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The Real Practice of Antibiotic Prophylaxis for Prostate Biopsy in Korea Where the Prevalence of Quinolone-Resistant *Escherichia coli* Is High

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Purpose: Transrectal ultrasonography-guided prostate biopsy (TRUS-Bx) is an essential procedure for diagnosing prostate cancer. The American Urological Association (AUA) Guideline recommends fluoroquinolone alone for 1 day during TRUS-Bx. However, this recommendation may not be appropriate in regions where the prevalence of quinolone-resistant *Escherichia coli* is high. We investigated the real practice of antibiotic prophylaxis for TRUS-Bx in Korea.

Materials and Methods: A total of 77 hospitals performing TRUS-Bx were identified and an e-mail was sent to the Urology Department of those hospitals. The questions in the e-mail included the choice of antibiotics before and after the procedure and the duration of antibiotic therapy after TRUS-Bx.

Results: A total of 54 hospitals (70.0%) responded to the e-mail. Before TRUS-Bx, all hospitals administered intravenous antibiotic prophylaxis. The percentage of hospitals that used quinolone, cephalosporin, and aminoglycoside alone was 48.1%, 20.4%, and 9.3%, respectively. The percentage of hospitals that used two or more antibiotics was 22.2%. After biopsy, all 54 hospitals prescribed oral antibiotics. The percentage of hospitals that prescribed quinolone alone, cephalosporin alone, or a combination of two or more antibiotics was 77.8%, 20.4%, and 1.8%, respectively. The duration of antibiotic use was more than 3 days in most hospitals (79.6%). Only four hospitals (7.4%) followed the AUA recommendation of a 1-day regimen.

Conclusions: The AUA recommendation was not followed by most hospitals in Korea. This clinical behavior might reflect the high quinolone resistance rate in Korea, and further studies on the most efficient prophylactic antibiotics after TRUS-Bx in Korea are warranted.

Keywords: *Antibiotic prophylaxis; Biopsy; Guideline*

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INTRODUCTION

Prostate cancer is the most prevalent cancer and the third most common cause of mortality in men in Western countries [1-4]. Transrectal ultrasonography-guided prostate biopsy (TRUS-Bx) is an essential procedure for diagnosing prostate cancer but may cause variable complications, including pain, hematuria, hemospermia, urethral injury, and urinary tract infection [5-7].

Among the complications, infective complications are clinically important because these can cause prostatitis or urosepsis, which are sometimes fatal to patients. The incidence rate of infective complications after TRUS-Bx was reported to range from 0.1% to 7% and has increased during

the past 10 years [8].

Antibiotic prophylaxis has been recommended to prevent infective complications [9]. For example, the American Urological Association (AUA) Guideline recommends antibiotic prophylaxis with fluoroquinolone for less than 24 hours as the first-line therapy and aminoglycoside combined with metronidazole or clindamycin for less than 24 hours as the second-line therapy [10]. The European Association of Urology (EAU) Guideline also recommends oral or intravenous antibiotic prophylaxis before biopsy, and quinolone is recommended as the drug of choice [11]. However, these recommendations would not be appropriate in a region where the prevalence of quinolone-resistant *Escherichia coli* is high. The recent increase in infective complications is possibly due to an increase in quinolone-resistant *E. coli* prevalence in the community.

Because overuse of antibiotics has not been strictly controlled in Korea, high resistance rates to various antibiotics have been reported [12]. A recent epidemiology study reported that the resistance rate to ciprofloxacin was over 24% in cystitis patients [12]. For this reason, Korean urologists hardly follow the AUA or EAU Guideline and instead use various combinations of antibiotics to prevent infective complications.

Considering the increase in quinolone-resistant pathogens worldwide, it is clinically significant to know the pattern of antibiotic prophylaxis in Korea, where the prevalence of quinolone-resistant *E. coli* is already high. Such data would give insight into the future of antibiotic prophylaxis in other countries where the quinolone resistance rate is still low but increasing. Therefore, we investigated the real practice of antibiotic prophylaxis to prevent infective complications of TRUS-Bx in Korea.

