Microbiological Characteristics of Acute Prostatitis After Transrectal Prostate Biopsy

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Purpose: We aimed to identify microbiological characteristics in patients with acute prostatitis after transrectal prostate biopsy to provide guidance in the review of prevention and treatment protocols.

Materials and Methods: A retrospective analysis of medical records was performed in 1,814 cases who underwent prostate biopsy at Seoul St. Mary’s Hospital and St. Vincent’s Hospital over a 5 year period from 2006 to 2011. Cases in which acute prostatitis occurred within 7 days after the biopsy were investigated. Before starting treatment with antibiotics, sample collections were done for culture of urine and blood. Culture and drug susceptibility was identified by use of a method established by the Clinical and Laboratory Standards Institute.

Results: A total of 1,814 biopsy procedures were performed in 1,541 patients. For 1,246 patients, the procedure was the first biopsy, whereas for 295 patients it was a repeat biopsy. Twenty-one patients (1.36%) were identified as having acute bacterial prostatitis after the biopsy. Fifteen patients (1.2%) had acute prostatitis after the first biopsy, and 6 patients (2.03%) experienced acute prostatitis after a repeat biopsy. Even though the incidence of acute bacterial prostatitis was higher after repeat biopsy than that after the first biopsy, there was no statistically significant intergroup difference in terms of incidence ($\chi^2=1.223, p=0.269$). When the collected urine and blood samples were cultured, *Escherichia coli* was found in samples from 15 patients (71.4%), *Klebsiella pneumoniae* in 3 patients (14.3%), *Enterobacter intermedius* in 1 patient (4.8%), *E. aerogenes* in 1 patient (4.8%), and *Pseudomonas aeruginosa* in 1 patient (4.8%). A fluoroquinolone-resistant strain was confirmed in 5 cases (23.8%) in total. Three cases of *E. coli* and 1 case of *Klebsiella* had extended-spectrum β-lactamase activity.

Conclusions: Empirical treatment of acute prostatitis should be done with consideration of geographical prevalence and drug resistance. This study will provide meaningful information for the management of acute prostatitis after transrectal prostate biopsy.

Keywords: Acute diseases; Beta-lactamases; Biopsy; Fluoroquinolone; Prostate

INTRODUCTION

Transrectal ultrasound (TRUS)-guided needle biopsy is the standard diagnostic method for diagnosing prostate cancer. The risks and complications of TRUS-guided needle biopsy are widely known; these are usually minor problems such as hematuria or hematospermia, but complications such as urinary tract infection and sepsis often have very serious consequences. Bacterial sepsis is the most serious complication. The postbiopsy incidence of bacteremia is in the range of 16% to 73%, whereas the incidence of bacteriuria is in the range of 35% to 44% [1-3]. In addition, fatal...
septic shock is sometimes induced after prostate biopsy [4,5]. The most commonly identified bacteria in urine culture and blood culture is *Escherichia coli* [1,2]. Administration of prophylactic antibiotics before biopsy has been widely used as a way to prevent serious infection-related complications, and a recent study showed that fluoroquinolone is the most effective treatment [6-8]. However, in some cases, fluoroquinolone-resistant infection has been reported because of the increase of bacterial strains resistant to the broad-spectrum antibiotic and, especially in recent years, the emergence of resistant strains that demonstrate extended-spectrum β-lactamase (ESBL) activity. In the present study, we aimed to identify microbiological characteristics in patients with acute prostatitis incurred after transrectal prostate biopsy to provide guidance in the review of prevention and treatment protocols.

