A prospective randomized trial of 1-day versus 3-day antibiotic prophylaxis for transrectal ultrasound guided prostate biopsy

Robert Sabbagh, MD, Michael Mc Cormack, MD, François Péloquin, MD, Raymond Faucher, MD, Jean-Paul Perreault, MD, Paul Perrotte, MD, Pierre I. Karakiewicz, MD, Fred Saad, MD

Division of Urology, Centre Hospitalier de l'Université de Montréal, Université de Montréal, Montréal, Québec, Canada

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Purpose: *To compare the incidence of infection between a 1 day and a 3 day antibiotic prophylaxis regimen for transrectal ultrasound (TRUS) guided prostate biopsy in a prospective, randomized open-label trial.*

Materials and methods: *TRUS examination was performed in the left lateral decubitus position using a Brüel and Kjaer 7 MHz rectal probe. Biopsies were carried out with an 18 gauge Tru-cut needle fired by the hand-held Biopsy gun. An average of eight core biopsies (range 6 to 12) was taken. From May 15, 2000 to May 16, 2001, 363 patients were enrolled in this study. Patients were randomized to receive either 1 day or 3 days of fluroquinolone antibiotic prophylaxis, consisting of either ciprofloxacin or levofloxacin orally. Antibiotics were begun at least 1 hour prior to biopsy. Seven days later, telephone follow-up was obtained.*

Results: *Two (0.55%) of the 363 patients, one in each group, had an episode of sepsis. No urinary tract infection was reported. Traumatic complications were only minor and no significant difference was observed between both groups: hematospermia ($p > 0.4$), hematuria ($p > 0.1$) and rectorragia ($p > 0.2$) being reported most frequently.*

Conclusion: *There is no clinically nor statistically significant difference between a 1 day and 3 day antibiotic prophylaxis regimen for patients undergoing TRUS guided biopsies.*

Key Words: transrectal ultrasound, antibiotic prophylaxis, prostate biopsy

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Address correspondence to Fred Saad, MD, Department of Urology, Centre Hospitalier de l'Université de Montréal, 1560 Sherbrooke Street East, Montreal, Quebec H2L 4M1 Canada

Introduction

Transrectal ultrasound (TRUS) guided prostate biopsy is a commonly performed procedure to obtain tissue

for the histological diagnosis of carcinoma of the prostate in patients with either an abnormal digital rectal examination (DRE) and/or an elevated prostate-specific antigen level (PSA). Most complications following TRUS-guided biopsies are minor and require no treatment.[1]

However TRUS guided prostate biopsy can be associated with traumatic and infective complications, of which the latter may be manifest as asymptomatic bacteriuria, urinary tract infection or septicemia, the latter being occasionally fatal. Several studies have shown that administration of prophylactic antibiotics results in a lower incidence of post biopsy febrile episodes[2,3] positive urine cultures[4,5] and bacteremia.[4,6] However, there is a lack of standardization in antibiotic prophylaxis regimens. Furthermore these regimens have widely varying costs. Most studies advocate the use of antibiotic prophylaxis and generally use a fluoroquinolone. However, few prospective studies have addressed the optimal length of use of fluoroquinolone prophylaxis as a single agent. A review of the literature shows that oral ciprofloxacin is effective, inexpensive and well tolerated at reducing the incidence of bacteremia and clinical sepsis following TRUS prostate biopsies.[7] In a retrospective analysis, Janoff et al[8] also showed that six doses of ciprofloxacin appear to be more effective than four doses in reducing the clinical and febrile infection rate following ultrasound guided biopsy of the prostate. No obvious financial benefit was observed.

In order to determine the optimal use of fluoroquinolone prophylaxis we conducted a prospective randomized open-label study to compare whether a 3-day antibiotic prophylaxis is more effective in reducing infection complication rate than a 1-day regimen.

Materials and methods

A total of 363 patients were enrolled in the study and underwent TRUS guided prostate biopsies. After obtaining consent, patients were randomized by permutation block to receive either 1 day of antibiotic prophylaxis (consisting of ciprofloxacin 500 mg twice daily for two doses or one dose of levofloxacin 500 mg orally) or 3 days of antibiotic prophylaxis (six or three doses of ciprofloxacin 500 mg or levofloxacin 500 mg, respectively). The first dose of antibiotic was given at least 1 hour prior to biopsy.

TRUS examination was performed in the left lateral decubitus position using Brüel and Kjaer 7 MHz rectal probes. Biopsies were carried out with an 18 gauge Tru-cut needle fired by the hand-held biopsy gun. An average of eight core biopsies (range 6 to 10) was taken. Neither bowel preparation was given nor urinalysis taken prior to the procedure. Seven days later, all patients were contacted by phone for follow-up. They were questioned as to whether they experience chills, fever, dysuria, voiding difficulty, hematuria, hematospermia or rectorragia.

The infection and traumatic rate in these two groups were compared using the chi-squared test.

