DETECTION OF FLUOROQUINOLONE-RESISTANT BACTERIA PRIOR TO TRANSRECTAL PROSTATE BIOPSY: ANALYSIS OF STOOL SAMPLES FACILITATES TARGETED PROPHYLAXIS

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ABSTRACT

Aims: *We used faecal culture to determine the prevalence of fluoroquinolone-resistant Escherichia coli in the intestinal flora of patients undergoing prostate biopsies. We sought to use faecal culture results to choose appropriate prophylaxis prior to prostate biopsy. In addition, we identified fluoroquinolone-resistant E. coli strains in faecal cultures, and the sensitivities thereof to other drugs that could be used for prophylaxis.*

Materials and methods*: This study included a total of 108 patients, who were subjected to a prostate biopsy on suspicion of prostate cancer; patients ranged in age from 46-74 years. Patients with histories of prostate biopsy and/or prostate surgical operations were excluded. Faecal culture results were obtained for each patient prior to biopsy, and infections occurring after biopsy were recorded. Patients were divided into two groups: those with fluoroquinolone-resistant E. coli strains, and those with fluoroquinolone-susceptible E. coli strains. The two groups were compared in reference to age, prostate-specific antigen level, and antibiotic use in the prior 6 months.*

Results*: E. coli strains were identified in 84 of the 108 patients for whom faecal culture results were available. In 20 such patients, fluoroquinolone-resistance was evident. No infectious complication developed in any patient. Mean patient age, median prostate specific antigen level prior to biopsy (lg/L), and use of fluoroquinolones <6 months prior to biopsy were analysis as possible risk factors. However, no significant difference between patients with fluoroquinolone-resistant and fluoroquinolone-susceptible E. coli was evident.*

Conclusion*: We found high numbers of fluoroquinolone-resistant E. coli in faeces collected prior to prostate biopsy. Thus, fluoroquinolones should not be used for prostate biopsy prophylaxis. We found no difference in the extent of quinolone-resistance in patients graded by age, prostate specific antigen level, or antibiotic use in the prior 6 months. In risky cases, faecal culture results may be used to choose appropriate prophylaxis.*

Key words*: Prostate biopsy, antibiotic prophylaxis, fluoroquinolon- resistance, Escherichia coli, complications.*

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Introduction

Transrectal ultrasound-accompanied biopsy is the gold-standard procedure for histological diagnosis of prostate cancer[1]. Several reports have shown that antibiotic prophylaxis reduces the frequency of infectious complications developing after prostate biopsy[2, 3]. However, inappropriate and excessive antibiotic use in prophylaxis causes development of bacterial resistance, and leads to financial expenditure[4]. The American Urological Association (AUA) and the European Association of Urology (EAU) recommend fluoroquinolone as the drug of first choice for prostate biopsy prophylaxis[5, 6]. Several studies have recently reported increases in complication rates caused by infection after prostate biopsy. A 4-fold increase was observed over 10 years from 1996 to 2005, primarily attributable to a rise

in the levels of infection-related complications. Although fluoroquinolones continue to be the most commonly used antibiotics, as recommended by the EAU, the most likely cause of the increased infection frequency is bacterial antibiotic resistance[7]. Recent study in occur, fluoroquinolone-resistant Escherichia coli has emerged as an important pathogen in the setting of post-biopsy sepsis, E. coli bloodstream isolates reporting fluoroquinolone resistance in 62% of post-transrectal ultrasound (TRUS) biopsy blood isolates, compared with 14% of blood isolates from other males within the same population (P<0.001)[8].

Furthermore, patients presenting with infectious complications, thus already colonized with infectious agents, may be at higher risk of infection. Antibiotic-resistant microorganisms from the intestinal flora may infect the bladder and bloodstream during prostate biopsy. An earlier report described prophylaxis choice based on the results of rectal swab cultures performed prior to prostate biopsy[9]. However, rectal swabbing is invasive. We suggest that faecal culture (of stool samples) can yield equivalent data. In the present study, we determined the prevalence of fluoroquinolone-resistant *E. coli* in the intestinal flora of patients undergoing transrectal ultrasonography-guided prostate biopsies accompanied by stool sampling. In addition, we evaluated whether stool data could be used to choose appropriate prophylaxis prior to prostate biopsy.

