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Korean Multicenter Study of Infectious Complications after Transurethral Prostate Surgery in Patients with Preoperative Sterile Urine

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Purpose: To evaluate the efficacy of antibiotic prophylaxis and determine the risk factors of infectious complications after transurethral surgery of the prostate.
Materials and Methods: Seven hundred and seventy-two patients who underwent transurethral resection of the prostate (TURP) or holmium laser enucleation of the prostate (HOLEP) were reviewed. Of these, this study enrolled 643 patients without bacteriuria who had not received antibiotics for urinary tract infections for two weeks before surgery. The patients were divided into two groups according to the duration of the antibiotics (Group 1: less than one day, n=396 vs. Group 2: more than one day, n=247).
Results: The overall incidence of postoperative infectious complications in 643 patients was 5.0% (32/643). When postoperative infectious complications were compared according to the duration of the antibiotics (Group 1 vs. Group 2), the infectious complications rates were 5.6% (22/396) vs. 4.0% (10/247), respectively (p=0.393). When postoperative infectious complications were compared according to the duration of antibiotics (Group 1 vs. Group 2) in the TURP and HOLEP groups, the infectious complications rates were 6.3% (12/192) vs. 1.0% (1/103) (p=0.035) and 4.9% (10/203) vs. 6.0% (8/134) (p=0.677), respectively. The duration of Foley catheterization was independently associated with infectious complications (p=0.003).
Conclusions: The results showed that prolonged postoperative catheterization affects postoperative infectious complications associated with transurethral prostate surgery. Although antibiotics administered for less than one day are effective for antibiotic prophylaxis of transurethral prostate surgery, a longer antibiotic therapy is recommended for TURP.

Keywords: Urinary tract infections; Transurethral resection of prostate; Risk factors; Antibiotic prophylaxis

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INTRODUCTION

Prophylactic antibiotic use aims to prevent local or systemic postprocedural infection. Four types of infection are commonly associated with urologic surgery. In the first, a urinary tract infection (UTI) is either a space or organ infection associated with both endoscopic and endoluminal interventions. It occurs with both open and laparoscopic surgeries, mostly coinciding with catheter and stent placement or an undetected harbored bacterial load. The second type is a wound infection after open and laparoscopic surgeries. The third form of infection is observed in the male genital system (prostatitis, epididymitis, and orchitis). In the fourth form, bloodstream-borne sepsis secondary to urologic instrumentation accounts for 10% to 12% of health-care-associated infections in urology wards [1].

Transurethral surgery of the prostate is considered the gold standard treatment for benign prostate surgery. Despite the progress made in prostate surgery (e.g., transurethral laser surgery), postoperative infectious complications, especially UTIs, are frequent, often progressing to bacteremia and life-threatening sepsis [2]. Furthermore, despite antibiotic prophylaxis for reducing postoperative infectious complications, controversy over antibiotic prophylaxis for prostatic surgery remains as for other urologic surgeries [3,4].

In the context of surgical field classification, transurethral resection of the prostate (TURP) can be categorized into a clean-contaminated or a contaminated operation depending on the patient's history of UTI/urogenital infection, catheterization, and sterile/nonsterile urine [4]. In this regard, the administration of prophylactic antibiotics is suitable for preventing postoperative infectious complications in transurethral prostate surgery. Unfortunately, there are few studies on the prophylactic effect of antimicrobial therapy and the risk factors associated with TURP and other prostate interventions (e.g., adenoma enucleation and laser ablation) [2,5-7].

There is currently a lack of information on the risk factors for infectious complications associated with prostate surgery in Korea. In addition, the Health Insurance Review & Assessment Service of Korea recently recommended prophylactic antibiotics for less than one day in patients undergoing prostate surgery without any evidence from studies on the Korean population. Therefore, this study evaluated the risk factors for infectious complications after transurethral surgery of the prostate and the efficacy of antibiotic prophylaxis according to the duration of antibiotic therapy.

