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Prevalence of Antibiotic-Resistant Bacteria on Rectal Swabs and Factors Affecting Resistance to Antibiotics in Patients Undergoing Prostate Biopsy

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Purpose: The prevalence of antibiotic-resistant bacteria on rectal swabs in patients undergoing transrectal ultrasound (TRUS)-guided prostate biopsy and the factors affecting resistance to antibiotics were evaluated.

Materials and Methods: Two hundred twenty-three men who underwent TRUS-guided prostate biopsy from November 2011 to December 2012 were retrospectively evaluated. Rectal swabs were cultured on MacConkey agar to identify antibiotic-resistant bacteria in rectal flora before TRUS-guided prostate biopsy. All patients were admitted and received intravenous antibiotics before prostate biopsy. Clinical variables including underlying disease, infectious complications, and antibiotics associated with resistance were evaluated. Logistic regression was used to determine the factors influencing antibiotic resistance.

Results: Of the 233 patients, 161 had positive rectal cultures. *Escherichia coli* was cultured in 130 (80.7%) and *Klebsiella pneumonia in* 16 (9.9%). The prevalence of quinolone resistance was 16.8% and the prevalence of extended-spectrum beta-lactamase (ESBL) positivity was 9.3%. A previous history of prostatitis was correlated with quinolone resistance and ESBL positivity (both p=0.001). The factors affecting quinolone resistance in the univariate analysis were a previous history of prostatitis (p=0.003) and previous exposure to antibiotics (p=0.040). Only a previous history of prostatitis was statistically significant in the multivariate analysis (p=0.014). Four patients had infectious complications.

Conclusions: The prevalence of quinolone resistance was 16.8% in rectal swabs performed before TRUS-guided prostate biopsy. A previous history of prostatitis was influential. In patients with a history of prostatitis, selection of prophylactic antibiotics before the biopsy may be reconsidered.

Keywords: *Bacteria; Biopsy; Drug resistance; Prostate; Risk factors*

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INTRODUCTION

Prostate cancer is the second most commonly diagnosed cancer in men and represents a significant health problem. Worldwide, more than 900,000 men are diagnosed with prostate cancer every year with an estimated 258,000 deaths in 2008 [1].

Transrectal ultrasound (TRUS)-guided needle biopsy of the prostate is generally accepted as the standard procedure for diagnosing prostate cancer. The risks and complications of TRUS-guided biopsy are well documented. Minor complications including hematuria or hematospermia occur in 25% to 50% of patients [2]. Major complications such as bacteremia and sepsis are much less common, in part because antibiotic prophylaxis is recommended before the procedure [2,3].

It is commonly accepted that the use of prophylactic antimicrobial agents will lower the incidence of infections after biopsy [4,5], but little consensus exists regarding the most appropriate antimicrobial regimens. Fluoroquinolones are the most commonly used prophylactic antimicrobial agents for TRUS-guided prostate biopsy because of their broad-spectrum coverage, pharmacokinetics, bioavailability, and ease of oral administration [6,7]. However, despite the use of prophylactic antibiotics, the incidence of infectious complications is from 2.1% to 3.0% [8,9]. *Escherichia coli* is the most common isolate identified in infections after TRUS-guided biopsy [10].

The percentage of fluoroquinolone-resistant *E. coli* recovered from urinary tract infections increased 4.4 folds from 2004 to 2006 and is predicted to reach 45% in the United States by 2013 [11,12]. In addition, fluoroquinolone-resistant *E. coli* in rectal flora are a risk factor of infectious complications after TRUS-guided biopsy [11,13, 14]. However, little is known concerning fluoroquinolone resistance in rectal flora and relevant risk factors in Korean patients.

The present study was undertaken to investigate the prevalence of antibiotic resistance in bacteria recovered from rectal swabs from Korean patients undergoing TRUS-guided prostate biopsy and the factors correlated with resistance.

