred for active UTI.
Results: The study groups were comparable regarding patient demographics, stone characteristics, operative time, and intra-operative complications. The overall hospitalization time was 1.68 ± 0.81 days. Postoperative, and overall complications were significantly higher in group 1 (15.6% vs. 6.3%, p = 0.04 and 26.6% vs. 17.2%, p = 0.047), respectively. Twenty patients (15.6 %) in the standard prophylaxis group were diagnosed with UTI in comparison to 8 patients (6.3 %) in the enhanced prophylaxis group (p = 0.047).
Conclusions: Urinary tract infection after FURS could be reduced significantly by utilizing the suggested enhanced prophylactic approach.

KEY WORDS: *Antibiotic; Prophylaxis; Ureteroscopy; Urinary tract infect.*

Submitted 13 December 2022; Accepted 22 January 2023

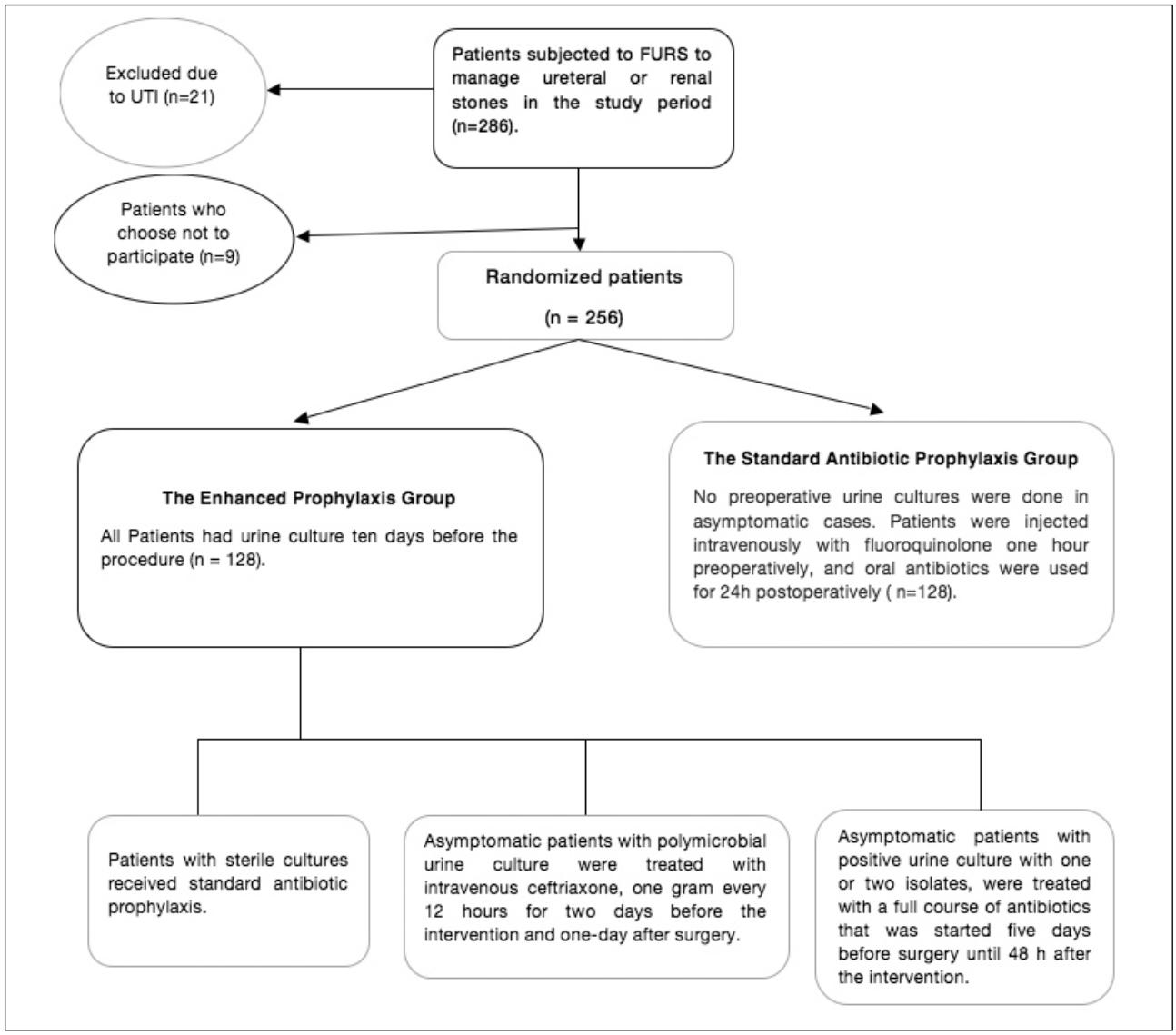
INTRODUCTION

Flexible ureteroscopy (FURS) has become one of the most reliable tools in upper urinary tract endourology. Thanks to creative ancillary instruments such as graspers and baskets, effective energy sources, and digital and robotic enhancements, FURS has expanded its diagnostic and therapeutic applications to many upper urinary tract pathologies beyond its common use in the management of renal stones (1). FURS can be used as a conservative treatment for *urothelial tumors of the upper urinary tract* (UTUC) and can be used in the follow-up after radical treatment of UTUC (2). However, the use of FURS is not without drawbacks. Significant complications, including *urinary tract infection* (UTI) and ureteric trauma, are frequently reported (3). In one study, febrile UTI was reported in 14.1% of patients submitted to flexible ureteroscopic lithotripsy (4). Unfortunately, prevention of postoperative UTI after FURS remains a debatable issue. Current practice lacks well-established clinical evidence based on randomized clinical studies and is mainly based on retrospective studies (5). To standardize the periprocedural systemic antimicrobial administration, the *American Urological Association* best practice policy statement was developed (6). However, real-world practice is widely variable, and observational studies show relatively low compliance with these recommendations (5-7). To guard against post procedural infection, the most common approach is single-dose antibiotic prophylaxis (8). On the other hand, some centers use more enhanced precautions, including centralized collection and examination of preoperative urine cultures, standardized antibiotic prophylaxis, and use of ureteral access sheath. Even with these precautions, postoperative UTI was encountered in 6.7% of patients (9). The present randomized study aimed to compare the rate of post-procedural UTI in patients subjected to the standard antibiotic prophylaxis alone versus enhanced prophylactic measures.

PATIENTS AND METHODS