MATERIALS AND METHODS

This cross-sectional observational study was performed in June 2013. We sent an e-mail to the Urology Departments of 77 hospitals in Korea. These hospitals were secondary or tertiary referral hospitals and covered most prostate biopsy cases in Korea.

The contents of the e-mail included questions about the real practice of TRUS-Bx as follows: (1) Which department has performed TRUS-Bx? (Department of Radiology or Urology), (2) How has biopsy been performed? (inpatient or outpatient setting), (3) Which type of enema has been performed? (4) Has betadine enema been performed? (5) Which kinds of antibiotics have been used prior to biopsy? (6) Which kinds of antibiotics have been used after the procedure? (7) How long did the patients take the medicine after prostate biopsy?

We analyzed the contents of the returned e-mails. According to the responses received, the prophylactic drugs in practice before and after TRUS-Bx were classified according to the type of antibiotic (quinolone, cephalosporin, aminoglycoside, and metronidazole), and we investigated the prevalence of each antibiotic regimen. In addition, duration of postbiopsy medication and the identity of the antibiotics used before and after biopsy were evaluated. All statistical analyses were performed by using SPSS ver. 17.0 (SPSS Inc., Chicago, IL, USA), and the prevalence was presented as the number of hospitals with percentages.

RESULTS

A total of 54 hospitals replied to our e-mail; the response rate was 70.1%. Two thirds of the responding hospitals indicated that the department of urology performed the prostate biopsy procedures (37 hospitals, 68.5%), and patients were admitted for TRUS-Bx in 33 hospitals (61.1%; Fig. 1). For rectal preparation before TRUS-Bx, various types of enema or suppositories were used in 48 hospitals (88.8%), and disinfection with povidone-iodine was used in 29 hospitals (53.7%; Fig. 2).

1. Antibiotics used before prostate biopsy

Various types of prophylactic antibiotics prior to prostate biopsy were used in each hospital (Table 1). A quinolone alone regimen was the most common (26 hospitals, 48.1%), followed by cephalosporin alone (11 hospitals, 20.4%), and aminoglycoside alone (5 hospitals, 9.3%). A combination of two or more antibiotics was used in 12 hospitals (22.2%).

2. Antibiotics used after prostate biopsy

The doctors of all hospitals that participated in this study prescribed oral antibiotics after TRUS-Bx (Table 2). The

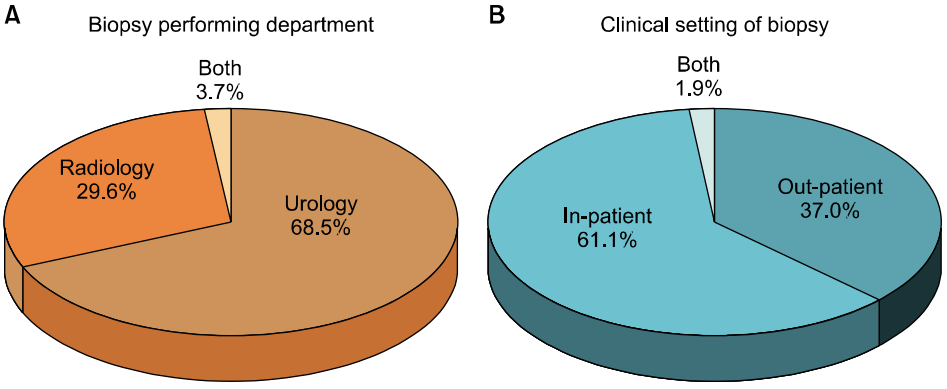

FIG. 1. The proportion of departments performing prostate biopsy (A), and the proportion of clinical settings performing prostate biopsy (B).