Results

Of the 363 eligible patients enrolled in this study, 181 patients had a 1-day antibiotic prophylaxis regimen and 182 patients had 3 days of antibiotic prophylaxis. The mean age and PSA serum levels were similar in each group Table 1. Mean number of biopsies and prostate volume were similar in both groups. Only two cases of septicemia, one in each group, were found. The first case involved a *serratia marcescens* septicemia following a 3-day antibiotic prophylaxis regimen. This patient received ciprofloxacin 12 hours and 1 hour prior to the procedure and continued this regimen for 2 additional days. The day following the prostate biopsies, the patient complained of chills and a fever up to 39ºC. He had no urinary symptoms. Blood cultures were positive for *serratia marcescens* sensitive to gentamycin and ciprofloxacin. Urinalysis and urine culture were both negative. He was hospitalized for 3 days and received ampicillin and gentamycin intravenously. Following this acute episode he received ciprofloxacin orally for a total of 14 days.

The second case of septicemia occurred in a patient receiving a 1-day antibiotic prophylaxis regimen. One week following TRUS, he was admitted to our institution for fever. Our medical and radiologic workup showed that the patient had developed endocarditis. He had no urinary symptoms. Urinalysis and urine culture were both negative. The cardiac surgeon involved in this case believed that the patient had a previously undetected valvular anomaly which predisposed the patient to endocarditis.

No symptomatic urinary tract infections were reported in this study Table 1. The overall incidence of hematospermia, hematuria and rectorragia was 58%, 62.3% and 18%, respectively.

There was neither clinically nor statistically significant difference regarding minor traumatic complications, which subsided within 4 weeks after the procedure.

TABLE 1. **Patients demographic, infection and traumatic rates in both groups.**

	1-day antibiotic prophylaxis	3-day antibiotic prophylaxis	p value
Number of patients	181	182	-
Patients age (yr)	65	68	
Mean PSA levels (ng/ml)	9.53	10.57	0.4667
Mean number of biopsies	8 (6-10)	8 (6-10)	> 0.99
Septiciemia	1	1	> 0.99
Hematospermia (%)	111 (61.3)	101 (55.5)	0.4
Hematuria (%)	130 (71.8)	111 (61.0)	0.1
Nectorragia (%)	37 (20.4)	30 (16.5)	0.2

PSA: prostatic specific antigen
UTI: urinary tract infection

Discussion

Transrectal ultrasound (TRUS) guided prostate biopsy is a commonly performed procedure. Most complications related to the biopsies are minor and require no treatment.[6,9] However serious infectious complications may occur. In order to prevent these complications antibiotic prophylaxis is generally recommended. Administration of prophylactic antibiotics results in a lower incidence of post biopsy febrile episodes,[1-3,8,10,11] positive urine cultures[4,5] and bacteremia.[4,6]

However no standard prohylactic regimen has been determined. Most authors advocate the use a fluoroquinolone. In his literature review Taylor concluded that oral ciprofloxacin is effective, inexpensive and well tolerated at reducing the incidence of bacteremia and clinical sepsis following TRUS prostate biopsies.[7]

Janoff et al[8] showed that six doses of ciprofloxacin appear to be more effective than four doses in reducing the clinical and febrile infection rate following ultrasound guided biopsy of the prostate.

In order to better determine the optimal use of fluoroquinolone prophylaxis we conducted a prospective randomized open-label study to compare whether a 3-day antibiotic prophylaxis is more effective in reducing infection complication rate than a 1-day regimen.

A total of 363 patients underwent TRUS guided prostate biopsies and were randomized to receive either a 1 day or a 3 day fluoroquinolone prophylactic regimen. The first dose of antibiotic was given at least 1 hour prior to biopsy. Patient evaluation was done by telephone 7 days after the biopsy. Patients were questioned as to whether they experienced chills, fever, dysuria, voiding difficulty, hematuria, hematospermia or rectorragia.

In our study hematospermia and hematuria were the most common complaints and occured in more than half of the patients. The overall incidence of hematospermia, hematuria and rectorragia was 58%, 62.3% and 18%, respectively. These symptoms disappeared after a few weeks in all patients.

Our study found two serious infections with one case of septicemia and one case of endocarditis. Although this represents a low infection rate (less than 1%) these major complications underline the need for antibiotic prophylaxis when performing TRUS guided prostate biopsies. We believe these two cases occurred from our trans-rectal biopsies and not from an underlying urine infection because both patients had positive blood cultures with negative urine cultures. No symptomatic urinary tract infections were reported in this study Table 1. While our symptomatic urinary tract infection rate seems lower than what is found in the literature, our febrile infection rate corresponds to the reported range.[8] In a study conducted by Griffith et al,[12] a single dose levofloxacin prophylaxis was administered for prostate biopsy in patients at low risk. The overall infection rate was 1 of 400 cases (0.25%). Routine blood or urine cultures were not performed because the study aim was to detect clinically apparent urinary tract infection, not the bacteriuria or bacteremia rate.

Conclusions

Based on these results of this study there appears to be little benefit in continuing prophylactic

fluoroquinolone antibiotics for longer than 1 day in patients undergoing TRUS guided biopsies. Most complications related to the biopsies are minor and require no treatment. Our study found two serious infections in 363 patients with one case of septicemia and one case of endocarditis. Although this represents a low infection rate (less than 1%) these major complications underline the need for antibiotic prophylaxis when performing TRUS guided prostate biopsies. We believe these two infections occurred from our trans-rectal biopsies and not from an underlying urine infection because both patients had positive blood cultures with negative urine cultures. □

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