A prospective randomized controlled study was conducted at the *Department of Urology, Armed Forces Hospital, Alhada, KSA*, from March 2018 to July 2022. The study protocol was approved by the local ethical committee of the institution, and informed written consent was obtained from all patients before enrollment. The study included all patients subjected to FURS to manage ureter-

Figure 1.
Flow chart of the study population.



al or renal stones. Exclusion criteria were symptomatic UTI, use of rigid ureteroscope, and antegrade ureteroscopy. Preoperatively, all patients were subjected to careful history taking, thorough clinical examination, and non-contrast computed tomography scan to evaluate the stone characteristics. Patients were equally and randomly allocated into one of the two treatment groups, including the standard antibiotic prophylaxis group and the enhanced prophylaxis group. The sample size was calculated utilizing the G-power software program for statistical power 80% and type II statistical error 20%. The total number of patients was 256, equally divided into the two groups (each group included 128 patients). Patients in the standard antibiotic prophylaxis group were injected intravenously with fluoroquinolone one hour preoperatively, and oral antibiotics were used for 24 hours postoperatively. Patients in the enhanced prophylaxis group had urine culture ten days before the procedure. Patients with sterile cultures received standard antibiotic prophylaxis. In contrast, patients with polymicrobial preoperative urine culture (defined by a urine culture isolating at least three microorganisms, of which none is predominant) were treated with ceftriaxone from 48 hours before the procedure until one day after surgery. Patients with positive urine culture were contacted to assess if they had symptoms of UTI. In asymptomatic cases, according to the specific pathogens identified, a full course of antibiotics was started five days before surgery until 48 h after the intervention (Figure 1). For those having a clinically significant infection, the intervention was deferred.

In addition to the antibiotic prophylaxis, hydrophilic-coated ureteral access sheaths were systematically used in all cases.

The primary outcome of the study was the occurrence of postoperative UTI within 30 days from treatment. Postoperative UTI was defined as the occurrence of a temperature higher than 38 °C associated with pyuria

and/or bacteriuria without any other focal infectious sites. In a symptomatic patient, no routine urine culture was requested.

Statistical analysis

Data obtained from the present study were presented as number and percent or mean and *standard deviation* (SD). Numerical data were compared using a t-test, while categorical data were compared using the chi-square test. Logistic regression was used to identify predictors of outcome. All statistical operations were computed using SPSS 25 (IBM, USA), and a p-value less than 0.05 was considered statistically significant.