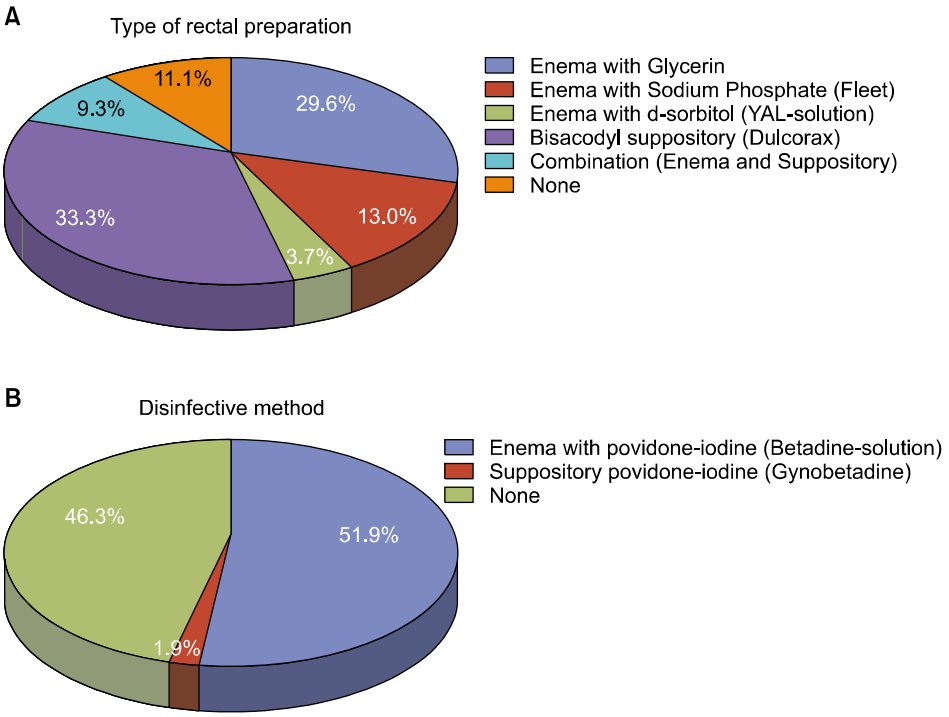

FIG. 2. Frequency of rectal preparation type (A) and disinfective method (B) used in hospitals performing biopsy.

TABLE 1. Types of prophylactic antibiotics used in clinical practice before prostate biopsy

Type of antibiotics prior to biopsy	No. of hospitals (%), (n=54)
Quinolone alone	26 (48.1)
Cephalosporin alone	11 (20.4)
Aminoglycoside alone	5 (9.3)
Quinolone+cephalosporin	3 (5.6)
Quinolone+aminoglycoside	4 (7.4)
Cephalosporin+aminoglycoside	3 (5.6)
Quinolone+metronidazole	1 (1.9)
Quinolone+aminoglycoside+metronidazole	1 (1.9)

TABLE 2. Type and duration of antibiotic treatment after prostate biopsy

Type and duration	No. of hospitals (%), (n=54)
Type of antibiotic	
Quinolone alone	42 (77.8)
Cephalosporin alone	11 (20.4)
Quinolone+cephalosporin	1 (1.8)
Duration of antibiotic treatment (d)	
1	4 (7.4)
2–3	7 (13.0)
4–6	21 (38.9)
7	22 (40.7)

most common type of postbiopsy medication was quinolone alone (42 hospitals, 77.8%). A cephalosporin alone regimen was used in 11 hospitals (20.4%), and only 1 hospital answered that oral quinolone and cephalosporin were routinely prescribed simultaneously. The treatment duration of postbiopsy antibiotics also varied among the hospitals (Table 2). Only 4 hospitals (7.4%) chose a 1-day regimen. Routine protocols of most hospital (43 hospitals, 79.6%) were treatment for 4 or more days with oral antibiotics after TRUS-Bx.

3. Overall type of antibiotics used around prostate biopsy

Among the 26 hospitals that chose quinolone alone before biopsy, 1 hospital (3.8%) changed the type of antibiotic to cephalosporin after biopsy. The other hospitals maintained an identical type of antibiotic during the post-biopsy period. Among the 11 hospitals using cephalosporin alone prior to TRUS-Bx, 3 hospitals (27.3%) cared for postbiopsy patients with oral quinolone. In contrast, the other 8 hospitals adhered to the same type of antibiotic used for the initial prophylaxis. Postbiopsy quinolone was used in all 3 hospitals that administrated aminoglycoside alone before TRUS-Bx. Overall, the proportion of hospitals using prophylaxis with a single type of antimicrobial agent before and after prostate biopsy was 61.1% (33 hospitals). On the other hand, various combinations of drugs were used in 21 hospitals (38.9%).

