

Risk factors of infectious complication after ureteroscopic procedures of the upper urinary tract

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Received: 25 February 2013 / Accepted: 29 May 2013 / Published online: 20 June 2013
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Abstract Ureteroscopic procedures are being commonly performed in urology, but only a few clinical studies have been conducted on infectious complications after these procedures, and overall understanding on the preoperative use of prophylactic antibiotics is insufficient. This study examined the incidence rate of infectious complications and the risk factors affecting incidence after ureteroscopic procedures. We retrospectively reviewed the medical records of 531 patients who underwent ureteroscopy and ureteroscopic lithotripsy in our hospital, including age, sex, past history, comorbidity, urine analysis, urine culture, blood test, hydronephrosis, urethral catheter or ureteral stent, and percutaneous nephrostomy placement from January 2002 to December 2011. A total of 20 patients (3.8 %) contracted infectious complications after various procedures in the upper urinary tract. Preoperative bacteriuria, hydronephrosis, and the placement of a urethral catheter or ureteral stent, and percutaneous nephrostomy are significant risk factors of infectious complication. No significant differences were shown in the types and start time of prophylactic antibiotics. Diagnostic ureteroscopy exhibited a higher incidence rate of infectious complications compared to ureteroscopic lithotripsy.

Keywords Ureteroscopy · Infectious complication · Risk factor

Introduction

Prophylactic antibiotics are commonly and conventionally used to prevent general or local infections and complications during various invasive examinations or surgical procedures in urology. The purpose of prophylactic antibiotic use is to prevent wound infection, as well as the occurrence of febrile infectious complications such as pyelonephritis, prostatitis, epididymitis, and urosepsis [1, 2]. Urologists frequently perform ureteroscopic procedures and ureteroscopic lithotripsy for the purpose of examining and treating the upper urinary tract. Those procedures are generally performed in cases of urinary stones or tumor and congenital anomalies, and they are also conducted for the evaluation of ureter stricture or hydronephrosis. Febrile infectious complications and urinary tract infections can occur during those procedures and have negative impact on the surgical outcome. For these reasons, urologists administer prophylactic antibiotics to prevent such complications. However, those alternative measures are not always desirable. Patient resistance on bacteriuria and bacteremia and potential complications must be taken into consideration to decide the needs of prophylactic antibiotic administration. Moreover, risk factors also need to be considered such as the type of ureteroscopic procedure, older age, anatomical abnormalities, history of chemotherapy or radiation therapy, or long-term hospital stay to determine the types of prophylactic antibiotics, their start time, and duration of administration [3]. Although ureteroscopic procedures are being commonly performed in urology, only a few clinical studies have been conducted on infectious complications after these procedures, and overall understanding on the preoperative use of prophylactic antibiotics is insufficient. Therefore, this study examined the incidence rate of infectious complications

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and the risk factors affecting incidence after ureteroscopic procedures.