Results

In total, 256 patients were included in the study; the mean age in years ± SD was 46.8 ± 12.9, the male to female ratio was 178/78, and all patients underwent FURS for stone disease with laser lithotripsy. The mean stone number ± SD of the entire cohort was 2.5 ± 1, and the largest stone diameter was 2.1 ± 0.78. The stones were recurrent in 50% of patients and were associated with moderate hydronephrosis in 21.9% and mild hydronephrosis in 48.4%, whereas no hydronephrosis was associated in 29.7%. Regarding the stone location, it was in the proximal ureter in 35.2%, in the kidney in 36.7%, and combined in 28.1%. Pre-FURS internal double J ureteric stents were placed in 26.5% of patients who presented with proximal ureteric obstructing stones and slight acute renal impairment, which was normalized after ureteric stenting. Group 1 included patients subjected to the standard antibiotic prophylaxis protocol (n = 128). Group 2 included patients subjected to the enhanced prophylaxis protocol (n = 128) who had sterile urine culture in 66 cases (51.6%), polymicrobial positive urine culture in 41 cases (32%), and isolated organism in 21 (16.4%). There were no significant differences between the study groups regarding patient demographics and stone characteristics, as illustrated in Table 1. The overall hospitalization time was 1.68 ± 0.81 days, comparable between groups 1 and 2 with no significant difference (p = 0.35) (Table 1). We reported an overall complication rate of 21.9% (56 cases). Intraoperative complications were comparable between the study groups. Conversely, postoperative, and overall total complications were significantly higher in group 1, as shown in Table 2. All the reported complications were MCCS grades I and II that were managed conservatively. Regarding post-FURS urinary tract infection, 20 patients (15.6%) in the standard prophylaxis group were diagnosed with UTI in comparison to 8 patients (6.3%) in the enhanced prophylaxis group with statistically significant difference (p = 0.047) (Table 2). Hospital readmission was mandatory in 10 cases (3.9%) for UTI and urosepsis. In these cases we collected urine and blood samples for culture and started with empirical intravenous meropenem (1 gram every 8 hours). Urine culture showed *E. coli* in 8 cases and Klebsiella pneumonia in two, all sensitive to meropenem, and all patients were discharged after ten days of antibiotic course after confirmation of sterile urine. Using binary logistic regression analysis, female gender [OR (95% CI): 0.09 (0.018-0.46) and operative time [OR (95%CI): 0.97 (0.94-0.99)] were significant predictors of postoperative UTI at univariate analysis. However, only female sex remained significant at multivariate analysis [OR (95% CI): 0.09 (0.017-0.49)] (Table 3).

Table 1.
Comparison between the studied groups regarding the preoperative, operative, and postoperative data.

Parameters	Standard prophylaxis Group 1 (n = 128)	Enhanced prophylaxis Group 2 (n = 128	P value
Age (years) mean ± SD	47.4 ± 11.8	46.1 ± 14.3	0.67
Male/female n	86/42	96/36	0.52
BMI (Kg/m^2) mean ± SD	30.4 ± 4.8	29.4 ± 4.2	0.42
Associated morbidities n (%)			
Hypertension	38 (29.9%)	34 (26.7%)	0.66
Diabetes mellitus	62 (48.4%)	56 (43.8%)	0.45
Previous stone operation n (%)	59 (45.3%)	70 (54.7%)	0.26
Preoperative ureteral stent n (%)	36 (28.3%)	32 (25 %)	0.72
Preoperative hydronephrosis n (%)			
None	36 (28.1%)	40 (31.3%)	0.52
Mild	66 (51.6%)	58 (45.3%)	
Moderate	22 (20.3%)	30 (23.4%)	
Stone location n (%)			
Kidney	44 (34.4%)	50 (39.1%)	0.7
Ureter	50 (39.1%)	40 (31.2%)	
Combined	34 (26.6%)	38 (29.7%)	
Stones number mean ± SD	2.6 ± 1.1	2.4 ± 1	0.43
Largest stone size (cm^3) mean ± SD	2 ± 0.9	2.2 ± 0.7	0.31
Operative time (min.) mean ± SD	117.4 ± 26.2	114.8 ± 22.7	0.63
Hospitalization time, days	1.53 ± 0.7	1.63 ± 0.8	0.34

Table 2.
Complications rate among studied groups.