MATERIALS AND METHODS

1. Study Population and Data Collection

This retrospective study was conducted from January 2020 to December 2021 in 11 Korean urologic institutions. Seven hundred and seventy-two patients with symptomatic benign prostatic hyperplasia or prostate cancer, who underwent transurethral prostate surgery, such as TURP, holmium laser enucleation of the prostate (HOLEP, Ho:YAG laser), or photovaporization (GreenLight laser) of the prostate, were included in this study. The inclusion criteria were as follows: no preoperative bacteriuria, no antibiotics within two weeks of the surgery, and age 18 years or older. Among the 772 patients who underwent transurethral prostate surgery during this period, 129 patients with preoperative bacteriuria or UTI history were excluded from the study.

Six hundred and forty-three patients included in the final analysis were divided into two groups according to the duration of the antibiotics (Group 1: less than one day, n=396 vs. Group 2: more than one day, n=247). All patients received an initial intravenous antibiotic 30 to 60 minutes before surgery. The oral antibiotics were the same type as the intravenous antibiotics used previously. The intravenous antibiotics were chosen according to physician preference. Most antibiotics were cephalosporins and quinolones. The other antibiotics included amikacin, gentamycin, fosfomycin, piperacillin and tazobactam, and imipenem.

Patient preoperative data, including age, body mass index (BMI), diabetes mellitus, maximal flow rate, prostate volume, prostate-specific antigen (PSA) level, and the presence of preoperative Foley catheterization and bladder stones, were obtained from the patients' medical records. This study reviewed perioperative data, such as resected prostate volume (fresh tissue weight in the operating room), operation time (minutes), duration of postoperative catheterization, operation method, type of antibiotics, duration of antibiotic therapy (intravenous or oral), and infectious complication rates for all patients.

Table 1. Preoperative characteristics of the patients

Characteristics	Total (n=643)	Group 1 (n=396)	Group 2 (n=247)	p-value
Age (y)	72.3±7.2	72.1±7.0	72.6±7.4	0.357
BMI (kg/m^2)	24.7±3.1	24.9±3.1	24.5±3.1	0.146
Comorbid condition				
DM	170 (26.4)	100 (25.3)	70 (28.3)	0.388
Immunosuppression	11 (1.7)	3 (0.8)	8 (3.2)	0.018
IPSS total	21.1±10.0	21.2±11.0	21.0±7.1	0.833
Qmax (mL/s)	9.2±5.9	9.1±6.0	9.4±5.6	0.521
PSA level (ng/mL)	8.0±33.1	7.2±27.1	9.6±42.9	0.521
Bladder stone	69 (10.7)	37 (9.3)	31 (12.6)	0.150
Prostate volume (mL)	60.4±29.3	60.6±29.8	59.8±28.2	0.743
Urinary retention	147 (22.9)	66 (16.7)	81 (32.8)	0.001
Foley catheterization before surgery	101 (15.7)	56 (14.1)	45 (18.2)	0.167

Values are presented as mean ± standard deviation or number (%).
Group 1 use of antibiotics for less than one day. Group 2 use of antibiotics for more than one day.
BMI: body mass index, DM: diabetes mellitus, IPSS: International Prostate Symptom Score, PSA: prostate-specific antigen.

2. Definition of Postoperative Infectious Complications

Because of the possible lack of the clinical significance of bacteriuria, the primary and secondary outcome parameters were symptomatic UTI, fever, sepsis, and bacteremia. Therefore, postoperative infectious complications were defined as febrile UTI and symptomatic bacteriuria. Febrile UTI and symptomatic bacteriuria were described according to the clinical guideline for diagnosing and treating UTIs in Korea [8]. Symptomatic bacteriuria and febrile UTI were defined as postoperative bacteriuria associated with the clinical signs of UTI (dysuria, frequency, and urgency) and a body temperature of ≥38℃, respectively. Bacteremia was defined as the existence of bacteria in blood culture. Sepsis was defined as systemic inflammatory response syndrome (SIRS) caused by infection. SIRS was defined as the presence of two or more of the following conditions: body temperature ≥38℃ or <36℃, heart rate >90 beats per minute, respiratory rate >20 breaths per minute or respiratory alkalosis, or a white blood cell count >12,000/mm^3 or <4,000/mm^3, or the presence of >10% immature band forms [9].