Patients and methods

Ureteroscopic procedures are mainly classified into diagnostic ureteroscopy and ureteroscopic lithotripsy that were performed in our hospital from January 2002 to December 2011. An 8-Fr. semi-rigid ureteroscope was utilized during the diagnostic ureteroscopy and ureteroscopic lithotripsy. We retrospectively reviewed the medical records of 531 patients who underwent ureteroscopy and ureteroscopic lithotripsy in our hospital, including age, sex, past history, comorbidity, urine analysis, urine culture, blood test, hydronephrosis, urethral catheter or ureteral stent, and percutaneous nephrostomy placement. The occurrence of infectious complication was defined as incidence within a 1-month period of surgery, a fever higher than 38 °C or chills, positive results in urine or blood bacterial culture, and the presence of sepsis. In addition, pyelonephritis, prostatitis, and epididymitis were included in the determination [4]. When a patient underwent different procedures, patient number was counted by taking each procedure as a case during the assessed period. The authors investigated the types and usage frequency of prophylactic antibiotics in each procedure, the postoperative incidence rate of infectious complications, and risk factors. Risk factors were established as male, older age, diabetes, history of chemotherapy or radiation therapy, renal insufficiency, hydronephrosis, preoperative bacteriuria, previous hospitalization, the placement of percutaneous nephrostomy, ureteral stent, or urethral catheter, procedure time, and start time of administering antibiotics, by reviewing references based on the criteria mentioned by Grabe et al. [5] and Yoon [6]. Patients aged more than 65 years were defined as old. A history of chemotherapy or radiation therapy implied a state of low immunity resulting from chemotherapy or radiation therapy. Renal insufficiency was defined as a glomerular filtration rate less than 60 ml/min/1.73 m². The journal article of Cietak and Newton [7] was used as a reference to classify hydronephrosis: grade 1 is no enlargement of the urinary tract; grade 2 is mild enlargement of the pelvis of the kidney but no deformation of the calyces; grade 3 is moderate enlargement of the pelvis and calyces simultaneously; grade 4 is severe enlargement of the pelvis and calyces simultaneously. Grade 2 and higher was defined as hydronephrosis. Also, bacteriuria was defined as more than 10⁴ CFU/ml before the surgery. Previous hospitalization indicated a long-term admission or hospital admission in the time period near to and preceding the surgical procedure. The time of antibiotic administration was categorized into a minimum of

12 h and immediately before the procedure (within 1 h) and a minimum of 3 h after the procedure. Levofloxacin 250 g was administered intravenously as prophylactic fluoroquinolone antibiotic, ceftriaxone 1 g was administered intravenously as cephalosporin antibiotic, and tobramycin 100 mg was administered intramuscularly as aminoglycoside antibiotic. One hour was set as the standard for the duration of the procedure. Statistical analysis was performed using a Fisher's exact test in the cross-tabulation analysis between the incidence rates of infectious complications caused by different surgical procedures and the start time of antibiotic administration. *P* values less than 0.05 were considered statistically significant. Statistical analysis was performed using the software SPSS version 18.0 (SPSS, Chicago, IL, USA).

Results

Analysis of patient characteristics

A total of 531 patients were classified according to the foregoing criteria. The results are shown in Table 1. The mean age of subjects was 59.07 years (range, 32–83), comprising 310 men (58.4 %) and 221 women (41.6 %). Of these patients, 205 (38.6 %) were more than 65 years old. There were 89 patients (16.8 %) with a history of

Table 1 Baseline characteristics of patients

Characteristics	Total (%)
Patients (number)	531
Mean age (years)	59.07 (32–83)
Sex	
Male	310 (58.4)
Female	221 (41.6)
Risk factors	
Old age (≥65 years)	205 (38.6)
Diabetes mellitus	59 (11.1)
History of chemotherapy or radiation therapy	89 (16.8)
Renal insufficiency ^a	38 (7.2)
Hydronephrosis	440 (82.9)
Bacteriuria	111 (20.9)
Previous hospitalization	47 (8.9)
Ureteral stent or nephrostomy	101 (19.0)
Duration of procedure (≤1 h)	469 (88.3)
Timing of antibiotic prophylaxis	
≥12 h before procedure	125 (23.5)
Just before procedure	340 (64.0)
≥3 h after procedure	28 (5.3)
No antibiotic prophylaxis	38 (7.2)

^a Glomerular filtration rate less than 60 ml/min/1.73 m²

chemotherapy or radiation therapy, and 440 patients (82.9 %) were confirmed with hydronephrosis; 101 patients (19.0 %) had already undergone placement of a ureteral stent, percutaneous nephrostomy, or urethral catheter. Because the ureteroscopic procedure takes a short period of time to perform, 469 patients (88.3 %) completed the procedure in less than an hour.

In analyzing start time of prophylactic antibiotics, 319 patients (63.7 %) were administered immediately before the procedure, 125 patients (23.5 %) were administered 12 h before the procedure, and 28 patients (5.3 %) were administered 3 h after the procedure. In principle, prophylactic antibiotics are administered before the procedure. However, some cases were administered with prophylactic antibiotics 12–24 h before the procedure depending on the preference of the attending physician, because diagnostic ureteroscopy were performed the day after admission under local anesthesia in some cases.