Parameters	Total (n = 256)	Group 1 (n = 128)	Group 2 (n = 128)	P value
Overall complications	56 (21.9%)	34 (26.6%)	22 (17.2%)	0.04
Intraoperative complications	28 (10.9%)	14 (10.9%)	14 (10.9%)	0.89
Postoperative complications	28 (10.9%)	20 (15.6%)	8 (6.3%)	0.047
MCCS grading of complications				
GRADE 1				
Ureteric mucosal injury	12 (4.7%)	6 (4.7%)	6 (4.7%)	0.98
Hematuria	16 (6.3%)	10 (3.9%)	6 (4.7%)	0.34
GRADE 2				
UTI	28 (10.9%)	20 (15.6%)	8 (6.3%)	0.047
Readmission (within 8 weeks)	10 (3.9%)	8 (6.3%)	2 (1.7%)	0.038

Table 3.
Predictors of postoperative UTI in the studied groups.

	Univariate analysis			Multivariate analysis		
	OR	95% CI	p value	OR	95% CI	p value
Age	0.99	0.94-1.03	0.54	-	-	-
Sex	0.09	0.018-0.46	0.004	0.09	0.017-0.49	0.005
Diabetes	0.53	0.14-2.02	0.36	-	-	-
Stone size	0.82	0.55-1.24	0.35	-	-	-
Operative time	0.97	0.94-0.99	0.032	0.97	0.95-1.01	0.063
Type of prophylaxis	0.22	0.044-1.09	0.063	0.19	0.033-1.14	0.069

Discussion

Urinary tract infections after FURS are commonly seen in clinical practice. Even in the absence of microbial invasion, the surgical procedure elicits a significant systemic inflammatory response related to the procedure's duration and can predispose to infectious complications (10). The present prospective study assessed the value of standard antibiotic prophylaxis versus enhanced prophylaxis in preventing UTIs after FURS. Postoperative UTI was diagnosed in twenty patients (15.6%) in the standard prophylaxis group versus eight patients (6.3%) in the enhanced prophylaxis group ($p = 0.047$). The beneficial effects of enhanced prophylaxis are attributed to additional measures included in the protocol, namely the preoperative culture and treatment of identified infections and use of coated ureteral access sheaths.

The relation between positive preoperative culture and postoperative UTI in patients submitted to FURS was discussed by the study by *Senocak et al.* (11). In their paper, positive preoperative urine culture with multidrug resistance isolates was recognized as an independent risk factor of postoperative UTI. Of note, none of our patients had such isolates. Also, in the study of *Alezra et al*. (12), positive day-1 culture was a significant predictor of severe UTI. In addition, the study of *Auge et al.* (13) highlighted the value of ureteral access sheath (UAS) in the reduction of postoperative UTI after FURS. Similar conclusions were reported by the randomized study of *Özkaya et al.* (14). They noted that using UAS in impacted mid-upper ureteral stones was related to fewer infectious complications.

The UAS reduces the irrigation pressures transmitted to the renal pelvis and parenchyma (13). Moreover, appropriate UAS selection is essential to optimize the renal blood flow during FURS. Adequate renal blood flow is critical to maintain local immune defensive mechanisms (15).

In our study, logistic regression analysis identified the female sex as an independent risk factor of postoperative UTI. This finding conforms with the study of *Baboudjian et al.* (9).

Their study showed preoperative polymicrobial urine culture and increased operative time as predictors of postoperative UTI.

Our conclusions are also supported by the recent meta-analysis of *Ma et al.* (16). In contrast, the study of *Baseskioglu et al.* (17) recognized preoperative infection history, comorbidity score, and residual fragments as significant predictors of UTI after FURS, while the relevant risk factors in the study of *Ozgor et al.* (18) were longer operation time, presence of renal abnormality and age ≤ 40 years.

Conclusions

Urinary tract infection after flexible ureteroscopy and laser lithotripsy could be reduced significantly by utilizing the suggested enhanced prophylactic approach. The female sex factor is the only independent predicting factor for the occurrence of post-FURS urinary tract infections.

References

1. Alenezi H and Denstedt JD. Flexible ureteroscopy: Technological advancements, current indications and outcomes in the treatment of urolithiasis. Asian J Urol. 2015; 2:133-141.

2. Cho SY. Current status of flexible ureteroscopy in urology. Korean J Urol. 2015; 56:680-688.

3. Osther PJS. Risks of flexible ureterorenoscopy: pathophysiology and prevention. Urolithiasis. 2018; 46:59-67.

4. Kim JW, Lee YJ, Chung JW, et al. Clinical characteristics of postoperative febrile urinary tract infections after ureteroscopic lithotripsy. Investig Clin Urol. 2018; 59:335-341.

