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Ureterorenoscopic Stone Removal without Antibiotic Prophylaxis

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Keywords
Urolithiasis · Ureteric stone · Kidney stone · Ureterorenoscopy · Urinary tract infection · Antibiotic prophylaxis · Antibiotic stewardship

Abstract

Introduction: The aim of this study was to assess the feasibility of sparing routine antibiotic prophylaxis in patients without preoperative urinary tract infection undergoing ureterorenoscopy (URS) for stone removal. ***Methods:*** A retrospective, monocentric study was conducted to evaluate the outcome of a modified perioperative antibiotic management strategy according to the principles of antibiotic stewardship. Patients with preoperative unremarkable urine culture received no antibiotic prophylaxis for URS stone removal (NoPAP). The NoPAP group was compared to a historic URS cohort, when antibiotic prophylaxis (PAP) was standard of care. Analysis focused on postoperative complications. ***Results:*** Postoperative fever occurred in 1% of the NoPAP and 2% of the PAP patients (p = 0.589). Clavien 1–3 complications did not differ between groups with 9% in the NoPAP and 6.2% in the PAP (p = 0.159). No Clavien 4–5 complications were seen. We identified a residual stone (p = 0.033) and an ASA score 3–4 (p = 0.004) as significant risk factors for postoperative fever. By sparing routine antibiotic prophylaxis, the overall antibiotic usage was reduced from 100% (PAP) to 8.3% (NoPAP). ***Conclusion:*** Sparing a routine antibiotic prophylaxis during URS for stone removal seems feasible in patients with unremarkable preoperative urine culture for most of the patients. A prospective validation is warranted.

Introduction

Antibiotic prophylaxis is usually administered before every endourological intervention. Regarding the increasing number of deaths associated with antibiotic resistance worldwide, it is crucial to avoid inappropriate antibiotic usage [1]. Therefore, the use of a perioperative administration of antibiotics should be adjusted based on the individual risk profile of the patient in the context of the antibiotic stewardship (ABS) principles [2].

Ureterorenoscopic (URS) stone removal is the standard procedure for ureteric and renal stones up to 20 mm [3]. According to current guideline recommendations, a perioperative antibiotic prophylaxis is advised before every URS [4, 5]. In patients with small distal ureter stones and low surgical risk, an antibiotic prophylaxis can be waived [6]. In case of a negative preoperative urine culture (UC), a single dose of intraoperative antibiotics is sufficient to prevent a postoperative urinary tract infection (UTI) [7, 8]. The aim of this study was to investigate the feasibility to omit routine perioperative antibiotic prophylaxis during URS in patients with an unremarkable preoperative UC.

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Table 1. Patient characteristics

	NoPAP	PAP	*p* value
Number of patients	155	96	
Gender, *n* (%)			0.963*
Male	107 (69)	66 (69)	
Female	48 (31)	30 (31)	
Body mass index, median, kg/m^2	27.7 (IQR: 7)	26.8 (IQR: 8)	0.414#
Age, median, years	54 (IQR: 24)	54 (IQR: 20)	0.136#
ASA score, *n* (%)			0.210*
1	32 (21)	17 (18)	
2	99 (64)	54 (57)	
3	23 (14)	21 (24)	
4	2 (1)	1 (1)	
Diabetes mellitus, *n* (%)			0.833*
No	137 (88)	84 (88)	
Yes	18 (12)	12 (12)	
Immunosuppression, *n* (%)			0.396*
No	151 (97)	95 (99)	
Yes	4 (3)	1 (1)	
Hydronephrosis preoperative, *n* (%)			0.164*
No	114 (73)	62 (65)	
Yes	41 (27)	33 (35)	
Intervention prior to URS, *n* (%)			0.291*
None	30 (19)	18 (19)	
Invasive[a]	117 (75)	68 (71)	
Noninvasive (SWL)	8 (5)	10 (10)	
Urinary diversion prior PCNL, *n* (%)			0.130*
None	45 (29)	30 (31)	
Ureteric stent	109 (70)	62 (65)	
Nephrostomy	1 (1)	4 (4)	
Taking anticoagulants, *n* (%)			0.596*
No	136 (88)	82 (85)	
Yes	19 (12)	14 (15)	
Dysuria or alguria, *n* (%)			0.260*
No	145 (94)	86 (90)	
Yes	10 (6)	10 (10)	
Stone position, *n* (%)			0.321*
Ureter	61 (39)	44 (46)	
Kidney	93 (60)	50 (52)	
Both	1 (1)	2 (2)	
URS type, *n* (%)			0.219*
Semirigid	45 (29)	31 (33)	
Flexible	83 (54)	55 (58)	
Both	27 (17)	9 (10)	
Ureteral access sheath, *n* (%)			0.887*
No	115 (74)	72 (75)	
Yes	40 (26)	24 (25)	
Hospital stay, median, days	2 (IQR: 0)	2 (IQR: 1)	0.029[b]

SD, standard deviation; IQR, interquartile range. [a]Invasive interventions summarize ureteric stent or nephrostomy placement, URS, PCNL. *χ^2 test. #*t* test. [b]Mann-Whitney U test.