Administration of prophylactic antibiotics by ureteroscopic procedure

Ureteroscopic lithotripsy was performed in 377 patients (71.0 %): 231 patients (61.3 %) of these patients received insertion of a ureteral stent and 146 (38.7 %) did not. Diagnostic ureteroscopy was conducted in 154 patients (29.0 %): 89 patients (57.8 %) of these patients received insertion of a ureteral stent and 65 (42.2 %) did not. Administered prophylactic antibiotics by procedure are shown in Table 2. A total of 499 patients (94.0 %) received prophylactic antibiotics, of which 255 (48.0 %) received quinolones, 159 (29.9 %) received cephalosporins, and 19 (3.6 %) received aminoglycosides. Moreover, 39 (7.3 %) and 27 (5.1 %) patients received other antibiotics and a combination of two antibiotics, respectively; combined antibiotics were mostly cephalosporins and aminoglycosides.

Table 2 Antibiotics prophylaxis for ureteroscopic procedures

	UL (n = 377)	DU (n = 154)	Total (n = 531)
Fluoroquinolones	160	95	255 (48.0 %)
Cephalosporins	119	40	159 (29.9 %)
Aminoglycosides	16	3	19 (3.6 %)
Other antibiotics	35	4	39 (7.3 %)
Combined antibiotics	22	5	27 (5.1 %)
No antibiotics	25	7	32 (6.1 %)

UL ureteroscopic lithotripsy, DU diagnostic ureteroscopy

Incidence rate of infectious complication by ureteroscopic procedure

A total of 20 patients (3.8 %) contracted infectious complications after procedures in the upper urinary tract. Infectious complications were detected in 9 (5.8 %) of those patients who underwent ureteroscopic procedures and 11 (2.9 %) of those patients who underwent ureteroscopic lithotripsy. When incidence rates of infectious complications were compared by procedure, a significant difference was found in the incidence of complications between two procedures ($P = 0.022$). According to the types of antibiotics, incidence rates were highest with 10.5 % (2/19) in aminoglycosides, 6.3 % (2/32) with no use of antibiotics, 3.7 % (1/27) in the use of combined antibiotics, 3.5 % (9/255) in quinolones, 3.1 % (5/159) in cephalosporins, and 2.6 % (1/39) in other antibiotics. No statistically significant differences were found ($P = 0.185$; Table 3). Eight of 20 patients with infectious complications showed a positive result in urine culture. Cultures were identified to be *Escherichia coli* in 6 patients and *Enterococcus* spp. and *Staphylococcus aureus* in 2 patients each. The identified *E. coli* was sensitive to all antibiotics in 1 case, resistant to ampicillin in 2 cases, and resistant to TMP/SMX in 1 case. Moreover, *E. coli* was resistant to fluoroquinolone and ampicillin in 1 case, and resistant to cephalosporin, ampicillin, and others in the other case. In addition, *S. aureus* was resistant to cephalosporin, aminoglycoside, and TMP/SMX whereas *Enterococcus* was resistant to all antibiotics. In this case, the patient received conservative care including prolonged use of antibiotics for reasons of a chronic disorder associated with colorectal cancer. Among 20 cases of infectious complications, 15 cases (75.0 %) were acute pyelonephritis, 1 case was (5.0 %) acute prostatitis, 1 case was (5 %) acute epididymitis, and 3 cases (15.0 %) were cause unknown. Of the acute pyelonephritis

Table 3 Febrile infectious complications and antibiotic prophylaxis

	UL (n = 377)	DU (n = 154)	Total (n = 531)
Incidence (%)*	11 (2.9 %)	9 (5.8 %)	20/531 (3.8 %)
Fluoroquinolones	5	4	9/255 (3.5 %)
Cephalosporins	2	3	5/159 (3.1 %)
Aminoglycosides	2	0	2/19 (10.5 %)
Other antibiotics	1	0	1/39 (2.6 %)
Combined antibiotics	0	1	1/27 (3.7 %)
No antibiotics	1	1	2/32 (6.3 %)