DISCUSSION

The incidence of acute prostatitis related to TRUS-Bx has been reported to range from 0.1% to 7% [13,14]. In Korea, the incidence of biopsy-related prostatitis was reported to

range from 1.4% to 1.9% [15,16]. Various studies have been undertaken to reduce the incidence of acute prostatitis after TRUS-Bx. One study reported that rectal preparation prior to biopsy with bisacodyl decreased biopsy-induced infectious complications significantly compared with a non–rectal-preparation group [17]. An intrarectal mixture of povidone-iodine and lidocaine gel also significantly decreased infectious complications in another study [18]. A povidone-iodine suppository has been shown to decrease the bacterial colony count [19]. Recently, Issa et al. [20] described that formalin disinfection of a biopsy needle after each core reduces the incidence of urinary tract infection and sepsis.

Among these prophylactic methods, antibiotic prophylaxis has been the standard method of preventing infectious complications. In particular, fluoroquinolones have traditionally been used as the primary prophylactic agent owing to their excellent prostatic penetration [9]. In the past, these agents also provided good coverage against the key pathogens implicated in infections after prostate biopsy [13].

However, fluoroquinolone resistance has dramatically increased recently. Lee et al. [21] analyzed a total of 1,994 strains from patients with community-acquired urinary tract infection from 34 hospitals in Korea from January 2008 to June 2009. In that study, the resistance rate to ciprofloxacin was reported to range from 20% to 38% in community-acquired uncomplicated cystitis and showed a tendency to increase [21]. The overall resistance rate to ciprofloxacin rapidly increased from 15.2% in 2002 to 24.8% in 2009. Furthermore, ciprofloxacin-resistant *E. coli* has been shown to be more prevalent in complicated urinary tract infection (40.9%) than in uncomplicated urinary tract infection (24.8%) in Korea [22].

Recent studies have reported that the prevalence of quinolone-resistant *E. coli* has also increased in Western countries [23,24]. However, the rate of quinolone resistance is lower than in Korea [16,22]. In the United States, fluoroquinolone-resistant bacteria were identified in 22% of samples from rectal swab cultures before TRUS-Bx [23]. In that study, Asian men had a higher risk of resistant rectal flora colonization (odds ratio, 2.8). In American men who developed acute prostatitis after TRUS-Bx, the fluoroquinolone-resistant rate was reported to be 57.1% [24]. In Korea, a study reported that 2.0% of patients who underwent TRUS-Bx developed acute prostatitis, and nearly all culture-positive specimens (96.3%) were identified as ciprofloxacin-resistant pathogens [16]. In that study, most quinolone-resistant pathogens were sensitive to cephalosporin and aminoglycoside. Therefore, several studies have evaluated the effect of cephalosporin combined with quinolone on the prevention of infectious complications after TRUS-Bx [25]. Some reports have suggested that adding aminoglycoside is helpful for preventing infectious complications in areas with a high antibiotic resistance rate [26].

The AUA Guideline does not recommend using multiple antibiotics during prostate biopsy [10]. In our study, 21 hospitals (38.9%) used two or more antimicrobial agents during TRUS-Bx. Cephalosporin alone or combined with other antibiotics was used in 19 hospitals (35.2%), and aminoglycoside alone or combined with other antibiotics was used in 13 hospitals (24.1%). Only 25 hospitals (46.2%) followed the AUA guideline recommending fluoroquinolone alone before and after TRUS-Bx. No hospitals used alternative antimicrobials (aminoglycoside with metronidazole or clindamycin). Regarding the duration of antibiotic treatment, fewer hospitals adhered to AUA Guidelines. Prophylactic antibiotic use of less than 24 hours was used by only 7.4% of the hospitals in our study, although several studies have suggested that there are no significant benefits of long-term use [9,27,28]. A recent Cochrane review revealed that there was no clinically nor statistically significant difference between a short course or a single-dose regimen compared with a longer course [29]. Our study revealed that a quinolone only regimen was the single most common method for prophylaxis, but less than half of hospitals used a quinolone only regimen for prophylaxis. Moreover, about 80% hospitals had used antibiotics for more than 3 days. These results showed that most hospitals did not follow the AUA or EAU Guidelines for various reasons.