Table 2. Postoperative outcome

	NoPAP	PAP	*p* value
Number of patients	155	96	
Residual stones postoperatively, *n* (%)			0.084*
No	138 (89)	78 (81.3)	
Yes	17 (11)	18 (19)	
Stone clearance, *n* (%)			
Ureter	60 (98)	40 (91)	0.077*
Kidney	77 (83)	37 (74)	0.212*
Both	1 (100)	1 (50)	0.386*
Stone composition[a], *n* (%)			<0.001*
Infectious stone	2 (1)	0 (0)	
Noninfectious stone	113 (73)	28 (29)	
Missing analysis	40 (26)	68 (71)	
Surgical time (cut-closure), min	32 (IQR: 32)	59 (IQR: 47)	<0.001[#]
With ureteral access sheath	58 (IQR: 32)	78 (IQR: 50)	0.007[b]
Without ureteral access sheath	26 (IQR: 23)	46 (IQR: 49)	<0.001[b]
Complications, Clavien-Dindo, *n* (%)			0.159*
0	141 (91)	90 (94)	
1–2	13 (8)	3 (3)	
3	1 (1)	3 (3)	
4–5	0 (0)	0 (0)	
Body temperature postoperatively, *n* (%)			0.589*
<38.2°C	147 (98)	91 (98.9)	
≥38.2°C	3 (2)	1 (1)	
PULS, *n* (%)			0.206*
0	131 (88)	70 (84)	
1	16 (11)	8 (10)	
2	1 (1)	4 (5)	
3	1 (1)	1 (1)	
4	0 (0)	0 (0)	

SD, standard deviation; IQR, interquartile range. *χ^2 test. [#]*t* test. [a]Infectious stone including apatite, struvite, ammonium components. [b]Mann-Whitney U test.

Table 3. Antibiotics postoperatively

	NoPAP	PAP	*p* value
Antibiotics postoperatively, *n* (%)	142 (91)	35 (37)	<0.001*
None	12 (8)	61 (63)	
Appropriate	1 (1)	0 (0)	

*χ^2 test.

Material and Methods

A retrospective database search was conducted to select patients who underwent a unilateral URS for removal of ureteric or renal urolithiasis at an university medical center in Germany. In the context of ABS program, the perioperative administration of antibiotics was modified in December 2015 in the urological department. Priorly, antibiotic prophylaxis was standard of care (SOC) during every URS for urolithiasis treatment. As a result of ABS, antibiotics were not administered anymore if the preoperative UC was unremarkable during URS. Perioperative antibiotics were only given to patients with significant bacteriuria revealed by the preoperatively obtained UC.

The observation period of this study splits in two separate intervals. From January 2013 until December 2014, patients received SOC perioperative antibiotic prophylaxis and were included

Table 4. Antibiotic usage postoperatively in the NoPAP group

Antibiotics usage, *n* (%)	
Yes	13 (9)
No	142 (91)
Reasons for antibiotics, *n* (%)	
Postoperative temperature ≥38.2°C	3 (23)
Intraoperatively suspected UTI	1 (8)
Second-look surgery for residual stone	9 (69)
Duration of antibiotic therapy, mean, days	6 (SD: 7)

in the PAP cohort. Patients who underwent an URS for urolithiasis in 2018, when SOC was no antibiotic prophylaxis, were included in the NoPAP cohort.

Only patients with negative preoperative UC or insignificant bacteriuria were included in this study. Patients with significant bacteriuria or symptomatic UTI always received a perioperative antibiotic treatment; therefore, these patients were excluded from further analysis. Patients without preoperative UC were also excluded.

A significant bacteriuria was defined as ≥ 10,000 colony-forming units (CFU)/ml of typical UTI pathogens. The UC was routinely done using clean catch of spontaneous midstream urine as part of the preoperative outpatient visit. Other exclusion criteria were bilateral urolithiasis, anatomic urinary tract variants (e.g., horseshoe kidney), urinary diversion, pregnancy, and coagulation disorders.

As part of the preoperative visit, all patients underwent ultrasound examination of the urinary tract to screen for hydronephrosis combined with one of the following optional imaging techniques: intravenous urography, non-contrast-enhanced computed tomography, or retrograde urography. Pre- and postoperative laboratory tests contained hemoglobin, white blood cell count, and glomerular filtration rate. Patients' records were screened for a history of recurrent UTIs, recent antibiotic usage, and prior therapies for urolithiasis within the last 90 days. Secondary diagnoses such as diabetes mellitus or immunosuppression were also recorded since these are known risk factors for UTI and potentially complicating factors. Symptoms like pollakiuria and strangury were registered as well as anticoagulants or immunosuppressants in long-term medication. The URS was performed as flexible, semirigid, or both. If necessary, lithotripsy was done with a 30-W holmium:YAG laser from Dornier MedTech® (Medials H Solvo®).

