Risk Factors for Acute Prostatitis after Transrectal Biopsy of the Prostate

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감사의 글

의과대학을 졸업하고 2년이 지난후 다시 대학원이라는 학업의 길을 시작한지가 엊그제 같은데 어느덧 2년이라는 세월이 흘러 논문을 쓰게 되었습니다.

먼저 아무것도 모르는 항상 부족한 저를 이끌어 주시고 지도해주신 김세중 교수님께 진심으로 감사의 말씀을 드립니다. 또한 항상 저를 지켜봐주시고 좋은 말씀을 해주신 김영수 교수님, 안현수 교수님, 최종보 교수님, 김선일 교수님, 조대성 선생님께도 깊은 감사를 드립니다.

전공의 생활과 동시에 해왔던 대학원이기에 제가 못했던 일들을 대신 해주었던 의국원 모두에게도 고맙다는 말을 전하고 싶습니다. 마지막으로 항상 저를 사랑해주시고 믿어주시는 부모님, 제 옆에서 변함없이 저를 아껴주는 사랑하는 가족들에게 감사의 마음을 전하고 싶습니다.

의학에 입문한지가 어느덧 10년이라는 시간이 되었지만 아직도 모르는 게 너무 많고 항상 질문에 부딪히곤 합니다. 앞으로도 더욱더 공부하고 노력하는 사람이 되어 저를 지켜봐주시는 모든 분들에게 부끄럽지 않은 사람이 되겠습니다.

감사합니다.

2010년 12월

김 상 진

- ABSTRACT -

Risk Factors for Acute Prostatitis after Transrectal Biopsy of the Prostate

Purpose: We investigate the incidence, clinical features, pathogenic bacteria and risk factors associated with acute prostatitis after transrectal prostate biopsy.

Materials and Methods: We retrospectively reviewed the medical records of 923 transrectal ultrasound-guided needle biopsy of the prostate on 878 patients performed in our institution from June 2004 to May 2009. The indications for transrectal prostate biopsy were generally serum prostate-specific antigen (PSA) elevation and/or abnormal findings on digital rectal examination. All biopsies were performed with the patient hospitalized except for 10 patients who refused to be hospitalized, and ciprofloxacin was administered as antibiotic prophylaxis. The incidence, clinical features, pathogenic bacteria and potential risk factors associated with acute prostatitis after prostate biopsy were evaluated.

Results: Acute prostatitis developed in 18 (2.0%) cases after transrectal prostate biopsy. Among them, 9 (1.0%) had bacteremia and 2 (0.2%) showed clinical features of sepsis. Of the total 50 urine or blood specimens sent for culture study, 27 (54.0%) specimens showed positive cultures, including E. coli in 25. Among 27 culture positive specimens, 26 (96.3%) were resistant to ciprofloxacin. Among the potential risk factors for acute prostatitis after prostate biopsy, biopsy performed as an outpatient procedure without cleansing enema (p=0.001) and past history of cerebrovascular accident (p=0.048) were statistically significant.

Conclusions: Fluoroquinolone is effective as antibiotic prophylaxis for transrectal prostate biopsy in the majority of cases. The incidence of acute prostatitis after transrectal prostate biopsy was 2.0% and almost all were caused by fluoroquinolone-resistant E. coli. Cleansing enema is recommended before transrectal prostate biopsy.

Key words: Biopsy, Prostate, Prostatitis

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I. INTRODUCTION

Transrectal ultrasound-guided needle biopsy of the prostate is generally accepted as the standard diagnostic procedure for detecting prostate cancer (Lee, 2004; Jeon et al, 2008; Chae et al, 2009; de la Rosette et al, 2009). Although transrectal ultrasound-guided prostate biopsy is generally considered to be a safe procedure, complications are occasionally encountered. They include minor complications such as hematuria, hemospermia and rectal bleeding as well as clinically significant major complications such as acute prostatitis and urosepsis, which may be fatal (Djavan et al, 2001; Raaijmakers et al, 2002; Berger et al, 2004; Nam et al, 2010).

Antibiotic prophylaxis before transrectal prostate biopsy is generally accepted to reduce the infection related complications. Fluoroquinolones, which are known to be delivered at high concentrations in the prostate, are considered to be effective in lowering the incidence of infective complications (Sieber et al, 1997; Aron et al, 2000; Shigehara et al, 2008; Yamamoto et al, 2008). However, there are recent reports of developing fluoroquinolone-resistant infections following transrectal prostate biopsy (Tal et al, 2003; Sieber et al, 2007; Feliciano et al, 2008; Özden et al, 2009).