**MATERIALS AND METHODS**

A retrospective analysis of medical records was performed in 1,814 cases (Seoul St. Mary’s Hospital, 935 cases; St. Vincent’s Hospital, 879 patients) who underwent prostate biopsy over a 5-year period from 2006 to 2011. Indications for prostate biopsy were an elevation of prostate-specific antigen or palpable nodules in the prostate noted during digital rectal examination. All prostate biopsy procedures were conducted transrectally as 10-core biopsies by use of an automatic biopsy gun with an 18-gauge needle. For prophylactic antibiotics, a single injection of Flomoxef (Flomox) was orally administered three times daily for 3 days. Cases in which acute prostatitis occurred within 7 days after the biopsy were admitted to the hospital and administered intravenous antibiotics. According to the culture identification results, ceftriaxone was used in 8 patients, fluoroquinolone in 4 patients, amikacin in 5 patients, and piperacillin/tazobactam in 4 patients. No cases resulted in septic shock or death.

**RESULTS**

From January 2006 to December 2011, 1,814 biopsy procedures were performed in 1,541 patients. For 1,246 patients, the procedure was the first biopsy, whereas for 295 patients it was a repeat biopsy. Patient demographics and bacteriologic findings are described in Table 1 and Table 2, respectively.

Twenty-one patients (1.36%) were identified as not having any other prebiopsy urinary tract infection or symptoms of acute prostatitis but as having acute bacterial prostatitis after the biopsy. Of these patients, 15 patients (1.2%) developed acute prostatitis after the first biopsy and 6 patients (2.03%) developed it after a repeat biopsy. Among the patients who were diagnosed with acute bacterial prostatitis after a repeat biopsy, none had experienced the same problem at a previous biopsy. Even though the incidence of acute bacterial prostatitis was higher after a repeat biopsy than after the first biopsy, there was no statistically significant intergroup difference in incidence ($\chi^2=1.223$, p=0.269).

The median age of the patients within the category was 63.7 years (range, 52 to 77 years). Patients had shown symptoms from 2 days after biopsy on average. All patients had a high fever ($\geq38^\circ C$), and 15 patients (71.4%) showed leukocytosis (white blood cell $>10,000$ cells/mL). All patients were admitted to the hospital and administered intravenous antibiotics. According to the culture identification results, ceftriaxone was used in 8 patients, fluoroquinolone in 4 patients, amikacin in 5 patients, and piperacillin/tazobactam in 4 patients. No cases resulted in septic shock or death.

All cases showed positive results for urine culture, whereas 42.8% (921) of patients showed positive results for blood culture. When the collected urine and blood samples were cultured, *E. coli* was found in samples from 15 patients (71.4%), *Klebsiella pneumoniae* in 3 patients (14.3%), *Enterobacter intermedius* in 1 patient (4.8%),...
| Biopsy no. | Culture | Bacteria | ESBL | Susceptibility |
|------------|---------|----------|------|----------------|
|            |         |          |      | AMK AUG AMPC AZT CFPM CTX CFXT CEZ GM TOBV IPM LVFX TAZC TMP/SMX |
| First      | + +     | *Escherichia coli* | - | S S S S S S S S S S S S S |      |
| First      | + -     | *Escherichia coli* | - | S S S S S S S S S S S | S |      |
| First      | + +     | *Klebsiella pneumoniae* | - | S - R S S S S S S S S - - |      |
| First      | + -     | *Enterobacter intermedius* | - | S - R S S S S S S R S S S S |      |
| First      | + +     | *Escherichia coli* | - | S - R S S S S S S S S S | S |      |
| First      | + +     | *Escherichia coli* | + | S S R R R R R R S S S S R |      |
| First      | + -     | *Enterobacter aerogenes* | - | S R R S S S S R R S S S S |      |
| First      | + +     | *Escherichia coli* | - | S - R S S S S I S S S S S | S |      |
| First      | + +     | *Escherichia coli* | - | S - R S S S S S S S S S | S |      |
| First      | + -     | *Klebsiella pneumoniae* | + | S S R R R R R R S S S S R |      |
| First      | + +     | *Escherichia coli* | - | S - R S S S S S S S S S | S |      |
| First      | + -     | *Escherichia coli* | - | S S R R S S S S R S S S | S |      |
| First      | + -     | *Pseudomonas aeruginosa* | - | S - - S S I - - S S S S R |      |
| First      | + +     | *Escherichia coli* | - | S I R S S S S S I S S S S S | R |      |
| Second     | + -     | *Escherichia coli* | + | S S R R R R R R S S S S | R |      |
| Second     | + +     | *Klebsiella pneumoniae* | - | S S R R S S S S S S S S S | S |      |
| Second     | + -     | *Escherichia coli* | + | S S R R R R R R S S S S R | S |      |
| Second     | + +     | *Escherichia coli* | - | S I R S S S S S S S S S | S |      |
| Third      | + +     | *Escherichia coli* | - | S S S S S S S S S S S | S |      |