UL ureteroscopic lithotripsy, DU diagnostic ureteroscopy

* $P < 0.05$, compared with ureteroscopic lithotripsy and diagnostic ureteroscopy

patients, 7 were hospitalized because of fever higher than 38 °C, and 5 of the patients were first given ceftriaxone intravenously until their body temperature dropped to normal levels, and then received ceftriaxone orally for 10–14 days. However, 1 of the patients diagnosed with acute pyelonephritis was found to have ceftriaxone-resistant *E. coli* and was given levofloxacin. Another patient was infected with *Enterococcus* sp., resistant to all antibiotics, so vancomycin was intravenously administered for 1 week after consulting with the Division of Infectious Diseases. Patients with acute prostatitis and acute epididymitis had temperatures above 38 °C and were given levofloxacin intravenously until their temperatures returned to normal. After temperatures returned to normal, they received urine analysis and were orally administered levofloxacin for 2–4 weeks.

Incidence rate of infectious complication by the start time of prophylactic antibiotics

Incidence rates of infectious complications by the start time of prophylactic antibiotics are shown in Table 4. The incidence rate was lowest with 2.4 % (8/340) when the antibiotics were administered immediately before the procedures. The incidence rates were found to be 5.3 % (2/38) with no use of antibiotics, 5.6 % (7/125) with use 12 h before the procedure, and 10.7 % (3/28) in with use 3 h after the procedure. Preoperative administration lowered the incidence rate of infectious complications compared to postoperative administration. However, no statistically significant differences were found ($P = 0.338$).

Analysis of risk factors affecting the incidence of infectious complications

In this study we performed multivariate analysis on risk factors affecting the incidence of infectious complications. Statistical significance was only observed in cases with bacteriuria, hydronephrosis, and the placement of a urethral catheter, ureteral stent, or percutaneous nephrostomy preoperatively. Old age, diabetes, history of chemotherapy or

radiation therapy, renal insufficiency, preoperative long-term hospital stay, operation time, start time of prophylactic antibiotics administration, and other factors were all statistically insignificant. After ureteroscopic procedures, a ureteral stent was inserted in 3 cases (3/89), although 6 cases (6/65) were not among the 9 patients with infectious complications. A statistically significant decrease was detected in infectious complications with ureteral stent insertion. After ureteroscopic lithotripsy, 4 cases (4/231) were inserted with ureteral stent while 7 cases (7/146) were not among 11 patients with infectious complications. A statistically significant decrease was also found in infectious complications with ureteral stent insertion. Therefore, preoperative bacteriuria, hydronephrosis, placement of a urethral catheter or ureteral stent, percutaneous nephrostomy, and the postoperative insertion of a ureteral stent were verified to be risk factors influencing the incidence of infectious complications ($P < 0.05$; Table 5).

Discussion

Prophylactic antibiotics are commonly and conventionally used to prevent infections in urological procedures performed for diagnosis and treatment purposes. Commonly performed urological procedures vary from urethral catheter insertion, cystoscopy, urodynamic study, and transrectal prostatic biopsy in the lower urinary tract to retrograde pyelography, diagnostic ureteroscopy, ureteral stent insertion, and percutaneous nephrostomy in the upper urinary tract. Many studies have been conducted on the use of prophylactic antibiotics in transrectal prostatic biopsy among surgical procedures of the lower urinary tract. The use of prophylactic antibiotics was verified to decrease fever and infectious complications such as urinary tract infection, establishing the need of prophylactic antibiotic use [8, 9]. However, reviews of literature are rarely performed, especially on the use of prophylactic antibiotics in other urological procedures. Lee et al. [10] reported in detail that the incidence rate of infectious complication after urethral catheter insertion in intensive care unit patients was 4.6 %, and the incidence rate of infectious complications reportedly ranged between 2.2 % and 7.8 % with urinary tract infection identified via urine culture after cystoscopic exam [11, 12]. According to Rané et al. [13], an incidence rate of 21 % of urinary tract infection decreased to 1–5 % with a single dose of antibiotics after cystoscopic exam without cases of general infection.