The number of prostate biopsies is bound to progressively increase with the advent of prostate-specific antigen (PSA) screening and increasing awareness of prostate cancer. Therefore, it becomes essential to have a clear understanding of the morbidity of transrectal prostate biopsy to allow for more appropriate patient counseling and management.

In this study, we investigated the incidence, clinical features, pathogenic bacteria and risk factors associated with acute prostatitis after transrectal prostate biopsy.

II. MATERIALS AND METHODS

We retrospectively reviewed the medical records of 923 prostate biopsies on 878 patients, including 77 repeated biopsies, performed in our institution from June 2004 to May 2009. The indications for prostate biopsy were serum PSA elevation and/or abnormal findings on digital rectal examination and/or transrectal ultrasonography. All prostate biopsies were performed transrectally under ultrasound guidance. An automatic biopsy gun with an 18-gauge needle was used to obtain biopsy specimens. Either 10- or 12-core biopsies were sampled depending on the time period the biopsy was performed. 10-core biopsies were performed from June 2004 to April 2008 and 12-core biopsies were performed since May 2008. Acetylsalicylic acid or oral anticoagulant agents were stopped 7 days before prostate biopsy with the approval of the prescribing physician as a rule. Urine samples were obtained for urinalysis in all cases except 5 and for urine culture in all cases except 10 before prostate biopsy.

All prostate biopsies were performed with the patient hospitalized except for 10 patients who refused to be hospitalized. In patients who were hospitalized, 200 mg ciprofloxacin was injected intravenously before and after the biopsy. All hospitalized patients received a cleansing enema before biopsy. They were discharged from the hospital on the following morning after the biopsy and received 250 mg ciprofloxacin orally twice daily for 7 days. Patients who underwent biopsy on an outpatient basis had not received a cleansing enema or parenteral injections of ciprofloxacin. These patients received 250 mg ciprofloxacin orally twice daily for 7 days, beginning on the morning before biopsy.

In case symptoms of acute prostatitis, such as fever, chill and voiding

difficulty developed after prostate biopsy, the patient was readmitted for treatment including intravenous antibiotics.

The incidence, clinical features and pathogenic bacteria of acute prostatitis after prostate biopsy were investigated. Variables such as patient's age, past medical history, prostate volume, biopsy core numbers, number of biopsy session, cleansing enema, and urinalysis and urine culture findings before biopsy were also assessed.

Statistical analysis was performed using the chi-square test or independent t-test with SPSS version 13.0 (SPSS Inc., Chicago, USA). The values of $p<0.05$ were considered to be statistically significant in all of the analyses.

III. RESULTS

Of the 923 prostate biopsy cases, acute prostatitis developed in 18 (2.0%) cases after prostate biopsy. Among 18 cases, 9 (1.0%) had bacteremia as confirmed by positive blood culture, and 2 (0.2%) showed clinical features of sepsis. The patients developed infective symptoms a median of 1 day (mean, 2.8 days; range, 1-25 days) after prostate biopsy.

Of the 18 cases with acute prostatitis, 13 (72.2%) cases had positive urine and/or blood cultures, including E. coli in 11, Klebsiella pneumoniae in 1 and Citrobacter freundii in 1. Of the total 50 urine or blood specimens sent for culture study, 27 (54.0%) specimens showed positive cultures, including E. coli in 25, Klebsiella pneumoniae in 1 and Citrobacter freundii in 1. Among 27 culture positive specimens, 26 (96.3%) yielded ciprofloxacin-resistant pathogens, including E. coli in 24, Klebsiella pneumoniae in 1 and Citrobacter freundii in 1. However, these pathogens were sensitive to cephalosporins and aminoglycosides (Table 1).

When stratified by year, there was no statistically significant difference in the annual rates of acute prostatitis developed after prostate biopsy (p=0.904) (Table 2).

The mean age of the patients who underwent prostate biopsy was 65.4 years (range 20-95). The mean ages of the patients who developed acute prostatitis and who did not were 59.3±13.0 years and 65.5±11.0 years, respectively, which showed no statistically significant difference (p=0.063) (Table 3).