3. Statistics

Statistical analysis was performed using SPSS software, version 23.0 (IBM Co., Armonk, NY, USA). Descriptive analysis was performed to assess the patients' demographics. Continuous variables are presented as means and standard deviations, and categorical variables are presented as frequencies (%). Univariate and multivariate logistic regression analyses (stepwise backward procedure) were performed to assess the associations of clinical parameters with infectious complications. The p-values <0.05 were considered significant for all analyses.

4. Ethics Statement

The study protocol was reviewed and approved by the institutional review board of the Chonnam National University Hwasun Hospital (IRB approved protocol: No. CNUHH-2021-006). The study was performed in accordance with the principles of the Declaration of Helsinki and the Ethical Guidelines for Clinical Studies.

RESULTS

1. Baseline Demographics

The 129 patients excluded with preoperative bacteriuria or a history of UTI showed higher postoperative infectious complications (12.4% vs. 5.0%, p=0.001). Table 1 lists the preoperative characteristics of the included patients. The mean age and BMI of the enrolled patients were 72.3±7.2 years and 24.7±3.1 kg/m^2, respectively. Regarding the prostate-related parameters, the International Prostate Symptom Score (IPSS), and uroflowmetric parameters, the PSA level, prostate volume, total IPSS, and Qmax, were 7.99±33.1 ng/mL, 60.4±29.3 mL, 21.1±10.0, and 9.17±5.92 mL/s, respectively. One hundred and one patients (15.7%) had undergone preoperatively indwelled Foley catheterization. As shown in Table 1, no significant difference was noted in the patients' preoperative characteristics, except

Table 2. Perioperative characteristics of the patients

Characteristics	Total (n=643)	Group 1 (n=396)	Group 2 (n=247)	p-value
Operative duration (min)	88.21±47.18	80.70±46.72	100.20±45.48	0.001
Operation type				0.223
KTP	11	1 (0.3)	10 (4.0)	
TURP	295	192 (48.5)	103 (41.7)	
HOLEP	337	203 (51.3)	134 (54.3)	
Resected prostate volume (mL)	24.2±18.78	25.01±18.45	22.77±19.32	0.179
Co-op Hx with prostate surgery	91 (14.2)	49 (12.4)	42 (17.0)	0.101
Type of prophylactic antibiotics				0.001
1st cephalosporin	55 (8.6)	44 (11.1)	11 (4.5)	
2nd cephalosporin	461 (71.7)	318 (80.3)	143 (57.9)	
3rd cephalosporin	26 (4.0)	10 (2.5)	16 (6.5)	
Quinolone	63 (9.8)	24 (6.1)	39 (15.8)	
Others	38 (5.9)		38 (15.4)	
Duration of Foley catheterization (d)	4.02±2.59	3.91±1.97	4.19±3.35	0.190
Histology				0.040
BPH	593 (92.2)	372 (93.9)	221 (89.5)	
Prostate cancer	50 (7.8)	24 (6.1)	26 (10.5)	
Infectious complications	32 (5.0)	(22/396) 5.6%	(10/247) 4.0%	0.393
TURP		(12/192) 6.3%	(1/103) 1.0%	0.035
HOLEP		(10/203) 4.9%	(8/134) 6.0%	0.677
KTP		(0/1) 0%	(1/10) 10%	0.740
Postop antibiotics				
Yes	257 (40.0)	150 (37.9)	107 (43.3)	0.171
Duration	4.12±7.11	4.31±7.55	3.82±6.35	0.040
Therapeutic	35 (5.4)	22 (5.6)	13 (5.3)	0.874
Sx palliative	222 (34.5)	128 (32.3)	94 (38.1)	0.137

Values are presented as mean ± standard deviation or number (%).
Group 1 use of antibiotics for less than one day. Group 2 use of antibiotics for more than one day.
KTP: potassium-titanyl-phosphate, TURP: transurethral resection of the prostate, HOLEP: Holmium laser enucleation of the prostate, Hx: history, BPH: benign prostate hyperplasia, Sx: symptom.

the presence of immunosuppression (0.8% vs. 3.2%, p=0.018) and a history of urinary retention (16.7% vs. 32.8%, p=0.001) between Groups 1 and 2.