ESBL, extended-spectrum β-lactamase; AMK, amikacin; AUG, amoxicillin-clavulanic acid; AMPC, ampicillin; AZT, aztreonam; CFPM, cefepime; CTX, cefotaxime; CFXT, ceftoxitin; CEZ, cefazolin; GM, gentamycin; TOBV, tobramycin; IPM, imipenem; LVFX, levofloxacin; TAZC, piperacillin/tazobactam; TMP/SMX, trimethoprim/sulfamethoxazole; S, sensitive; R, resistant; I, intermediate.
TABLE 3. Susceptibility of isolated Escherichia coli (n=15)

| Antibiotic                           | Susceptibility (%) |
|--------------------------------------|--------------------|
| Amikacin                             | 100.0              |
| Amoxicillin-clavulanic acid           | 80.0               |
| Ampicillin                           | 20.0               |
| Aztreonam                            | 80.0               |
| Cefotaxime                           | 80.0               |
| Cefoxitin                            | 100.0              |
| Cefazolin                            | 46.7               |
| Gentamycin                           | 86.7               |
| Tobramycin                           | 92.9               |
| Imipenem                             | 100.0              |
| Levofloxacin                         | 73.3               |
| Piperacillin/tazobactam              | 100.0              |
| Trimethoprim/sulfamethoxazole        | 60.0               |

Enterobacter aerogenes in 1 patient (4.8%), and Pseudomonas aeruginosa in 1 patient (4.8%). A fluoroquinolone-resistant strain was confirmed from 5 cases (23.8%) in total, and 3 cases of E. coli and 1 case of Klebsiella were ESBL(+). The antibiotic susceptibility of E. coli is described separately in Table 3.

DISCUSSION

Administration of prophylactic antibiotics before transrectal prostate biopsy significantly reduces the likelihood of urinary tract infection. However, despite the use of prophylactic antibiotics, fever of 38 degrees or more occurs in 1% to 5% of cases [6,9-12]. Many drugs have been proposed for prophylactic use, and Taylor and Bingham [8] summarized these to 13 different antibiotics. In general, because fluoroquinolone has higher bioavailability in the prostate, this drug family is the most commonly used in transrectal biopsy for the purpose of prophylactic antibiotics [6,8, 11-13]. However, some studies have reported patients developing fluoroquinolone-resistant infections after prostate biopsy. Tal et al. [14] also reported that fluoroquinolone-resistant E. coli was the most critical cause of urinary tract infection incurred after transrectal prostate biopsy, and Otrock et al. [15] reported that 50% of patients were admitted to the hospital and treated for urinary tract infection owing to fluoroquinolone-resistant E. coli incurred after transrectal prostate biopsy.

Feliciano et al. [16] reported that in postbiopsy acute prostatitis, the incidence of fluoroquinolone-resistant E. coli was 86% and that fluoroquinolone resistance appeared to increase as shown by a survey of over 1,273 patients for 2 years. In other research, all isolated E. coli was resistant to levofloxacin, although the relevant cases were small in number [17]. In Korea, the rate of fluoroquinolone-resistant pathogens in postbiopsy acute prostatitis was reported to be 96.3% [18].

