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Original Article

Optimizing prophylactic antibiotic regimen in patients admitted for transrectal ultrasound-guided prostate biopsies: A prospective randomized study

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ABSTRACT

Background: Transrectal ultrasound-guided prostate biopsies (TRUSBx), in spite of being one of the most frequently performed urological office procedures, are associated with a spectrum of complications, most significantly including infection. The aim of the study is to evaluate the prevalence of fluoroquinolone-resistant bacteria in rectal swabs from our local population prior to TRUSBx and to identify risk factors among a patient population harboring fluoroquinolone-resistant organisms.

Methods: We prospectively included 541 men who were submitted for TRUSBx in our center from March 2011 to June 2015. The indications for TRUSBx were an elevated prostate-specific antigen level and/or abnormal digital rectal exam. All patients were randomly divided into two groups: Group 1 (n = 279 cases) who received standard empirical prophylactic antibiotics and Group 2 who received targeted prophylaxis based on a rectal swab culture and susceptibility result. Differences in risk factors between quinolone-resistant and nonresistant patients were compared. Univariate and multivariate analyses were performed to identify independent potential risk factors associated with fluoroquinolone-resistant rectal flora.

Results: Sixteen out of 271 men developed infectious complications after TRUSBx in the group receiving standard empirical prophylaxis (5.7%). No men in the group who received targeted prophylactic antibiotic guided by rectal swab developed infectious complications. Among the 262 patients who underwent prebiopsy rectal swab cultures, 76 men (29%) displayed fluoroquinolone-resistant rectal flora (29%). In the multivariate analysis, a history of antibiotic exposure before prostate biopsy was the only independent factor associated with an increased risk of fluoroquinolone resistance.

Conclusion: Determining the prevalence of fluoroquinolone resistance in rectal flora has important implications in the selection of targeted prophylactic antibiotic regimens. Antimicrobial profiles guided by rectal swabs may prove useful to optimize prophylaxis prior to TRUSBx; this strategy is effective at reducing the rates of infectious complications, including sepsis, especially in men at higher risk of infectious complications.

1. Introduction

Transrectal ultrasound-guided prostate biopsies (TRUSBx), in spite of being a frequently performed urological procedure, are associated with a spectrum of complications, most significantly including infection, which affects up to 5% of patients.[1] In the most severe cases, infection leads to sepsis, which poses significant morbidity to patients with inpatient hospital stays, intensive care requirements, and even death. *Escherichia coli* is the pathogen most commonly associated with infections after TRUSBx.[2–4]

Antibiotic prophylaxis with fluoroquinolones (FQ) is currently used on a regular routine basis for preventing sepsis after TRUSBx because of its broad spectrum activity against gram-positive and gram-negative organisms and the convenience of using an oral agent with a high sustained concentration in urine and prostate tissue;[5–7] however, there is growing evidence that the infection rate after TRUSBx is on the rise and it continues to be a problem, frequently caused by an increasing prevalence of FQ-resistant organisms.[8–12]

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In an attempt to reduce the rate of infectious complications, there are an increasing number of publications citing different prophylaxis regimens.[13–15] The aim of this study is to evaluate the prevalence of FQ-resistant bacteria in rectal swabs from men presented to the outpatient department at Alexandria University Hospital, Egypt, prior to TRUSBx and to identify the risk factors among a patient population harboring FQ-resistant organisms.

2. Materials and methods

We prospectively included 541 men who were submitted for TRUSBx in our center from March 2011 to June 2015. All patients were randomly divided into two groups: Group 1 ($n = 279$ cases) who received standard empirical prophylactic antibiotic with oral ciprofloxacin 500 mg and metronidazole 500 mg at least 1 hour before biopsy and continued this twice daily for 3 days (a total of 6 doses of each antibiotic) and Group 2 who received targeted prophylaxis based on a rectal swab culture and susceptibility results performed 1 week before TRUSBx provided in a 3-day regimen on the day before the biopsy, the day of the biopsy, and the day after the biopsy (Fig. 1).

Sealed opaque envelopes were used as the method of randomization which were placed into a box and mixed. Allocation concealment was achieved using an independent person ("biopsy nurse") who selected one of the sealed opaque envelopes blindly. Thus patients were randomly allocated to Group 1 or Group 2 before the procedure. The study was approved through the Institutional Review Board.

Demographic data were obtained for all patients, as well as diabetic status, recurrent urinary tract infections (UTI), presence of a urinary catheter, prior FQ exposure within 6 months before the biopsy, and past TRUS biopsies (Table 1). The results of rectal swabs and infectious complications within 30 days of the biopsy were also recorded. The definition of post-TRUSBx infection was distinct clinical presentations, including fever > 38.5°C, UTI, pyelonephritis, bacteremia, prostatitis, systemic inflammatory response syndrome, and sepsis. The indications for TRUS biopsies were an elevated prostate-specific antigen level (PSA) and/or abnormal digital rectal exam. All TRUSBx were performed at our institution in an office-based setting.