Among the 643 patients, 337, 295, and 11 underwent HOLEP, TURP, and potassium titanyl phosphate laser transurethral prostate surgery, respectively. The mean duration of the operation and postoperative Foley catheter placement were 88.2±47.2 min and 4.0±2.5 days, respectively. First- or second-generation cephalosporin was administered to 516 (80.3%) patients and a third-generation cephalosporin to 26 (4.0%) patients. Postoperative infectious complications developed in 32 (5.0%) patients. When postoperative infectious complications were compared according to the duration of the antibiotics (Group 1 vs. Group 2), the overall incidences of the infectious complications were 5.6% (22/396) versus 4.0% (10/247), respectively (p=0.393). On the other hand, when postoperative infectious complications were compared according to the duration of the antibiotics in the TURP and HOELP groups, the infectious complications rates were 6.3% (12/192) vs. 1.0% (1/103), (p=0.035), and 4.9% (10/203) vs. 6.0% (8/134), (p=0.677) respectively, as shown in Table 2.

Table 3 lists the results of logistic regression analysis for the clinical parameters associated with postoperative infectious complications. In univariate analysis, the duration of Foley catheterization (odds ratio [OR], 1.15; 95% confidence interval [CI], 1.06-1.24, p=0.001) and age (OR, 1.07; 95% CI, 1.02-1.13, p=0.010) were risk factors for postoperative infectious complications. Multivariate analysis showed that the duration of Foley catheterization (OR, 1.13; 95% CI, 1.04-1.23, p=0.003) was independently associated with postoperative infectious complications.

DISCUSSION

Although transurethral prostate surgery is one of the most common urological procedures, it carries a risk of postoperative infectious complications, similar to other urologic procedures. Prophylactic antibiotics are recom-

Table 3. Associations between clinical parameters and infectious complications after transurethral surgery and multivariate analysis of clinical parameters independently affecting infectious complications after transurethral surgery

Univariate analysis (n=643)		
Variables	Unadjusted OR (95% CI)	p-value
Age	1.07 (1.02-1.13)	0.010
BMI	0.94 (0.84-1.06)	0.296
DM	1.72 (0.82-3.59)	0.150
Immunosuppression	-	0.990
Foley catheterization before surgery	1.25 (0.50-3.13)	0.628
Urinary retention	0.77 (0.31-1.91)	0.571
Prostate volume	1.01 (0.99-1.02)	0.325
IPSS	0.95 (0.89-1.01)	0.085
Co-op Hx with prostate surgery	0.86 (0.30-2.51)	0.783
Resected prostate volume	1.01 (0.99-1.03)	0.166
Operative duration (min)	1.00 (0.99-1.01)	0.347
Duration of Foley catheterization (d)	1.15 (1.06-1.24)	0.001
Antibiotic use for more than one day	0.717 (0.33-1.54)	0.395
OP method (reference; HOLEP)		
TURP	0.82 (0.39-1.70)	0.588
KTP	1.77 (0.22-14.6)	0.595
Type of antibiotics (reference; 1st cephalosporin)		
2nd cephalosporin	1.52 (0.35-6.59)	0.577
3rd cephalosporin	1.06 (0.09-12.2)	0.963
Quinolone	0.87 (0.12-6.38)	0.890
Others	1.47 (0.19-10.9)	0.705
Multivariate analysis (n=643)		
	Adjusted OR (95% CI)	p-value
Age	1.05 (0.99-1.11)	0.073
Duration of Foley catheterization (d)	1.13 (1.04-1.23)	0.003

OR: odds ratio, CI: confidence interval, BMI: body mass index, DM: diabetes mellitus, IPSS: International Prostate Symptom Score, OP: operation, Hx: history, TURP: transurethral resection of the prostate, HOLEP: Holmium laser enucleation of the prostate, KTP: potassium-titanyl-phosphate.

mended to reduce postoperative infectious complications. Although effective in practice [10,11], the optimal antibiotic regimen and duration of antibiotics are still debatable. Therefore, a multicenter study in Korea was conducted to evaluate the efficacy of antibiotic prophylaxis and determine the risk factors of infectious complications after transurethral prostate surgery. The duration of Foley catheterization was an independent, predictive factor of postoperative infectious complications after prostate-related surgery. In addition, these results suggest that although antibiotics administered for less than one day are effective as antibiotic prophylaxis for transurethral prostate surgery, a longer antibiotic therapy is recommended for TURP.