Intraoperative parameters such as surgery duration, intraoperative complications, number of stones, and residual stones by endoscopic view were extracted from the surgical report. Residual stones were defined as fragments larger than 1 mm. Additionally, every patient underwent ultrasound examination of the urinary tract postoperatively, to screen for residual stones or hydronephrosis.

The stone material obtained was analyzed by infrared spectroscopy, depending on the surgeon's discretion. The auricular body temperature was measured daily as part of the postoperative inpatient monitoring. Postoperative fever was defined as a body temperature greater than 38.0°C [9]. Postoperative complications were classified according to Clavien-Dindo and intraoperative ureteric trauma by the Post-Ureteroscopic Lesion Scale (PULS) [10, 11].

Statistical analysis was performed using SPSS 21.0 (SPSS Inc. Chicago, IL, USA) applying the *t* test for continuous variables with normal distribution and the Mann-Whitney U test for variables with nonnormal distribution. Metric variables were checked for normal distribution using the Shapiro-Wilk test. The χ^2 test was used for binary variables. The significance level was defined as $p < 0.05$.

Results

During the study periods, 375 patients underwent URS for treatment of ureteric or renal stones. A total of 124 patients were excluded because of a significant bacteriuria revealed by the preoperative UC or missing report of the UC in our database.

A total of 251 patients (173 males, 78 female) qualified for statistical analysis, of whom 96 were assigned to the PAP group and 155 to the NoPAP group. Antibiotic prophylaxis in the PAP group was given as a perioperative single shot (70.8%) or preoperative antibiotic prophylaxis (53.1%). The mean duration of the preoperative antibiotic treatment was 2.5 days (SD: 1.8). There were no significant differences in the patient characteristics between both groups (Table 1).

Known risk factors for the development of a symptomatic postoperative UTI were balanced between NoPAP and PAP with diabetes mellitus (11.6% vs. 12.5%), immunosuppression (2.1% vs. 1%), and preoperative hydronephrosis (27% vs. 35%). The surgical techniques and the stone position were also comparable in both groups.

Postoperative complication rates did not differ between the two groups (Table 2). Postoperative fever occurred equally in NoPAP and PAP groups (2% vs. 1%).

Few patients received antibiotics in the NoPAP group postoperatively (Table 3). Nine patients received an antibiotic prophylaxis due to a planned second look intervention for residual stones, and 3 patients received an antibiotic treatment due to postoperative fever. In 1 case, antibiotics were administered due to intraoperative cloudy urine and suspected UTI (Table 4). In this patient, preoperative UC was unremarkable, and postoperatively, no fever occurred (Table 3).

Postoperative complications correlated with increased surgical time above median (11.1% vs. 4.8%; $p = 0.065$), residual stone postoperatively (17.6% vs. 6.5%; $p = 0.031$), and an ASA score of 3–4 (12.8% vs. 6.9%; $p = 0.185$) (Table 5). With regard to postoperative fever, we identified a residual stone ($p = 0.033$) and an ASA score 3–4 ($p = 0.004$) as significant risk factors. Stone fragmentation shows a trend for a potential risk factor ($p = 0.126$) (Table 6).

Table 5. Risk factors for postoperative complications

	Complications, Clavien-Dindo 1–5	*p* value
Stone position Kidney versus ureter stone	7.7% versus 8.6%	0.849*
Stone count Multiple versus one	8.2% versus 7.8%	0.927*
Complications PULS 0 versus PULS 1–3	7.5% versus 9.7%	0.668*
Previous operation within 90 days Yes versus no	8.6% versus 6.1%	0.505*
Hydronephrosis preoperatively Yes versus no	8.1% versus 8.0%	0.967*
Leukocytosis (≥11.0*10 9/L) preoperatively Yes versus no	12.0% versus 7.9%	0.483*
Diabetes mellitus Yes versus no	6.7% versus 8.1%	0.779*
Stone fragmentation Yes versus no	10.4% versus 5.7%	0.377*
Surgical time ≤Median (40 min) versus >median (41+ min)	11.1% versus 4.8%	0.065*
Residual stone postoperatively Yes versus no	17.1% versus 6.5%	**0.031***
ASA score 3–4 versus 1–2	12.8% versus 6.9%	0.185*

*χ^2 test.

Discussion

Due to the omission of a routine perioperative antibiotic prophylaxis in patients undergoing a URS for treatment of urolithiasis, we were able to reduce the antibiotic usage by 91.7%. This approach did not result in an increased rate of infectious complications in our study cohort.