Materials and methods

This retrospective study included 108 of 126 patients who underwent a prostate biopsy between April 2012 and January 2014, under suspicion of prostate cancer, and who ranged in age from 46-74 years (mean age: 61.4 years). A stool sample was obtained from each patient 3-7 days before prostate biopsy. Postoperative infections were recorded. All patient specimens were barcoded to ensure anonymity; patients were identifiable only by specimen barcode/number. Only one stool sample was collected from each patient.

Stool samples were cultured on standard sheep blood (SB) and Eosin Methylene Blue (EMB) agar. Bacterial identification and assessment of antimicrobial susceptibilities were achieved using both the VITEK 2 automated system (bio-Mérieux, Marcy-l'Étoile, France), and conventional microbial diagnostic techniques analyzing the cultural, physiological, and biochemical characteristics of bacterial strains, and antimicrobial susceptibilities based on guidelines of the Clinical and Laboratory Standards Institute (CLSI S100 M20; 2010). Antibiogram quality control was ensured by evaluating reference American Type Culture Collection strains recommended by the CLSI.

Patients with histories of prostate biopsy and/or prostate surgical operations were excluded. Also, those who did not follow antibiotic prophylaxis guidelines, and those who had been hospitalized in the prior 6 months for any reason, were excluded.

Prostate biopsy

Biopsy was achieved transrectally (using a 12-core needle array) under ultrasound guidance employing a fully automated biopsy gun fitted with 18-Gauge needles, with patients in the lateral decubitus position. We commenced 5-day ciprofloxacin treatment (2x500 mg daily) on the night before operation. We prescribed targeted prophylaxis (cephalosporin, tetracycline), informed by the results of faecal cultures in patients exhibiting microbial quinolone-resistance.

Patients were divided into two groups: those with quinolone-resistant bacteria, and those with quinolone-susceptible bacteria. All postoperative complications were recorded. The two groups were compared in terms of age, prostate-specific antigen (PSA) level, and antibiotic use in the prior 6 months. Descriptive statistics were recorded, Mann-Whitney U test and Fisher's exact test were used to compare between-group differences with the aid of statistical package for the social sciences (SPSS) version 17.0 (SPSS Inc., Chicago, IL USA). The level of significance was set at $p < 0.05$.

This was a clinical chart-based study; we did not meet with any patient. All patient information and culture data were carefully excerpted from clinical and laboratory reports.

Results

We obtained stool samples from 108 of 126 patients, and in 84 culture-positive patients, *E. coli* was the dominant microorganism. In 20 (23.7%) of these patients, fluoroquinolone-resistance was evident (Table 1). No infections were noted in these patients.

Mean age, median PSA level before biopsy (lg/L), and use of fluoroquinolones <6 months

before biopsy were analyzed as possible risk factors, but no significant difference was evident between the two groups (Table 2).

Drug	Number	%
Ciprofloxacin	20	23.7
Ampicillin	13	15.4
Gentamicin	8	9.5
Ampicillin-sulbactam	6	7.1
Ceftazidime	2	2.3
Cefazolin	2	2.3
Amikacin	1	0.8

Table 1: *E. coli* drug-resistance rates in faecal cultures.

Properties	sensitive (N. 64)	resistant (N: 20)	*p*
Mean age (years)	61,9	61,4	0.788
Median PSA level before biopsy (lg/L)	7,2	7,4	0.678
Use of fluoroquinolones <6 months before biopsy	14	5	0.781

Table 2: Risk factors for the presence of fluoroquinolone (Ciprofloxacin)-resistant microorganisms.
PSA: prostate specific antigen

Discussion

The gastrointestinal (GI) tract is the natural reservoir of *E. coli*, and antibiotic use (for any reason) may alter the GI flora profile[10,11]. Quinolone-resistance of *E. coli* strains in the rectal flora may be a risk factor for development of infectious complications after prostate biopsy[12]. The levels of antibiotic-resistant *E. coli* are increasing worldwide, and the widespread use of fluoroquinolones has triggered the emergence of fluoroquinolone-resistant *E. coli*.