MATERIALS AND METHODS

We retrospectively evaluated the records of all patients (n=233) who underwent prostate biopsy at our institution from November 2011 to December 2012. The indications for biopsy were elevation of prostate-specific antigen or abnormal digital rectal examination findings. We investigated age, underlying disease, prostate-specific antigen, prostate volume, kind of prophylactic antibiotics, infectious complications after biopsy, results of rectal swabs, and pathophysiologic results. Demographic data were obtained for all patients, as were histories of previous prostate biopsies within the preceding 24 months and antibiotic use within the 6 months preceding biopsy. Two weeks before the initial prostate biopsy, rectal swab samples were obtained for aerobic culture. Rectal swab samples (KOMED, Seongnam, Korea) were plated directly onto MacConkey agar (KOMED) and incubated overnight at 37°C in ambient air. All isolates were further characterized (identification and antimicrobial susceptibilities). All patients received prophylactic antibiotics; 74% received quinolone and 26% received third-generation cephalosporin provided in a 3-day regimen on the day before biopsy, the day of biopsy, and the day after biopsy. A third-generation cephalosporin was selected for patients with diabetes mellitus as an underlying disease or according to the preferences of the attending physicians. The patients were also instructed to instill a Colclean enema approximately 4 hours before the biopsy. Rectal cleansing with povidone-iodine was done before TRUS-guided prostate biopsy. All biopsies were performed by use of a LOGIQ E9 TRUS device (General Electric, Milwaukee, WI, USA). An Acecut automatic biopsy gun (CIVCO Medical Solutions, Kalona, IA, USA) with an 18-gauge needle was used to obtain 12-core biopsies by use of the same protocol. All biopsies were performed by the same physician. Statistical analyses were performed with IBM SPSS ver. 19.0 (IBM Co., Armonk, NY, USA). Differences in underlying disease between quinolone-resistant and nonresistant patients and extended-spectrum beta-lactamase (ESBL) positivity were compared by using Fisher exact test. Univariate and multivariate logistic regression was performed to determine the factors influencing quinolone resistance. Statistical significance was set at $p < 0.05$ for all analyses.

RESULTS

Among 233 patients, 161 had positive rectal swab cultures. The mean age of the patients was 67.7±8.8 years. Common underlying diseases were hypertension (n=75, 46.6%), diabetes (n=26, 16.1%), and cardiovascular accident or disease (n=11, 6.8%). The mean prostate-specific antigen concentration (logarithmically adjusted) was 0.9±0.5 ng/mL and the mean prostate volume was 35.2±22.6 mL. Six patients had previous therapeutic exposure to antibiotics owing to chronic prostatitis. Of these, five men displayed fluoroquinolone-resistant rectal flora. Twenty-four patients (14.9%) had a history of exposure to antibiotics before prostate biopsy and six patients (3.7%) had a previous prostate biopsy. Of the 161 bacterial isolates, 80.7% were *E. coli* and 9.9% were *Klebsiella pneumonia*. Of the 161 patients, 27 (16.8%) had a rectal swab culture positive for fluoroquinolone-resistant rectal flora and 15 (9.3%) had ESBL-positive rectal flora (Table 1).

There were infectious complications in four patients with fever, but no patients displayed bacteremia or sepsis. All four patients had fluoroquinolone-sensitive and ESBL-negative rectal flora. Isolated bacteria were *E. coli* (two cases), *K. pneumonia* (one case), and *Enterobacter cloacae* (one case). Three patients received prophylactic fluoroquinolone and one patient received a third-generation cephalosporin. None of the four patients had a history of prostatitis or previous prostate biopsy. We could not check the results of urine and blood culture in two patients with infectious complications because they were treated at another hospital. Another two patients were negative for urine and blood culture. A history of prostatitis was associated with quinolone resistance and ESBL positivity (p=0.001). Antibiotic exposure before prostate biopsy had borderline significance (p=0.05) (Table 2). In the univariate analysis, prior exposure to antibiotics and prostatitis history increased the risk of fluoroquinolone resistance (odds ratio [OR], 1.84; 95% confidence interval [CI], 0.65–5.18; p=0.040, and OR, 30.6; 95% CI, 3.24–289.7; p=0.003, respectively) and ESBL positivity (OR, 3.34; 95% CI, 1.03–10.84; p=0.044; and OR, 26.1; 95% CI, 4.30–159.1; p=0.001; respectively) (Table 3). In the multivariate analysis, a his-

tory of prostatitis was the only independent factor associated with increased risk of fluoroquinolone resistance (OR, 28.00; 95% CI, 1.988–394.40; p=0.014) and ESBL positivity (OR, 34.0; 95% CI, 2.43–474.5; p=0.009) (Table 4).