In urologic surgical practice, preventing postoperative infectious complications is important, but few studies evaluated the methods of antibiotic prophylaxis and risk factors for postoperative infectious complications in such settings [2,5-7]. Although the current classes of surgery/surgical field contamination were developed and updated for open surgery and to determine the relative risk of surgical wound infection [12] and the current guidelines for surgical site infection focus on gastrointestinal surgery [13]. Thus, urological interventions have not been classified, and the current definitions do not include endoscopic surgery. In addition, the criteria for assessing contamination categories in open surgery are the type of incision, level of spillage, and evidence of infection or inflammation [12]; UTI is not included in these criteria. Therefore, these guidelines cannot be adapted to transurethral prostatic surgery because many urological procedures are associated with urine exposure and endourological procedures.

In the context of surgical field classification, transurethral prostate surgery can be categorized into a clean-contaminated or contaminated operation depending on the patient's history of UTI/urogenital infection, catheterization, and sterile/nonsterile urine [4]. In cases of negative urine culture, whether the opening of the urinary tract should be classified as clean or clean-contaminated surgery remains controversial; the same applies to transurethral surgery. On the other hand, several studies have suggested that these procedures should be considered clean-contaminated because urine culture is not always a predictor of the bacterial burden, and the lower genitourinary tract is colonized by microflora, even in the presence of sterile urine [3,14]. In addition, the recent criteria for assessing the level of surgical class/surgical field contamination in prostatic urological procedures suggest that these procedures should be considered contaminated in the presence of a previous history of UTI/urogenital infection (prostatitis), presurgical catheterization, or controlled bacteriuria [4]. Therefore, clean-contaminated urologic operations should be extended for practical and strategic reasons. In an extension, this classification could theoretically be widened also to cover endoscopic urological procedures, the surgical site being the urinary tract and the surgical site infection being UTI.

The principal complications after transurethral prostate surgery are postoperative UTI and bacteremia. According to systematic reviews by Berry and Barratt [10] and Qiang et al. [11], the incidences of postoperative bacteriuria and bacteremia that were more severe than UTI without antibiotic prophylaxis were approximately 26.0% and 4.4%, respectively. The sources of infection after transurethral prostate surgery have not been elucidated. On the other hand, several factors, including inflammatory foci within the prostatic adenoma, urethral flora, intraoperative or postoperative contamination, urethral catheter colonization, or infection from distant foci, are considered the sources of infection [15]. In this regard, they concluded that antibiotic prophylaxis significantly decreases the development of post-TURP bacteriuria, post-TURP fever, sepsis, and the need for additional antibiotics after TURP. In addition, there was a trend suggesting higher efficacy with a short course (<72 hours) of antibiotic prophylaxis than with a single-dose regimen in patients who underwent TURP [10,11]. Nevertheless, the optimal antibiotic regimen and duration of prophylaxis remain to be determined.

In the present study, the postoperative infectious complications rate with antibiotic prophylaxis was 5%. In addition, there was no significant difference in postoperative infectious complications according to the duration of antibiotics (less than one day vs. more than one day). On the other hand, in subgroup analysis, according to the type of transurethral prostate surgery, the postoperative infectious complications rate was higher in the TURP group with the short duration of antibiotics. This is in concordance with the results of systematic reviews by Berry and Barratt [10] and Qiang et al. [11] that the prophylactic effect of multiple doses of cephalosporins for 24 to 72 hours is more effective than that of a single dose in patients undergoing TURP. Since 2000, the Health Insurance Review and Assessment Service of Korea has recommended using prophylactic antibiotics in surgery for less than one day [16]. HoLEP has the benefit of less extensive injury to prostatic tissue than TURP [17], postsurgical local inflammation may not be as severe as with TURP [18], and the use of prophylactic antibiotics in surgery for less than one day is appropriate for patients undergoing HOLEP. Regarding TURP, in addition to the above reasons, the duration of Foley catheterization is longer in TURP than in HoLEP due to more hematuria [17]. In addition, considering the reports that the incidence of antibiotic resistance in Asia is higher than that in Western or European countries [19,20], antibiotic prophylaxis within three days of surgery might be appropriate for patients who have undergone TURP.

