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Original article

# Adding gentamicin to fluoroquinolone-based antimicrobial prophylaxis reduces transrectal ultrasound-guided prostate biopsy-related infection rate

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ABSTRACT

*Objective:* Transrectal ultrasound-guided prostate (TRUS) biopsy is the standard method for the diagnosis of prostate cancer. Quinolone-based prophylaxis before a TRUS biopsy of the prostate is the most common regimen worldwide. In this retrospective study, we evaluated the efficacy and cost effectiveness of adding gentamicin to a fluoroquinolone-based prophylaxis regimen.

*Materials and methods:* In total, our study included 263 patients classified into two groups. Group 1 consisted of 129 patients who received one oral dose of levofloxacin (500 mg) daily 2 days before the biopsy, on the day of the biopsy, and for 2 days after the biopsy. Group 2 consisted of 134 patients who received a single intramuscular (IM) gentamicin injection (80 mg) 30 minutes before the biopsy in addition to the same oral levofloxacin protocol as Group 1. We recorded and analyzed data including age, indication for a TRUS biopsy of the prostate, prostate volume, comorbidity, infectious complications, and blood and urine culture results.

*Results:* The mean prostate-specific antigen level was 38.6 ng/mL ± 312.9 ng/mL (range, 4.4–2626 ng/mL) in Group 1, and 34.8 ng/mL ± 127.1 ng/mL (range, 2.11–1423 ng/mL) in Group 2. The groups were similar in terms of mean age, indication for a biopsy, prostate volume, number of biopsy cores taken, and comorbidities. Infection-related complications occurred in eight of 129 (6.2%) and in one of 134 (0.74%) patients in Groups 1 and 2, respectively ($p = 0.02$).

*Conclusion:* The addition of IM gentamicin (80 mg) was beneficial in improving the efficacy of fluoroquinolone and reducing the post-TRUS biopsy infection rate. Gentamicin is relatively inexpensive and readily available in daily practice and has good compliance for patient use.



## 1. Introduction

Transrectal ultrasound-guided prostate (TRUS) biopsy is the standard method for the diagnosis of prostate cancer.[1] It is generally a safe procedure with acceptable complication rates. Infectious complications after a prostate biopsy include fever, urinary tract infections, acute bacterial prostatitis, epididymo-orchitis, and sepsis.[2] The reported incidence of urinary tract infections after a TRUS biopsy typically ranges between 2% and 6%, with approximately 30–50% of these patients exhibiting accompanying bacteremia.[3,4] Bacteremia is frequently accompanied by severe sepsis, which has a reported overall incidence of 0.1–2.2% following a TRUS biopsy.[3] A Canadian study reported increasing rates of hospitalization within a 30-day period following a TRUS biopsy, from 1.0% in 1996 to 4.1% in 2005 ($p < 0.0001$).[5] Similarly, using data derived from Medicare records, researchers from the United States also reported an increasing frequency of infectious complications following a TRUS biopsy, increasing from 0.4% in 1991 to 1.1% in 2007 ($p < 0.0001$).[6] Therefore, reducing the postbiopsy infection rate is a challenge in the TRUS biopsy era.

Fluoroquinolone is one of the most commonly used prophylactic antibiotics for TRUS biopsies and has been used in our hospital for the past years. The American Urological Association guidelines for

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the use of prophylactic antibiotics for a TRUS biopsy of the prostate state that all recommended antibiotics are acceptable in the outpatient setting.[7] Furthermore, Western countries have reported and recommend aminoglycosides in combination with metronidazole, or fluoroquinolones and cephalosporins for TRUS biopsies. The incidence of prostate cancer varies from one country to another, with the highest incidence being found in the Western world and the lowest in Asian countries.[8] Therefore, owing to the relatively low incidence of prostate cancer, there could be different views regarding the feasibility and cost effectiveness of such formula used in Asian countries.

In this study, we compared infectious complication rates in patients undergoing a TRUS biopsy of the prostate who were given prophylactic levofloxacin only with those given levofloxacin combined with a single dose of intramuscular (IM) gentamicin (80 mg) to evaluate the efficiency of adding IM gentamicin to standard prophylaxis in reducing infection-related complications after a TRUS biopsy.

## 2. Materials and methods

We conducted this retrospective study from January 2008 to August 2011. The charts of patients who received a TRUS biopsy in this period were reviewed. The patients who did not receive levofloxacin as a prophylactic antibiotic were excluded. Patient's history was reviewed, including age, diabetes mellitus (fasting plasma glucose level ≧ 130 mg/dL), hypertension (blood pressure ≧ 140/90 mmHg), and other comorbidities. In total, the study included 263 patients. Group 1 consisted of 129 patients who received one oral dose of levofloxacin (500 mg) daily 2 days before the biopsy, on the day of the biopsy, and for 2 days after the biopsy. Group 2 consisted of 134 patients who received a single IM gentamicin injection (80 mg) 30 minutes before the biopsy in addition to the same oral levofloxacin protocol as Group 1. Whether or not to add gentamicin as an adjunctive is decided by the attending doctor.