DISCUSSION

One of the most common risks of TRUS-guided prostate biopsy is infectious complications, most seriously sepsis. Antibiotic prophylaxis has significantly decreased the rate of infectious complications associated with prostate biopsy, and it is evident that prophylaxis is effective [5]. Fluoroquinolones have been the antibiotics of choice for prophylaxis since the 1980s, mostly because of their potent activity against a large spectrum of clinically relevant pathogens in the urogenital tract [15,16]. Kapoor et al. [5] noted that using ciprofloxacin before trans-rectal prostate biopsy significantly reduced the rates of infection compared with the placebo group. The American Urological Association best practice statement on antibacterial prophylaxis recommends the use of a fluoroquinolone as a first-line agent for the prevention of infection from transrectal prostate biopsy [7]. In addition, the European Association of Urology guideline recommends quinolones, with ciprofloxacin superior to ofloxacin [17]. However, infectious complications after prostate biopsy are increasing owing to fluoroquinolone-resistant *E. coli* [11,18], which is a risk factor for infectious complications after TRUS-guided prostate biopsy [11,13,14].

Fluoroquinolone-resistant *E. coli* in rectal flora can be a risk factor for infectious complications after TRUS-guided prostate biopsy [19]. However, the risk factors associated with fluoroquinolone resistance in rectal flora remain unclear. In Korea, few data exist concerning the prevalence of fluoroquinolone-resistant *E. coli* and ESBL positivity in rectal flora. Thus, we investigated the prevalence of antibiotic-resistant bacteria from rectal swabs performed in patients undergoing TRUS-guided prostate biopsy and the factors affecting resistance to antibiotics. The prevalences of quinolone resistance and ESBL-positive rectal flora before TRUS-guided prostate biopsy were 16.8% and 9.3%, respectively. A previous history of prostatitis was influential.

In our study, only *E. coli* was resistant to fluoroquinolone in rectal flora. In other studies, the main causative microorganisms of fluoroquinolone resistance in rectal flora were *E. coli*, *K. pneumonia*, and other gram-negative rods [20]. Other studies have reported positive rates for fluoroquinolone-resistant E. coli in the rectal flora of 12% to 22% [10,13,14]. The present 16.8% rate of prevalence of fluoroquinolone resistance (ESBL positivity was 9.3%) in our study was comparable, as was the trend toward increased

TABLE 1. Baseline characteristics of the patients and clinical parameters

Parameter	Result
No. of patients	161
Age (y)	67.7±8.8
Prostate-specific antigen[a] (ng/mL)	0.9±0.5
Prostate volume (mL)	35.2±22.6
Underlying disease	
Hypertension	75 (46.6)
Diabetes mellitus	26 (16.1)
Cardiovascular accident	11 (6.8)
Prior prostate biopsy	6 (3.7)
Antibiotic exposure before biopsy	24 (14.9)
Prostatitis history	6 (3.7)
Biopsy results	
Benign prostate hyperplasia	97 (60.2)
Prostate cancer	64 (39.8)
Culture	
Escherichia coli	130 (80.7)
Klebsiella pneumonia	16 (9.9)
Others	15 (9.4)
ESBL	
Negative	146 (90.7)
Positive	15 (9.3)
Quinolone resistance	
Sensitive	134 (83.2)
Resistant	27 (16.8)
Infectious complications	4 (2.5)

Values are presented as mean±standard deviation or number (%).
ESBL, extended-spectrum beta-lactamase.
[a]:Logarithmically adjusted.

TABLE 2. Differences between underlying disease and quinolone resistance and extended-spectrum beta lactamase (ESBL) positivity

Variable	Quinolone resistance			ESBL		
	Sensitive	Resistant	p-value[a]	Negative	Positive	p-value[a]
Hypertension	62 (82.7)	13 (17.3)	1	68 (90.7)	7 (9.3)	1
Diabetes mellitus	23 (88.5)	3 (11.5)	0.570	24 (92.3)	2 (7.7)	1
Cardiovascular accident	10 (90.9)	1 (9.1)	0.690	11 (100)	0 (0)	0.600
Antibiotics exposure before biopsy before biopsy	18 (75.0)	6 (25.0)	0.244	19 (79.2)	5 (20.8)	0.050
Prior prostate biopsy	6 (100)	0 (0)	0.591	6 (100)	0 (0)	1
Prostatitis history	1 (16.7)	5 (83.3)	0.001	2 (33.3)	4 (66.7)	0.001

Values are presented as number (%).
[a]:Fisher exact test.