Peschers et al. [14] reported that prophylactic antibiotics were ineffective in urinary incontinence patients undergoing a urodynamic study. According to Payne et al. [15], the incidence rate of urinary tract infection was higher in females than males after urodynamic study. Based on those

Table 4 Timing of the start of antibiotic prophylaxis and incidence of febrile infectious complication

Timing of antibiotic prophylaxis	Febrile infectious complication		Total
	Yes	No	
≥12 h before procedure	7 (5.6 %)	118 (94.4 %)	125
Just before procedure	8 (2.4 %)	332 (97.6 %)	340
≥3 h after procedure	3 (10.7 %)	25 (89.3 %)	28
No antibiotic prophylaxis	2 (5.3 %)	36 (94.7 %)	38

Table 5 Risk factors for febrile complication

Risk factors	Patients	Infectious complication	<i>P</i> value
Old age			
<65 years	326	12	
≥65 years	205	8	0.534
Diabetes mellitus			
Absent	472	16	
Present	59	4	0.172
History of chemotherapy or radiation therapy			
Absent	442	15	
Present	89	5	0.232
Renal insufficiency			
Absent	493	19	
Present	38	1	0.573
Hydronephrosis			
Absent	91	2	
Present	440	18	0.022 ^a
Bacteriuria			
Absent	420	8	
Present	111	12	0.000 ^a
Previous hospitalization			
No	484	17	
Yes	47	3	0.257
Catheterization ^b			
Absent	430	9	
Present	101	11	0.000 ^a
Duration of procedure			
≤1 h	469	17	
>1 h	62	3	0.420
Timing of antibiotic prophylaxis			
≥12 h before procedure	125	7	
Just before procedure	340	8	
≥3 h after procedure	28	3	
No antibiotic prophylaxis	38	2	0.064

^a Statistically significant

^b Ureteral stent or nephrostomy

outcomes, procedures of the lower urinary tract showed somewhat aligned views. In cases of simple diagnostic procedures such as cystography, urodynamic study, and cystoscopy, prophylactic antibiotic use was not considered essential when strains did not grow in urine culture. In contrast, the use of prophylactic antibiotics needs to be taken into account in patients with a history of bacteriuria, urethral catheter placement, urinary tract infection, etc. [3, 6, 16]. As an exception, prophylactic antibiotic use must be considered in all patients undergoing transrectal prostatic biopsy.

Similarly, ureteroscopic procedures and ureteroscopic lithotripsy in the upper urinary tract are also commonly performed as often as the procedures of the lower urinary tract. However, fewer systematic reviews have been made than on lower urinary tract procedures. Some literature reports on prophylactic antibiotic use in ureteroscopic procedures differ from our study methods because they comprise complex endoscopic surgery including extracorporeal shock wave lithotripsy and percutaneous nephrolithotomy. Yoon [6] reported that few cases of infections were detected after upper urinary tract procedures such as ureteroscopy, agreeing with our study. They suggested that the effects of prophylactic antibiotics have not yet been clarified, and treatments need to be distinguished between procedures with fewer risk factors, such as diagnostic ureteroscopy, ureteral stent insertion, and distal ureteroscopic lithotripsy, and procedures with more risk factors, such as proximal ureteroscopic lithotripsy and percutaneous nephrolithotripsy [17].

The ratio of patients administered prophylactic antibiotics was 94.0 %, agreeing with 76–95 % of patients identified in a study by Koh et al. [3] on the use of prophylactic antibiotics in urological clinics nationwide in 2009. According to the European Association of Urology Guidelines [6], cephalosporin or fluoroquinolone was recommended as prophylactic antibiotic for diagnostic ureteroscopy and ureteroscopic lithotripsy. In the present study, cephalosporin or fluoroquinolone was most commonly used as the prophylactic antibiotic, similar to the EAU guideline.