The mean prostate volume of the patients who underwent prostate biopsy was 50.2 cc (range 12.2-383.3). The mean prostate volumes of the patients who developed acute prostatitis and who did not were 44.7±20.1 cc and

50.3±29.3 cc, respectively, which showed no statistically significant difference (p=0.261) (Table 3).

Among the other potential risk factors for acute prostatitis after prostate biopsy, biopsy performed as an outpatient procedure without cleansing enema (p=0.001) and past history of cerebrovascular accident (p=0.048) were statistically significant (Table 4).

Table 1. Susceptibility of ciprofloxacin-resistant E. coli to antibiotics in 24 urine and blood culture specimens

Antibiotics	% Susceptible
Trimethoprim/sulfamethoxazole	67
Ampicillin	38
Amoxicillin/clavulanic acid	86
Piperacillin	64
Piperacillin/tazobactam	100
Aztreonam	100
Imipenem	100
Tetracycline	50
Nitrofurantoin	100
Ceftazidime	100
Cefepime	100
Cefazolin	92
Cefoxitin	88
Cefotaxime	100
Ceftriaxone	100
Amikacin	100
Gentamicin	96
Netilmicin	100
Tobramycin	100

Table 2. Annual rates of acute prostatitis developed after prostate biopsy

Year	No. of prostate biopsies	No. of cases with acute prostatitis (%)	p-value
2004	77	2 (2.6)	
2005	124	1 (0.8)	
2006	155	4 (2.6)	0.904
2007	218	5 (2.3)	
2008	227	4 (1.8)	
2009	122	2 (1.6)	
Total	923	18 (2.0)	

Table 3. Patient's age and prostate volume relating to acute prostatitis

	Total	With acute prostatitis	Without acute prostatitis	p-value
Mean age ± SD (years)	65.4±11.1	59.3±13.0	65.5±11.0	0.063
Mean prostate volume ± SD(cc)	50.2±29.1	44.7±20.1	50.3±29.3	0.261

Table 4. Potential risk factors and rates of acute prostatitis after prostate biopsy

Risk factors	No. of prostate biopsies	No. of cases with acute prostatitis (%)	p-value
Diabetes mellitus			0.095
Yes	131	5 (3.8)	
No	792	13 (1.6)	
Hypertension			0.840
Yes	338	7 (2.1)	
No	585	11 (1.9)	
Cerebrovascular accident			0.048
Yes	54	3 (5.6)	
No	869	15 (1.7)	
Pyuria before biopsy			0.941
Yes	57	1 (1.8)	
No	861	14 (1.6)	
Urine culture before biopsy			0.771
Positive	46	1 (2.2)	
Negative	867	14 (1.6)	
No. of biopsy core			0.709
10	652	12 (1.8)	
12	271	6 (2.2)	
No. of biopsy session			0.645
1st	846	18 (2.1)	
2nd	63	0 (0)	
3rd	12	0 (0)	
4th	2	0 (0)	
Cleansing enema			0.001
Yes (biopsy in IPD)	913	15 (1.6)	
No (biopsy in OPD)	10	3 (30.0)	

IPD: inpatient department, OPD: outpatient department

IV. DISCUSSION

Although a few studies have demonstrated that antibiotic prophylaxis may not be required for transrectal prostate biopsy (Enlund and Varenhorst, 1997), antibiotic prophylaxis before transrectal prostate biopsy is generally accepted to decrease the rate of infective complications (Sieber et al, 1997; Aron et al, 2000; Shigehara et al, 2008; Yamamoto et al, 2008). However, there is much variability in the type, dosage and duration of antibiotic prophylaxis (Shandera et al, 1998; Lee et al, 2007).

Fluoroquinolones are the most frequently used antibiotics for prophylaxis before transrectal prostate biopsy because of their broad spectrum of action, adequate for common urinary and colorectal flora, their high concentration within the prostatic tissue, and the ease of oral administration (Cormio et al, 2002). Numerous studies have demonstrated the decrease in infective complications with fluoroquinolone use to rates of less than 1% to 4% (Sieber et al, 1997; Feliciano et al, 2008; Jang et al, 2008; Shigehara et al, 2008; Yamamoto et al, 2008). In our study, the rate of acute prostatitis was 2.0%, which was consistent with the previously reported rates. This means that fluoroquinolone is effective as antibiotic prophylaxis for transrectal prostate biopsy in the majority of cases.