TABLE 3. Univariate logistic regression analysis of factors influencing quinolone resistance and extended-spectrum beta lactamase (ESBL) positivity

Variable	OR (95% CI)	p-value
Quinolone resistance		
Age (≥69 y)	0.95 (0.39–2.35)	0.958
Underlying disease	0.85 (0.34–2.09)	0.853
Hypertension	0.47 (0.10–2.18)	0.342
Diabetes mellitus	1.07 (0.43–2.64)	0.875
Prostatitis history	30.6 (3.24–289.7)	0.003
Prior prostate biopsy	-	0.999
Antibiotic exposure before biopsy	1.84 (0.65–5.18)	0.040
ESBL positivity		
Age (≥69 y)	1.50 (0.50–4.42)	0.463
Underlying disease	1.38 (0.47–4.02)	0.549
Hypertension	0.99 (0.34–2.89)	0.995
Diabetes mellitus	1.27 (0.27–6.03)	0.756
Prostatitis history	26.1 (4.30–159.1)	0.001
Prior prostate biopsy	-	0.999
Antibiotic exposure before biopsy	3.34 (1.03–10.84)	0.044

OR, odds ratio; CI, confidence interval.

TABLE 4. Multivariate logistic regression analysis of factors influencing quinolone resistance and extended-spectrum beta lactamase (ESBL) positivity

Variable	OR (95% CI)	p-value
Quinolone resistance		
Antibiotic exposure before biopsy	1.10 (0.23–5.32)	0.899
Prostatitis history	28.0 (1.98–394.4)	0.014
ESBL positivity		
Antibiotic exposure before biopsy	1.33 (0.16–11.1)	0.787
Prostatitis history	34.0 (2.43–474.5)	0.009

OR, odds ratio; CI, confidence interval.

rates.

In a prospective study, 31% of patients who had fluoroquinolone-resistant *E. coli* in stool cultures developed acute bacterial prostatitis after biopsy [13]. In contrast, none of the 87 patients who had normal *E. coli* had acute bacterial prostatitis [13]. Compared with these prior results, in the present study, none of the patients who had fluoroquinolone-resistant *E. coli* developed acute bacterial prostatitis after prostate biopsy. However, four patients who had fluoroquinolone-sensitive rectal flora had acute bacterial prostatitis. A possible reason for this discrepancy may be that all patients in the present study had undergone rectal cleansing with povidone-iodine prior to TRUS-guided prostate biopsy. This rectal cleansing approach is safe and is associated with a 42% relative risk reduction of infectious complications after prostate biopsy [19].

Infectious complications after prostate biopsy can be increased owing to fluoroquinolone-resistant *E. coli* in rectal flora [19], which can be a risk factor for infectious complications after TRUS-guided prostate biopsy. In our study, a history of prostatitis was associated with antibiotic resistance of rectal flora. Patients with chronic prostatitis are usually treated with empirical fluoroquinolone antibiotics, which may increase the antibiotic resistance of rectal flora. In a prior study, 29 patients with acute prostatitis were treated with ciprofloxacin for one month; half of the patients were transiently colonized with new fluoroquinolone-resistant strains of *E. coli* [21].

In a prospective study, a history of fluoroquinolone use was reported as the only statistically significant risk factor for an increase in fluoroquinolone-resistant *E. coli* in rectal culture [13]. Fluoroquinolone use in the previous 6 months before prostate biopsy is a common risk factor for fluoroquinolone-resistant *E. coli* in rectal flora [22]. In our study, histories of previous antibiotic exposure and prostatitis were risk factors for fluoroquinolone-resistant rectal flora. Therefore, it is assumed that fluoroquinolone exposure as the result of chronic prostatitis before TRUS-guided prostate biopsy might be a risk factor for increasing fluoroquinolone resistance in rectal flora.

One of the mechanisms of fluoroquinolone resistance is the activity of ESBLs that enzymatically mediate resistance to extended-spectrum third-generation cephalosporins and monobactams, while not affecting carbapenems [9].