Almost all of the above-mentioned studies debated the use of fluoroquinolone as a prophylactic antibiotic in transrectal prostate biopsy. As a necessity, the microbiological cause of post biopsy acute prostatitis is subject to show a high rate of resistance to fluoroquinolone.

The results of the present study on microbiological characteristics after transrectal prostate biopsy are similar to the results of previously reported studies in terms of the overall infection rate and the variety of isolated pathogens [14-17,19]. Regarding antibiotic resistance, however, there were considerable differences between our results and those of previous studies. In this study, fluoroquinolone resistance was expressed in 23.8% (5/21) of strains, which differs from the previous study of postbiopsy acute prostatitis but is similar to another E. coli-related general urinary tract infection study that reported that the fluoroquinolone resistance rate was approximately 20% to 30%. This fact is broadly similar to other Korean data concerning acute prostatitis contingent upon urological manipulation in which a resistance rate of 28.6% of E. coli to ciprofloxacin was reported [20]. In the hospitals where this study was conducted, fluoroquinolone was not frequently used as a prophylactic antibiotic after 2006; flomoxef is used at present. This may be one of the reasons the postbiopsy acute prostate did not show a high fluoroquinolone resistance rate, unlike other prostate studies but similar to other general urinary tract infection studies.

The wide use of these medications is considered to be the reason for the increase in fluoroquinolone resistance in the first place. In addition, some studies reported that an increased expression of quinolone-resistant E. coli was found in the stool of patients who were treated with fluoroquinolone prophylaxis [21]. Shigehara et al. [17] suggested that the previous use of levofloxacin triggered bacterial selection inside the rectum, which led to the emergence of levofloxacin-resistant E. coli. This phenomenon has something in common with the study of Ha et al. [22], who reported that the effectiveness of ciprofloxacin was low in patients with a prior history of urological manipulation.

The use of aminoglycoside or cephapirin as prophylactic antibiotics before prostate biopsy has been researched in a few studies, but these agents did not show significant superiority over fluoroquinolone [23-26]. Because it is highly likely that fluoroquinolone-resistant E. coli may increase further, not only the use of fluoroquinolone as a preprostate biopsy prophylactic antibiotic but also the use of other antibiotics such as high-dose aminoglycoside or cephapirin should be considered. Our study may serve to provide basic information for various prophylactic antibiotics research.

When the difference between the first biopsy and a repeat biopsy was reviewed, the frequency of acute prostatitis was somewhat higher in the repeat biopsy group (2.03% vs. 1.20%), but the difference was not statistically significant. This outcome is similar to a previous report about postbiopsy complications [10,17,22]. The results of our study may have some distinctions from other studies of first and repeat biopsy complications in terms of the methods used for prophylactic antibiotic treatment.

Other than the aforementioned, many studies are being
conducted on the emergence of ESBL-producing \textit{E. coli}. ESBL is an enzyme that neutralizes broad-spectrum antibiotics such as the third-generation cephalosporins or monobactams. Bacteria including \textit{E. coli} and \textit{Klebsiella pneumonia} that often cause urogenital tract infection are potentially ESBL-producing microorganisms. The existence of ESBL-producing organisms can cause therapeutic failure in infectious diseases. In our study, 19.0\% (4/21) of bacteria were ESBL-producing strains. The emergence of ESBL activity is thought to be related to the high frequency of use of broad-spectrum antibiotics [27,28]. It is very important to make an accurate differentiation of ESBL-producing microorganisms. ESBL-producing \textit{E. coli}-induced bacteremia has far higher mortality than non-ESBL-producing \textit{E. coli}-induced bacteremia [29,30].

In our study, it would be difficult to directly identify the prevalence of ESBL activity or its sequelae because the study did not include many cases with postbiopsy acute prostatitis. In the future, more extensive research is needed to determine the effects of ESBL activity.