Postoperative fever did not differ between the PAP and NoPAP groups (1% vs. 2%). No high-grade complications (Clavien 4–5) were observed. Further risk factors might be considered preoperatively.

Our data show that longer surgery duration and ASA score 3–4 increase the risk of complications. The CROES URS Global Study showed similar results [12]. An explanation can be the higher probability of bacteremia due to prolonged manipulation in the urinary tract. Increased morbidity is also compatible with an increased infection rate.

Yet, our approach does not fully correspond to the current guideline recommendations, which suggest a single-shot antibiotic prophylaxis for patients with unremarkable preoperative UC [4, 6]. The guideline recommendations are primarily based on studies examining postoperative bacteriuria as the primary study end point.

It has been shown that a single dose of antibiotics significantly reduces the risk of postoperative bacteriuria after URS (12.5% PAP vs. 1.8% NoPAP) [13]. A systematic retrospective meta-analysis of 11 studies with 4,591 patients confirmed that a single dose of preoperative antibiotics results in a significantly lower risk of pyuria and bacteriuria [14].

In the context of ABS and our increasing knowledge about the urobiome, the question should be raised if an asymptomatic bacteriuria is the appropriate study end point to recommend antibiotic usage [15]. Severe UTI-associated complications like fever or urosepsis are rare

Table 6. Risk factors for postoperative fever

	Complications, Clavien-Dindo 1–5	*p* value
Antibiotic prophylaxis PAP versus nPAP	1.1% versus 2%	0.589*
Stone position Kidney versus ureter stone	1.4% versus 2%	0.938*
Surgical time ≤Median (40 min) versus >median (40+ min)	0.8% versus 2.5%	0.305*
Intraoperative complication PULS 0 versus PULS 1–3	1.5% versus 0%	0.489*
Leukocytosis (≥11.0*10 9/L) preoperatively Yes versus no	0% versus 1.9%	0.493*
Hydronephrosis preoperatively Yes versus no	1.4% versus 1.8%	0.844*
Diabetes mellitus Yes versus no	3.6% versus 1.4%	0.397*
Stone fragmentation Yes versus no	3.4% versus 0%	0.126*
Stone count Multiple versus one	3.3% versus 0.7%	0.119*
Residual stone postoperatively Yes versus no	6.1% versus 1.0%	**0.033***
Prior surgery within 90 days Yes versus no	2.2% versus 0%	0.227*
ASA score 3–4 versus 1–2	6.7% versus 0.5%	**0.004***

*χ^2 test.

after URS for urolithasis and scale between 1.1% and 1.72% [12, 16]. But these results mainly base on cohorts with short- or long-term perioperative antibiotic usage. To the author's knowledge, there are no studies that analyze the influence of a single dose of antibiotics compared to not using antibiotics with the endpoint of symptomatic UTI-related events.

Our simple approach by using the preoperative obtained UC for discrimination is not flawless since 2% of the NoPAP cohort developed fever. One explanation might be the known risk of a discrepancy between the urine from the renal pelvis compared to urine from the bladder [17]. Another reason might be our threshold of ≥10,000 CFU/mL for a significant bacteriuria in the preoperative UC. It is hypothetic if a stricter threshold of ≥1,000 CFU/mL would have reduced the incidence of symptomatic postoperative UTIs. On the other hand, a more conservative cutoff for antibiotic omission will decrease the number of patients eligible for antibiotic sparing approach.

In our study, there is a very low rate of infectious stones. It has to be noted that the rate of infectious stones is region-dependent and should be taken into account in a risk-adapted antibiotic prophylaxis strategy [18]. No conclusions can be made in this study with regard to stone analysis, due to the insufficient number of patients in the PAP group receiving a stone analysis. Another limitation of our study is the retrospective, single-center design.

In the perspective of the rising need of tailored antibiotic usage, we hope this trail can be an impulse for a prospective, multicentric, international validation of our hypothesis. We identified a residual stone, stone fragmentation, and an ASA score 3–4 as possible risk factors for postoperative fever, which might help for further

preoperative risk stratification. Based on our results, we suggest further prospective, multicentric investigation about routine antibiotic prophylaxis during URS.

Statement of Ethics

This article does not contain any studies with animals performed by any of the authors. Patient consent was not required as this study was based on publicly available data. All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional and/or National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study protocol (#17–818-104) was approved by the Ethics Committee of the University of Regensburg.

Conflict of Interest Statement

All other authors declare to have no conflicts of interest.

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Author Contributions

M.R.M.: conceptualization, methodology, project administration, formal analysis, and writing – original draft. E.-M.P.: data curation and investigation. P.J.S. and C.C.: writing – review and editing and validation. M.B.: supervision. M.J.S.: conceptualization, methodology, project administration, formal analysis, writing – review and editing, and investigation.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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