Regarding the antibiotic type, there is a lack of evidence suggesting the routine use of one class of antibiotics versus another, with aminoglycosides, fluoroquinolones, cephalosporins, and trimethoprim-sulfamethoxazole all demonstrating efficacy in large meta-analyses [10]. Ciprofloxacin and second- or third-generation cephalosporins are the most commonly used antibiotics in transurethral prostate surgery worldwide [21]. On the other hand, as the rate of quinolone resistance in Korea is relatively high [22], the Health Insurance Review and Assessment Service of Korea recommends using first- or second-generation cephalosporins as prophylactic antibiotics in transurethral prostate surgery. In the present study, the prophylactic efficacy did not differ according to the antibiotic type. Further trials on the efficacy of different types of antibiotics are needed in the future.

Several studies have investigated the risk factors for postoperative infectious complications after TURP [5,7,14,23,24]. The well-documented risk factors in these studies are preoperative bacteriuria, duration of the operation, rupture of closed drainage systems, and duration of postoperative catheterization [5,7,14,23,24]. These risk factors can cause infectious complications, even in clean operations; hence, information on these risk factors is fundamental for reducing infectious complications [12]. In the present study, the duration of postoperative catheterization was an independent risk factor for postoperative infectious complications. In contrast, neither the duration of antibiotic administration nor the type of surgery affected the rate of postoperative infectious complications. In addition, a history of preoperative or recent UTI was not a risk factor for postoperative complications in the present study because the patients with preoperative bacteriuria or who had received antibiotics because of UTI within two weeks of the surgery were excluded. The results of the present study can serve as appropriate evidence for the guidelines for antibiotic prophylaxis in transurethral prostate surgery, given the lack of information on the risk factors for infectious complications associated with prostate surgery in Korea.

This study had some limitations. First, the antimicrobial regimens and durations were not standardized. In line with the recent evaluation of prophylactic antibiotic use for prostate surgery, various antibiotics are being used prophylactically with varying duration depending on the hospital. Thus, these findings should be interpreted cautiously because each center has different clinical practice guidelines for antimicrobial prophylaxis in surgery. There is possible bias related to the quality control between different centers. Second, locoregional antimicrobial resistance was not considered in the selection of antibiotics. Third, heterogeneous populations and operative methods can lead to the possibility of an unknown cofounder associated with infectious complications. Finally, in the present study, the definition of postoperative infectious complications did not include asymptomatic bacteriuria. The importance of postoperative asymptomatic bacteriuria, which is observed in most patients, is unknown.

The evidence concerning perioperative infections in the urological field is still limited. Further studies to gather additional evidence will be needed to establish Korean guidelines. In addition, further studies on long-term complications in patients with postoperative UTI, such as patients with chronic prostatitis and urethral stricture, will be required. Nevertheless, to the best of the authors' knowledge, this is the first study in Korea to evaluate postoperative infectious complications after transurethral prostate surgery. With the paucity of Korean data addressing this issue, the present study will serve as a basis for future prospective research.

CONCLUSIONS

These results suggest that prolonged postoperative catheterization affects postoperative infectious complications associated with transurethral prostate surgery. Antibiotics administered for less than one day are effective as antibiotic prophylaxis for transurethral prostate surgery; nevertheless, longer antibiotic therapy is recommended for TURP. Additional research with multicentric, prospective, well-designed, randomized, controlled trials will be needed to evaluate infectious complications further after TURP and HOLEP.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTIONS

S.I.J., T.K. conception, and design; S.H.Y., S.I.J., E.C.H., T.H.K., J.D.C., K.H.Y., J.W.L., D.H.K., S.B., S.O.Y., J.C., S.K.M., and H.C. acquisition of data; E.C.H. and S.I.J. analysis and interpretation of data; S.H.Y. drafting the manuscript; S.I.J. editing the manuscript. All authors read and approved the final manuscript.

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