2.1. TRUSBx technique

All patients provided informed consent before the biopsy after they had been instructed by the physician regarding all possible complications. Patients were strictly advised not to take nonsteroidal anti-inflammatories and anticoagulant medications for a week before the application.

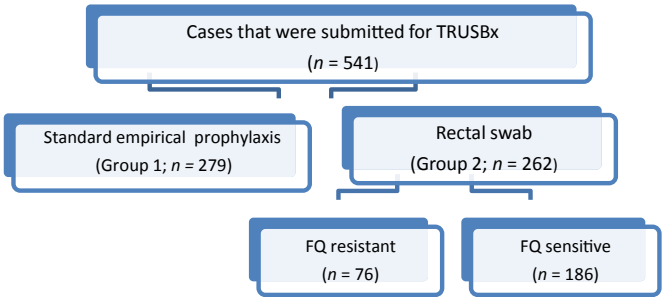

Fig. 1. Study cases. FQ, fluroquinolones; TRUSBx, transrectal ultrasound-guided prostate biopsies.

A standard prebiopsy preparation was applied for all patients. No enema was used. Patients only fasted the night before. The biopsy procedure was carried out under local periprostatic anesthesia. TRUS-guided biopsies were achieved through transrectal ultrasonography using a 7-MHz probe attached. Biopsies were carried out with the patient in the left decubital position using an automated biopsy gun with a disposable 18-G biopsy needle.

All biopsies were carried out through a systematic approach (a standard 12-core biopsy taken from the base, mid gland, and the apex of the right and left sides of the lateral and far-lateral peripheral zone). Two transitional zone biopsies were added in cases of a previous history of negative biopsies.

Patients were advised to present to the emergency department if they developed symptoms of sepsis within 30 days of the biopsy.

All patients with sepsis, as defined as fever > 38°C in the presence of constitutional symptoms, were admitted for inpatient management. Empiric treatment with meropenem 1 g [intravenous (i.v.)] twice daily was commenced after collecting blood and urine for culture.

The main outcome criterion was the incidence of bacteriuria (defined as $\geq 10^3$colony-forming units/mL) within 30 days of biopsy. Secondary endpoints included the incidence of clinical symptoms of fever, flushing, chills, or any weakness on physical examination and UTI, defined as the association of leukocyturia (>5 cells/high-power field) and bacteriuria, or any significant change in the biological results suggesting an infection including a blood cell count and C-reactive protein.

2.2. Statistical analysis

Differences in risk factors between quinolone-resistant and nonresistant patients were compared using a Fisher exact test with statistical significance ascribed at $P < 0.05$. Univariate and multivariate analyses were performed to identify independent potential risk factors associated with FQ-resistant rectal flora. Statistical analyses were performed with SPSS version 21.0 (SPSS Inc., Chicago, IL, USA) statistical software package.

3. Results

The mean age of patients was 63.6 years and 65.2 years in Group 1 and Group 2, respectively ($P = 0.4$).There was no difference in mean PSA value ($P = 0.62$) or age-adjusted Charlson comorbidity score ($P = 0.25$) between the two groups.

Sixteen men out of 279 men developed infectious complications after TRUSBx in the group receiving standard empirical prophylaxis (5.7%) in the form of fever and pyelonephritis including two cases of sepsis. None of the two men admitted for sepsis required intensive care treatment and all were successfully managed with i.v. fluids and i.v. meropenem (1 g twice daily). No men in the group who received targeted prophylactic antibiotic guided by rectal swab developed infectious complications. This result was statistically significant ($P = 0.003$). Culture and susceptibility results for the two men with sepsis demonstrated FQ resistant extended-spectrum β-lactamase-producing *Escherichia coli*.

Among the 262 patients who underwent prebiopsy rectal swab cultures, 76 men (29%) displayed FQ-resistant rectal flora (29%). Of the 76 bacterial isolates, 84.2% were *E. coli* and 10.5% were *Klebsiella pneumonia*. Antimicrobial susceptibility testing to FQ-resistant strains obtained by rectal swab showed the highest resistance notably to cotrimoxazole (85%), followed by cefotaxime (63%), and the highest sensitivity shown to carbapenems (92.1%), fosomycin (85.5%), amikacin (79%), followed by nitrofurantoin (63%), and sulbactam/cefoperazone (42.1%; Fig. 2).