This study had several limitations. First, we could not evaluate the incidence of infectious complications nor the changes in complications after modifying the antibiotic regimen at each hospital because this study was a cross-sectional observational study. In addition, we could not include the practice pattern of nonresponding hospitals. Furthermore, we could not assess why the current practice was selected in each hospital. Because there are no randomized controlled trials comparing the effectiveness of antibiotics for TRUS-Bx in Korean populations, and because current recommendations for antibiotic prophylaxis for TRUS-Bx are derived from studies performed in Western countries, we can assume that the current prophylactic antibiotic regimens are based on clinical experience. Therefore, the results of this study do not mean that other antibiotic regimens are more effective for preventing acute prostatitis after TRUS-Bx than the quinolone-alone regimen. Nonetheless, this is still the first study that has reported the practical use of antibiotics during TRUS-Bx. As such, the results of this study could be helpful for establishing a health policy in countries with increasing antibiotic resistance.

CONCLUSIONS

The AUA recommendation was not followed by most hospitals and a combination regimen was used by nearly half of the responding hospitals in Korea. This clinical practice pattern might be a result of the struggle to reduce infective complications after TRUS-Bx in a country where the quinolone resistance rate is high. To justify this empirical use of antibiotics, further studies evaluating the most efficient prophylactic antibiotic regimen are warranted.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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EDITORIAL COMMENT

Although transrectal prostate biopsy is an essential procedure for diagnosing prostate cancer, it leads to acute prostatitis in certain patients. In addition, if not treated appropriately and immediately, acute prostatitis can rapidly lead to septic conditions and patient death. To prevent this serious complication, antibiotic prophylaxis is generally recommended worldwide [1]. Two guidelines, those of the American Urological Association (AUA) and the European Association of Urology (EAU), can serve as cornerstones for the establishment of national guidelines [2].

The authors stressed that a guideline must be modified or adjusted to a region's antibiotic resistance pattern [3].

I completely agree with the authors' opinion. But we may become entrapped in preoccupation with setting the guideline for antibiotic prophylaxis in Korea, with initially high overuse of antibiotics, and consequently a high antibiotic resistance rate, and finally strong antibiotic prophylaxis for biopsy.

It is generally accepted that antibiotic-resistant pathogens have been detected at a high rate in the Asia-Pacific region in recent years. Moreover, some Asian countries do not currently consider fluoroquinolones as a first-line treatment for recurrent cystitis [4,5]. I agree with the above points: (1) The antibiotic resistance rate is high in patients with urinary tract infection in Asian countries; (2) *Escherichia coli* in urine cannot easily be eradicated with fluoroquinolones in certain Asian countries; (3) Women who have recurrent cystitis attacks or who have undergone previous antibiotic treatment may reveal drug resistance patterns in Korea. However, biopsy-related acute prostatitis may be directly related to antibiotic-resistant rectal flora, instead of the drug-resistant pathogens in urine. Furthermore, all patients with acute prostatitis are male, not female as in urinary tract infection.

Is there any strong evidence for the correlation between the high antibiotic resistance rate in urinary pathogens and the high rate of antibiotic-resistant pathogens in rectal flora or the high incidence of acute prostatitis? Even though the characterization of patients with biopsy-related acute prostatitis is very important, it is also imperative to study antibiotic resistance rates in rectal flora in the normal population in Korea. With these basic data, we can form an ideal guideline for antibiotic prophylaxis before transrectal prostate biopsy.

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