A 2006 study of infections developing after prostate biopsy reported fluoroquinolone-resistance rates of up to 90% in causative *E. coli* strains[13]. This means that appropriate antimicrobial agents must be selected for prophylaxis and treatment of biopsy-associated infections. Detection of rectal colonize with fluoroquinolone-resistant *E. coli* is of critical importance to prevent infections by these bacteria after prostate biopsy.

The role of antimicrobial prophylaxis in preventing infections after prostate biopsy is well-established. Although many antimicrobial regimes have been suggested, fluoroquinolones are the most commonly used prophylactic materials. Several recent studies have highlighted the alarming increase in the extent of fluoroquinolone-resistance, rendering fluoroquinolones unsuitable as prophylactics. It is possible that increases in the extent of resistance to ciprofloxacin and other antimicrobials will greatly influence the success of prophylactic antimicrobial therapy. Thus, studies of the local prevalence of antimicrobial-resistance traits are essential to guide such choices[13-19].

Strong correlations were evident between the antimicrobial sensitivities of coliforms from rectal swabs and those cultured from urine or blood. Almost 15% of patients with ciprofloxacin-resistant coliforms in rectal swabs became infected with ciprofloxacin-resistant organisms[20,21]. If the antimicrobial sensitivity of organisms isolated from rectal swabs and urine or blood differ, it is likely that rectal swabbing may not have sampled all of the gastrointestinal flora, or that the laboratory methods used had certain limitations. It is also possible that infectious organisms were not derived from the GI tract.

Infectious complication rates after prostate biopsy have risen in recent years[13, 22], and targeted prophylaxis has been recommended to deal with this problem[9, 23]. Taylor et al.[9] found no infectious complications in 112 patients from whom rectal swabs had been obtained, but 9 such complications (1 which one was sepsis) were observed in 345 patients given prophylactic treatment. Taylor et al.[9] performed rectal swabbing 5-7 days before biopsy; again, this procedure is invasive. When rectal swabbing is performed at the same time as biopsy, results are available in 24-72 h; thus, targeting of prophylaxis is not possible. We used faecal culture results to plan prophylaxis.

Rectal swabs are taken immediately prior to biopsy. Rectal swab culture is not easy, may not reveal all colonic flora, and distresses patients. However, stool samples are readily obtained and stool culture results are very reproducible. Periodic culture of rectal swabs or stool samples from populations exhibiting high or increasing rates of antimicrobial resistance would be appropriate.

We found high levels of fluoroquinolone-resistant *E. coli* in stool samples obtained prior to

prostate biopsy. Thus, in risky cases, faecal culture data may be useful to prescribe appropriate prophylaxis. Faecal cultures identify organisms causing gastrointestinal symptoms and disease.

Lower urinary tract symptoms (LUTS) are noted in males over the age of 50 years, and the incidence increases with age[24]. The most frequent cause of LUTS is benign prostate hyperplasia. However, all of prostate cancer, narrowing of the urethra, neurological disorders, urinary tract infection, and diabetes mellitus may cause LUTS[25]. The frequency of such symptoms renders diagnosis difficult, and especially on first presentation, triggers unnecessary antibiotic prescription to older geriatric males[26]. The extent of quinolone-resistance increased with prescription of quinolones in the prior 6 months[27]. However, we did not detect any significant association between quinolone use in the prior 6 months and quinolone-resistance in prostate biopsy patients.

In conclusion, we believe that stool samples should be cultured prior to prostate biopsy to screen for fluoroquinolone-resistant *E. coli*. This is easy to do and eliminates the embarrassment associated with rectal swabbing. We found high numbers of fluoroquinolone-resistant *E. coli* in faecal cultures performed prior to prostate biopsy. Thus, fluoroquinolones should not be preferred for prostate biopsy prophylaxis. We found that patient age, PSA level, or antibiotic use in the prior 6 months did not affect the levels of quinolone-resistant bacteria. In risky cases, faecal culture data may be useful for choosing the appropriate prophylaxis.

Study Limitations

Relatively small population is the major limitation of this study. Although our results occur high numbers of fluoroquinolone-resistant *E. coli* in faecal cultures, this finding should be better investigated through well designed, prospective and randomized trials, possibly performed in larger cohorts.

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