The indications for a TRUS biopsy included elevated prostate-specific antigen (PSA) level (>4 ng/mL), abnormal digital rectal examination, findings in a first prostate biopsy that necessitated a repeat biopsy such as the presence of an atypical gland or persistent elevation of PSA.

Almost all of the patients received the TRUS biopsy as an outpatient procedure except those who came for consultation for prostate biopsy during admission. Urine analysis, coagulation profile, and serum creatinine were all examined before the TRUS biopsy. Bowel movements were ensured with Bisacodyl (Dulcolax) suppositories given the previous night, and all patients had a cleansing enema before the procedure. With the patient in the left decubitus position, the TRUS biopsy was performed by an urologist with a multiplanar, multifrequency probe (75 MHz) attached to an ultrasound scanner. The prostate volume was calculated using the prostate ellipsoid formula: volume ($V$) = 0.52 ($L \times W \times H$), where $L$ is the cephalocaudal diameter, $W$ is the width, and $H$ is the anteroposterior diameter. The patients with superhigh PSA levels demonstrating osteoblast bone metastasis received 10 cores prostate biopsy; all other patients received 12–16 cores biopsy. The prostate biopsies were taken with an 18-gauge × 20-cm needle with an automated spring loaded gun mechanism (Bard Biopsy Gun). The biopsies were obtained at the apex, middle, and base of the bilateral prostate lobes in the parasagittal plane.

The patients were informed to return to the hospital if they developed a fever (>38.5°C), chills, or newly developed severe lower urinary tract symptoms and macroscopic hematuria with blood clots. The patients who experienced the aforementioned symptoms within 14 days of the procedure in the absence of other clinically apparent sources of infection were defined as having "post-TRUS biopsy infection-related complications."

Mean and standard deviations were determined. These two groups were compared with respect to descriptive characteristics and factors before and after biopsy using the Chi-square, Fisher exact test, and the student $t$ test. A $p$ value ≦0.05 was considered statistically significant.

## 3. Results

The characteristics of patients in the two groups are listed in Table 1. They were similar in terms of mean age (68.4 years ± 8.747 years in Group 1 and 69.20 years ± 10.394 years in Group 2), indication for biopsy, prostate volume (32.65 mL ± 10.82 mL in Group 1 and 35.46 mL ± 12.35 mL in Group 2), and the number of biopsy cores taken. The mean PSA level was 38.653 ng/mL ± 312.9249 ng/mL (range, 4.4–2626 ng/mL) in Group 1, and 34.843 ng/mL ± 127.1309 ng/mL (range, 2.11–1423 ng/mL) in Group 2. The percentage of patients with hypertension and diabetes was 31% (40/129) and 17% (22/129) in Group 1, 34.3% (46/134) and 14.9% (20/134) in Group 2, respectively. The comorbidities are comparable in both groups.

As shown in Figure 1 and Table 1, infection-related complications occurred in eight of 129 (6.2%) and one of 134 (0.74%) patients in Groups 1 and 2, respectively ($p$ = 0.02). Table 2 shows the possible etiological risk factors (including antibiotic prophylaxis, diabetes mellitus, hypertension, age, prostate cancer, and biopsy core number) and predisposing infection-related complications after a prostate biopsy. There was no statistically significant association between comorbidities including diabetes, hypertension, age, biopsy core number, and the pathology with postbiopsy infection-related complications, except antibiotics prophylaxis.

The patients with infection-related complications were hospitalized for intravenous antibiotics treatment. All organisms isolated were tested for antibiotic susceptibility to second- and third-generation cephalosporins as shown in Table 3. Over our study period, there were four blood cultures and one urine culture that were positive for *Escherichia coli* in nine cases of post-TRUS biopsy-related sepsis. Three of the four positive blood cultures were resistant to levofloxacin with only one exhibiting sensitivity. Of the four positive blood cultures, three were sensitive to gentamicin.

## 4. Discussion

Currently, TRUS biopsy of the prostate remains the most common procedure for the detection of prostate cancer. Although the procedure is generally considered to be safe and well-tolerated, postbiopsy complications are reported in up to 50% of cases, including pain, hematuria, hematospermia, urinary retention, and infection.[9] Septicemia is the most dangerous complication following the procedure and requires emergency admission and administration of intravenous antibiotics. The most common pathogen implicated in post-TRUS biopsy sepsis is *E. coli*, accounting for approximately 75–90% of infectious complications in published series.[10] In our fluoroquinolones-only prophylactic group, infection-related complications occurred in eight of 129 (6.2%) patients, which was comparable with previous reports.[3,4] Our results indicated that fluoroquinolones were effective as prophylaxis for TRUS prostate biopsies in 86.6% of patients. *E. coli* was the only causative organism identified in our positive cultures. Over our study period, there were four positive blood cultures and one positive urine culture in nine cases of post-TRUS biopsy-related sepsis. This finding is consistent with other reports, and thus, we directed our antibiotic prophylactic treatment at *E. coli*. Tal et al[2] also identified *E. coli* as the most common pathogen in their series.