However, recent reports have shown that fluoroquinolone-resistant infections following transrectal prostate biopsy are emerging (Tal et al, 2003; Sieber et al, 2007; Feliciano et al, 2008; Özden et al, 2009). Shigehara et al reported that all of the urine cultures of the patients with acute prostatitis developed after transrectal prostate biopsy yielded levofloxacin-resistant E. coli (Shigehara et al, 2008). Feliciano et al showed that 61% of the patients with infective complications after transrectal prostate biopsy had positive

urine and/or blood cultures. Of the positive cultures, those from 89% of patients yielded E. coli and 90% were fluoroquinolone-resistant. The incidence of infective complications and fluoroquinolone-resistant infections in 2006 were 3 times and 3.3 to 4.3 times higher compared to 2004 and 2005, respectively (Feliciano et al, 2008). Özden et al reported that 61% of the patients with acute prostatitis after transrectal prostate biopsy had positive cultures, with E. coli being the most common pathogen (82%). Among the patients infected with E. coli, 93% showed fluoroquinolone-resistance and 43% harbored extended-spectrum β-lactamase-producing E. coli (Özden et al, 2009). In our study, 72.2% of cases with acute prostatitis developed after transrectal prostate biopsy had positive urine and/or blood cultures. Of the positive cultures, 96.3% were resistant to ciprofloxacin. However, in contradiction to the findings by Feliciano et al, there was no significant difference in the annual rates of acute prostatitis after prostate biopsy.

Özden et al suggested that the increasing fluoroquinolone-resistance might be due to the previous wide use of these drugs (Özden et al, 2009). Shigehara et al considered that the previous use of levofloxacin might cause bacterial selection in the rectum, and levofloxacin-resistant E. coli might then appear in the rectum for a certain period (Shigehara et al, 2008). In their reports, acute prostatitis developed more frequently after repeat biopsy compared to the first biopsy (Shigehara et al, 2008; Özden et al, 2009). However, in our study, the rate of acute prostatitis was not different according to the number of biopsy session and all cases of acute prostatitis occurred after the first biopsy.

Because our results demonstrated that ciprofloxacin-resistant pathogens were sensitive to cephalosporins and aminoglycosides, empirical treatment with cephalosporins or aminoglycosides is recommended to be initiated for

patients with acute prostatitis developed after transrectal prostate biopsy until culture specific therapy can be implemented.

The impact of cleansing enema before transrectal prostate biopsy on the infective complications is still controversial. Whereas some studies have shown that a cleansing enema is not required or recommended before biopsy (Carey and Korman, 2001; Kang et al, 2008), others have suggested that a cleansing enema before biopsy may decrease bacteremia and bacteriuria after prostate biopsy (Brown et al, 1981; Lindert et al, 2000). A cleansing enema has the advantage of producing a superior acoustic window for prostate imaging by decreasing the amount of feces in the rectum. Furthermore, a cleansing enema and empty rectal vault may reduce bacterial seeding of the prostate (Ramey et al, 2007).

In our series of 923 prostate biopsy cases, all patients except 10 (1.1%) received a cleansing enema. Acute prostatitis developed more frequently in cases without cleansing enema compared to those with cleansing enema before biopsy, which was statistically significant. Because only 1.1% of our cases had not received a cleansing enema, a large prospective randomized study will be needed to clarify the impact of cleansing enema on the infective complications.

In our study, biopsy performed as an outpatient procedure without cleansing enema and past history of cerebrovascular accident were statistically significant risk factors for acute prostatitis after transrectal prostate biopsy. Pyuria and positive urine culture before biopsy were not significant risk factors, which were consistent with the findings by Ecke et al that positive microbiology in urine before prostate biopsy was not a risk factor for a higher infection rate (Ecke et al, 2008). Chiang et al suggested that patients with larger prostate (>45ml) had a significantly higher risk of

developing acute prostatitis and acute urinary retention after prostate biopsy compared to those with smaller prostate (<45 ml) (Chiang et al, 2007). However, in our study, prostate volume was not a significant risk factor for acute prostatitis after prostate biopsy.