Although the prevalence of ESBL *E. coli* varies globally, the presence of such strains is a risk factor for infectious complications after prostate biopsy. Shin et al. [23] reported that 11 of 2,348 patients (0.4%) developed infectious complications after prostate biopsy. In their report, *E. coli* was the pathogen responsible for postbiopsy infections in all patients with positive blood cultures, which confirmed ciprofloxacin-resistant *E. coli*, with one isolate producing ESBL. Duplessis et al. [10] reported that of 235 patients who had rectal cultures before TRUS-guided prostate biopsy, 3 (1.3%) harbored ESBL-producing isolates. On the other hand, Siriboon et al. [24] reported that 37 of 144 patients (25.7%) yielded ESBL-producing isolates. In addition, several case-control studies have shown that previous use of third-generation cephalosporins and the previous use of fluoroquinolones remain independent risk factors for infections caused by ESBL-producing organisms [9]. Kanafani et al. [25] reported that the most notable risk factor for acquiring infections with ESBL-producing organisms was antibiotic consumption within 30 days of infection. Lautenbach et al. [26] also showed that the previous use of fluoroquinolone increases the risk of ESBL-producing *E. coli* and *K. pneumonia* infections. Similar to those results, histories of prostatitis and exposure to antibiotics before prostate biopsy were associated with ESBL positivity in the present study. However, there were no infectious complications among the 15 patients (9.3%) who were positive for ESBL bacteria. This is probably because of a prophylactic effect of quinolones to ESBL-positive organisms without in vitro resistance [27]. The presence of an ESBL-producing organism in rectal flora can also increase infectious complication. Therefore, there is a need for continuous monitoring of the distribution and antibiotic resistance patterns of pathogens.

Several recent studies have suggested that rectal swab cultures before biopsy may be useful in the selection of appropriate antimicrobial agents for prophylaxis and decreased overall cost of care. Duplessis et al. [10] showed that rectal cultures obtained before TRUS biopsy with the use of selective media to identify fluoroquinolone-resistant Enterobacteriaceae facilitate targeted antibiotic prophylaxis and appear to be highly efficacious in reducing infectious complications. Taylor et al. [28] reported no infectious complications in 112 men who received targeted antimicrobial prophylaxis, whereas there were 9 cases (including one of sepsis) among 345 patients receiving empirical therapy (p=0.12). More comparative studies are needed to compare the infectious complication rate and overall cost of care after TRUS-guided biopsy between targeted antimicrobial prophylaxis and traditional empirical fluoroquinolone antimicrobial prophylaxis. In the wake of the increased fluoroquinolone resistance of *E. coli* strains, several interventional studies have compared different antibiotic prophylactic regimens for TRUS prostate biopsy [29, 30]. In those studies, the authors replaced an oral fluoroquinolone with another antibiotic, either piperacillin-tazobactam or ceftriaxone, or added another antibiotic to an oral fluoroquinolone (cefoxitin, gentamicin, or amikacin). More studies are needed to enforce target antibiotic prophylactics and choice of prophylactic antibiotics.

In our study, there was some discrepancy between rectal flora on the rectal swabs and infectious complications. There were some infectious complications in cases without antibiotic-resistant rectal flora and no infectious complications in cases with antibiotic-resistant rectal flora. Thus, we cannot recommend routine rectal swabs before prostate biopsy. However, we can consider the selective application of rectal swabs before prostate biopsy in patients with risk factors such as a history of prostatitis. Such selective application will allow for appropriate selection of prophylactic antibiotics and immediate treatment of infectious complications according to the results of the rectal swab.

Our study had some potential limitations. First, the number of patients was relatively small, because there were many cases with no bacterial growth on the rectal swab. Second, histories of antibiotic use and prostatitis were based on patient recall. It is possible that some patients might have forgotten these past events. Therefore, our study might have recall bias and we may have underestimated the total number of patients with a history of antibiotic use and prostatitis.

CONCLUSIONS

The prevalence of fluoroquinolone resistance was 16.8% in rectal swabs taken before TRUS-guided prostate biopsy. A previous history of prostatitis was influential. Therefore, in patients with a history of prostatitis, selection of prophylactic antibiotics before the biopsy may be reconsidered. Further prospective investigations are needed to clarify the risk factors associated with fluoroquinolone resistance. More comparative studies are needed to better understand the infectious complication rate and the overall cost of care after TRUS-guided biopsy through targeted antimicrobial prophylaxis or extended prophylactic antibiotics.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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