**CONCLUSIONS**

In acute prostatitis after transrectal prostate biopsy, it is essential to administer appropriate antibiotics immediately. Recently, however, more cases are caused by fluoroquinolone-resistant microorganisms or ESBL-producing microorganisms. Therefore, any empirical treatment should take into account geographical prevalence and drug resistance. To achieve this, microbiological data should be collected to optimize clinical guidelines. These efforts are essential to reduce the indiscriminate use of antibiotics. This study will provide meaningful information for the management of acute prostatitis after transrectal prostate biopsy.

**REFERENCES**

1. Crawford ED, Haynes AL Jr, Story MW, Borden TA. Prevention of urinary tract infection and sepsis following transrectal prostatic biopsy. J Urol 1982;127:449-51.
2. Lindert KA, Kabalin JN, Terris MK. Bacteremia and bacteriuria after transrectal ultrasound guided prostate biopsy. J Urol 2000;164:76-80.
3. Raebush TK 2nd, McConville JH, Calia FM. A double-blind study of trimethoprim-sulfamethoxazole prophylaxis in patients having transrectal needle biopsy of the prostate. J Urol 1979;122:492-4.
4. Hasegawa T, Shimomura T, Yamada H, Ito H, Kato N, Hasegawa N, et al. Fatal septic shock caused by transrectal needle biopsy of the prostate; a case report. Kansenshogaku Zasshi 2002;76:893-7.
5. Hoshi A, Nitta M, Hongo S, Hanai K, Nishikawa Z, Kobayashi Y, et al. Sepsis following transrectal prostate biopsy: a report of 2 cases and reviewed similar cases in Japan. Hinyokika Kyō 2006;52:645-9.
6. Kapoor DA, Klimberg IW, Malek GH, Wegenke JD, Cox CE, Patterson AL, et al. Single-dose oral ciprofloxacin versus placebo for prophylaxis during transrectal prostate biopsy. Urology 1998;52:552-8.
7. Aron M, Rajeev TP, Gupta NP. Antibiotic prophylaxis for transrectal needle biopsy of the prostate: a randomized controlled study. BJU Int 2000;85:682-5.
8. Taylor HM, Bingham JB. Antibiotic prophylaxis for transrectal prostate biopsy. J Antimicrob Chemother 1997;39:115-7.
9. Rietbergen JB, Kruger AE, Kranse R, Schroder FH. Complications of transrectal ultrasound-guided systematic sextant biopsies of the prostate: evaluation of complication rates and risk factors within a population-based screening program. Urology 1997;49:875-80.
10. Djavan B, Waldert M, Zlotta A, Dobroński P, Seitz C, Remezi M, et al. Safety and morbidity of first and repeat transrectal ultrasound-guided prostate needle biopsies: results of a prospective European prostate cancer detection study. J Urol 2001;166:856-60.
11. Griffith BC, Morey AF, Ali-Khan MM, Canby-Hagino E, Foley JP, Rozanski TA. Single dose levofloxacin prophylaxis for prostate biopsy in patients at low risk. J Urol 2002;168:1021-3.
12. Shigemura K, Tanaka K, Yasuda M, Ishihara S, Muratani T, Deguchi T, et al. Efficacy of 1-day prophylaxis medication with fluoroquinolone for prostate biopsy. World J Urol 2005;23:356-60.
13. Drusano GL, Preston SL, Van Guilder M, North D, Gombert M, Oefelein M, et al. A population pharmacokinetic analysis of the penetration of the prostate by levofloxacin. Antimicrob Agents Chemother 2000;44:2046-51.
14. Tal R, Livne PM, Lask DM, Baniel J. Empirical management of urinary tract infections complicating transrectal ultrasound guided prostate biopsy. J Urol 2003;169:1762-5.
15. Otrock ZK, Oghlakian GO, Salamoun MM, Haddad M, Bizri AR. Incidence of urinary tract infection following transrectal ultrasound-guided prostate biopsy at a tertiary-care medical center in Lebanon. Infect Control Hosp Epidemiol 2004;25:873-7.
16. Feliciano J, Teper E, Ferrandino M, Macchia RJ, Blank W, Grunberger I, et al. The incidence of fluoroquinolone resistant infections after prostate biopsy: are fluoroquinolones still effective prophylaxis? J Urol 2008;179:952-5.
17. Shigeoka H, Miyagi T, Nakashima T, Shimamura M. Acute bacterial prostatitis after transrectal prostate needle biopsy: clinical analysis. J Infect Chemother 2008;14:40-3.
18. Kim SJ, Kim SI, Ahn HS, Choi JB, Kim YS, Kim SJ. Risk factors for acute prostatitis after transrectal prostate biopsy. Korean J Urol 2010;51:426-30.
19. Ozden E, Bostanci Y, Yakupoglu KY, Akdeniz E, Yilmaz AF, Tulek N, et al. Incidence of acute prostatitis caused by extended-spectrum beta-lactamase-producing Escherichia coli after transrectal prostate biopsy. Urology 2009;74:119-23.
20. Le DD, Le DH, Park YY, Shim BS. A comparative study of clinical symptoms and treatment outcomes of acute bacterial prostatitis according to urine culture. Korean J Urol 2011;52:119-23.
21. Aparicio JR, Such J, Pascual S, Arroyo A, Plazaas J, Girona E, et al. Development of quinolone-resistant strains of Escherichia coli in stools of patients with cirrhosis undergoing norfloxacin prophylaxis: clinical consequences. J Hepatol 1999;31:277-83.
22. Ha US, Kim ME, Kim CS, Shim BS, Han CH, Lee SD, et al. Acute bacterial prostatitis in Korea: clinical outcome, including symptoms, management, microbiology and course of disease. Int J Antimicrob Agents 2008;31 Suppl 1:S96-101.
23. Bosquet Sanz M, Gimeno Argente V, Arlandis Guzman S, Bonillo Garcia MA, Trassierra Villa M, Jimenez Cruz JF. Comparative study between tobramycin and tobramycin plus ciprofloxacin in transrectal prostate biopsy prophylaxis. Actas Urol Esp 2006;30:

Korean J Urol 2013;54:117-122
24. Cam K, Kayikci A, Akman Y, Erol A. Prospective assessment of the efficacy of single dose versus traditional 3-day antimicrobial prophylaxis in 12-core transrectal prostate biopsy. Int J Urol 2008;15:997-1001.

25. Reach MB, Figueroa TE, McBride D, George WJ, Neal DE Jr. Ciprofloxacin versus gentamicin in prophylaxis against bacteremia in transrectal prostate needle biopsy. Urology 1991;38:84-7.

26. Brewster SF, MacGowan AP, Gingell JC. Antimicrobial prophylaxis for transrectal prostatic biopsy: a prospective randomized trial of cefuroxime versus piperacillin/tazobactam. Br J Urol 1995;76:351-4.

27. Kanafani ZA, Mehio-Sibai A, Araj GF, Kanaan M, Kanj SS. Epidemiology and risk factors for extended-spectrum beta-lactamase-producing organisms: a case control study at a tertiary care center in Lebanon. Am J Infect Control 2005;33:326-32.

28. Lautenbach E, Patel JB, Bilker WB, Edelstein PH, Fishman NO. Extended-spectrum beta-lactamase-producing Escherichia coli and Klebsiella pneumoniae: risk factors for infection and impact of resistance on outcomes. Clin Infect Dis 2001;32:1162-71.

29. Hyle EP, Lipworth AD, Zaoutis TE, Nachamkin I, Bilker WB, Lautenbach E. Impact of inadequate initial antimicrobial therapy on mortality in infections due to extended-spectrum beta-lactamase-producing enterobacteriaceae: variability by site of infection. Arch Intern Med 2005;165:1375-80.

30. Melzer M, Petersen I. Mortality following bacteraemic infection caused by extended spectrum beta-lactamase (ESBL) producing E. coli compared to non-ESBL producing E. coli. J Infect 2007;55:254-9.