In our study, patient's age, diabetes mellitus, hypertension, and number of biopsy core were not significant risk factors for acute prostatitis after prostate biopsy, which was consistent with the results by Chiang et al (Chiang et al, 2007). Past history of cerebrovascular accident was a statistically significant risk factor for acute prostatitis after prostate biopsy in our study, but not in the report by Chiang et al (Chiang et al, 2007). The possible explanation is that the patients with history of cerebrovascular accident may have altered bowel function and constipation (Krogh et al, 2001; Bracci et al, 2007), which may result in the change of bacterial flora in the rectum. They also could have consumed fluoroquinolones before prostate biopsy. These combined might lead to the appearance of fluoroquinolone-resistant pathogens in the rectum and increase in the infective complications after transrectal prostate biopsy.

A limitation of our study is that it was retrospective in nature, and the sample size of the groups was limited because of the low incidence of acute prostatitis after transrectal prostate biopsy. All patients, except 10 (1.1%), were hospitalized and received a cleansing enema before transrectal prostate biopsy. Further prospective studies would be necessary to confirm the impact of cleansing enema before transrectal prostate biopsy on the infective complications.

V. CONCLUSION

Fluoroquinolone is effective as antibiotic prophylaxis for transrectal prostate biopsy in the majority of cases. The incidence of acute prostatitis after transrectal prostate biopsy was 2.0% and almost all were caused by fluoroquinolone-resistant E. coli. Cleansing enema is recommended before transrectal prostate biopsy. Empirical treatment with cephalosporins or aminoglycosides should be initiated for patients with acute prostatitis after transrectal prostate biopsy until culture specific therapy can be implemented.

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-국문 요약-

경직장전립선생검 후 발생한 급성전립선염의 위험인자

아주대학교 대학원 의학과

김 상 진

(지도교수: 김 세 중)

목적: 경직장전립선생검은 현재 전립선암의 진단에 표준적인 방법으로 시행되고 있으나 치명적일 수도 있는 합병증인 급성전립선염의 위험이 있다. 저자들은 경직장전립선생검 후 발생한 급성전립선염의 빈도, 임상 양상, 위험인자, 균주의 특성 등을 알아보았다.

대상 및 방법: 2004년 6월부터 2009년 5월까지 본원에서 878명의 환자를 대상으로 923례의 경직장전립선생검을 시행하였으며 이들의 의무기록을 후향적으로 분석하였다. 전립선생검은 일반적으로 전립선특이항원 수치가 4ng/ml이상이거나 직장수지검사에서 결절이 있는 경우에 시행하였다. 전립선생검은 입원을 거부한 10명을 제외하고는 모두 입원해서 시행하였고, ciprofloxacin을 예방적 항생제로 투여하였다. 전립선생검 후 발생한 급성전립선염의 빈도, 임상 양상, 균주 및 위험인자를 평가하였다.

결과: 총 923례의 전립선생검 중 급성전립선염은 18례 (2.0%)에서 발생하였다. 그중 9례 (1.0%)에서 혈액균배양검사 양성 소견을 보여 균혈증이 있었으며, 2례 (0.2%)는 패혈증의 증세를 보였다. 이들 환자에서 총 50개의 혈액 또는 소변 균배양검사를 실시하였고, 그중 27개 (54%)에서 양성 소견을 보였다. 이중 E. Coli 25개, Klebsiella pneumoniae 1개, Citrobacter freundii 1개가 배양되었으며, ciprofloxacin에 내성균이 총 26개 (96.3%)였으나 cephalosporin, aminoglycoside 계열에는 대부분 감수성이 있었다. 급성전립선염의 잠재적 위험인자인 연령, 당

뇨, 과거 뇌경색, 고혈압, 생검횟수, 입원여부, 관장시행여부, 생검 전 농뇨, 생검 전 소변배양검사양성, 생검갯수, 전립선 용적 중 외래에서 관장 미시행 후 시행한 경우 (p=0.001)와 과거 뇌경색 (p=0.048)이 의미있는 위험인자였다.

결론: Fluoroquinolone은 대부분의 경직장전립선생검에서 급성전립선염을 예방하기에 효과적이었다. 경직장전립선생검 후 급성전립선염의 발생률은 약 2%였으며, 대부분 fluoroquinolone 내성 E.Coli가 원인균이었다. 이의 예방을 위해서는 관장 등의 생검 전 처치를 철저히 준수해야 하며 복합 예방적 항생제 사용도 고려되어야 할 것이다.

핵심어: 생검, 전립선, 전립선염