5. Greene DJ, Gill BC, Hinck B, et al. American Urological Association Antibiotic Best Practice Statement and Ureteroscopy: Does Antibiotic Stewardship Help? J Endourol. 2018; 32:283-288.

6. Wolf JS Jr, Bennett CJ, Dmochowski RR, et al. Best practice policy statement on urologic surgery antimicrobial prophylaxis [published correction appears in J Urol. 2008; 180:2262-3]. J Urol. 2008; 179:1379-1390.

7. Bapir R, Bhatti KH, Eliwa A, et al. Infectious complications of endourological treatment of kidney stones: A meta-analysis of randomized clinical trials. Arch Ital Urol Androl. 2022; 94:97-106.

8. Pietropaolo A, Bres Niewada E, Skolarikos A, et al. Worldwide survey of flexible ureteroscopy practice: a survey from European Association of Urology sections of young academic urologists and uro-technology groups. Cent European J Urol. 2019; 72:393-397.

9. Baboudjian M, Gondran Tellier B, Abdallah R, et al. Predictive risk factors of urinary tract infection following flexible ureteroscopy despite preoperative precautions to avoid infectious complications. World J Urol. 2020; 38:1253-1259.

10. Zhong W, Leto G, Wang L, et al. Systemic inflammatory response syndrome after flexible ureteroscopic lithotripsy: a study of risk factors. J Endourol. 2015; 29:25-28.

11. Senocak C, Ozcan C, Sahin T, et al. Risk Factors of Infectious Complications after Flexible Uretero-renoscopy with Laser Lithotripsy. Urol J. 2018; 15:158-163.

12. Alezra E, Lasselin J, Forzini T, et al. Prognostic factors for severe infection after flexible ureteroscopy: Clinical interest of urine culture the day before surgery? Prog Urol. 2016; 26:65-71.

13. Auge BK, Pietrow PK, Lallas CD, et al. Ureteral access sheath provides protection against elevated renal pressures during routine flexible ureteroscopic stone manipulation. J Endourol. 2004;18:33-36.

14. Özkaya F, Sertkaya Z, Karabulut I, et al. The effect of using ureteral access sheath for treatment of impacted ureteral stones at mid-upper part with flexible ureterorenoscopy: a randomized prospective study. Minerva Urol Nefrol. 2019;71:413-420.

15. Sener TE, Tanidir Y, Bin Hamri S, et al. Effects of flexible ureteroscopy on renal blood flow: a prospective evaluation. Scand J Urol. 2018; 52:213-218.

16. Ma YC, Jian ZY, Yuan C, et al. Risk Factors of Infectious Complications after Ureteroscopy: A Systematic Review and Meta-Analysis Based on Adjusted Effect Estimate. Surg Infect (Larchmt). 2020; 21:811-822.

17. Baseskioglu B. The Prevalence of Urinary Tract Infection Following Flexible Ureterenoscopy and the Associated Risk Factors. Urol J. 2019; 16:439-442.

18. Ozgor F, Sahan M, Cubuk A, et al. Factors affecting infectious complications following flexible ureterorenoscopy. Urolithiasis. 2019; 47:481-486.

Correspondence

El-Sayed I. El-Agamy, MD
abuamr1978@yahoo.com
Mohamed A. Elhelaly, MD
elhelalymohammed@yahoo.com
Department of Urology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt & Department of Urology, Armed Forced Hospital, Alhada, KSA

Tamer A. Abouelgreed, MD (Corresponding Author)
dr_tamer_ali@yahoo.com
tamerali.8@azhar.edu.eg
Department of Urology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt. & Gulf Medical University, UAE

Abdrabuh M. Abdrabuh, MD
abdo197871@yahoo.com
Mohamed F. Elebiary, MD
dr_elebiary@yahoo.com
Adel Elatreisy, MD
dr_adelelatreisy@yahoo.com
Osama M. Ghoneimy, MD
elgendyosama787@gmail.com
Basem A. Fathi, MD
basemhara@gmail.com
basemabdalla.8@azhar.edu.eg
Department of Urology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

Mohamed Zamra, MD
mohamedzomrah@gmail.com
Department of Urology, AlQasemi Hospital, Sharjah, UAE

Khalid Kutub, MD
abanis35@gmail.com
Department of Urology, Al Sharq Hospital, Fujairah, UAE

Conflict of interest: The authors declare no potential conflict of interest.