The incidence rate of infectious complications was 3.8 % after endourological procedures of the upper urinary tract in our study. The rate was slightly lower than the incidence rate of 4.5 % reported in a similar study conducted by Matsumoto et al. [18]

Diagnostic ureteroscopy was higher in the incidence of infectious complications compared to ureteroscopic lithotripsy. The outcome is thought to be attributable to higher risk for infection in diagnostic ureteroscopy, generally performed together with biopsy, generating bleeding and tissue damage, compared to ureteroscopic lithotripsy. Furthermore, the incidence of infectious complications was reduced when a ureteral stent was placed in both diagnostic ureteroscopy and ureteroscopic lithotripsy. The reduction is thought to be attributable to facilitated urinary drainage through ureteral stent placement. Kim [16] and Yoon [6] also suggested the accumulated experience of surgeons and internal bleeding within tissues as risk factors that increase the incidence of complications. No statistically significant differences were found in incidence rate by comparing antibiotics, showing that incidence of complications was not influenced by type of antibiotics.

According to the American Urological Association Guidelines, prophylactic antibiotics should be administered within 1 h after skin insertion, and the intravenous injection of fluoroquinolone or vancomycin must be made within 2 h to prevent antibiotics-related complications, in principle. The European Association of Urology Guidelines also principally recommend the administration within 2 h preoperatively, not to surpass a maximum of 3 h preoperatively. As evidence, Stone et al. [19] proved that wound infection rate was lowest in patients administered with prophylactic antibiotics within 1 h preoperatively. In contrast, wound infection rate was significantly higher in patients administered the antibiotics within 1–4 h postoperatively. Furthermore, the infection rate of these patients was similar to that of patients who did not receive prophylactic antibiotics. In 1992, Classen et al. [20] reported the relationship between the start time of prophylactic antibiotics and wound infection in clean or clean-contaminated surgery. Wound infection rate was lowest, up to 0.6 %, in the group administered antibiotics within 2 h preoperatively. In contrast, wound infection rate was 1.4 %, 2.4 times higher, in the group administered antibiotics 3 h postoperatively. Moreover, wound infection rates increased to 3.3 %, 5.8 times higher, in the group administered antibiotics within 3–24 h postoperatively. The group receiving antibiotics within 2–24 h preoperatively showed a wound infection rate of 3.8 %, 6.7 times higher than that of the group administered antibiotics within 2 h preoperatively. Based on the foregoing results, Classen et al. [20] recommended administering prophylactic antibiotics within 2 h preoperatively. Similarly, most previous studies reported that the incidence rate of infectious complications was lowest when the antibiotics were administered within 2 preoperative hours. Although the incidence rate was lowest, 2.4 %, when the administration was made before the procedure in this study, no statistically significant differences were shown. The outcome is thought to be attributable to the administration of different antibiotics compared to other previous studies. In addition, errors incurred because the study was a retrospective study performed with a small-scale population.

In regard to the risk factors affecting the incidence of infectious complications, predictors were identified to be preoperative bacteriuria, hydronephrosis, and the placement of a urethral catheter or ureteral stent and percutaneous nephrostomy in this study, agreeing with the results of previous literature reviews. However, Grabe et al. [5] pointed out bacteriuria, ureteral stent, and percutaneous nephrostomy as risk factors with definite evidence, whereas age, renal insufficiency, operation time, diabetes, and previous administration of prophylactic antibiotics were risk factors with insufficient evidence. Yoon [6] suggested urethral catheter placement, the history of urinary tract

infection, and preoperative long-term hospital stay as the three major risk factors. In addition, Matusmoto et al. [18] noted hydronephrosis and bacteriuria as statistically significant risk factors.

Risk factors were verified to be preoperative bacteriuria, hydronephrosis, previous placement of urethral catheter, ureteral stent, and percutaneous nephrostomy.

Conflict of interest There is no conflict of interest, and there are no financial or commercial interests.

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