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Detection of Fluoroquinolone-Resistant Organisms from Rectal Swabs by Use of Selective Media Prior to a Transrectal Prostate Biopsy▽

Michael A. Liss,[1] Amy N. Peeples,[2] and Ellena M. Peterson[2]*

Department of Urology, University of California, Irvine,[1] and Department of Pathology and Laboratory Medicine, University of California, Irvine,[2] Irvine, California

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Sepsis caused by fluoroquinolone-resistant *Escherichia coli* is a risk for patients undergoing an ultrasound-guided, transrectal prostate biopsy. A method incorporating selective broth and media was evaluated using rectal swabs obtained from 136 patients prior to a biopsy procedure. Fluoroquinolone-resistant organisms were isolated from 22% of the patients included in this study.

Transrectal ultrasound-guided biopsy is the standard procedure for the histological diagnosis of prostate carcinoma, and approximately 800,000 biopsies are performed in the United States each year (4). Infectious complications from the prostate biopsy, which include urinary tract infections, prostatitis, and sepsis, have increased substantially every year (3, 5, 6, 10, 12, 15). The most common organism responsible for these infectious complications is *Escherichia coli* (3, 6, 15). It is proposed that the resistant organisms are introduced into the bladder and bloodstream from the rectum during the biopsy procedure. Since fluoroquinolones are common antibiotics administered before the procedure, patients already colonized with these resistant organisms may be at higher risk for infection (13). A logical approach to providing accurate prophylaxis is to identify the patients that are harboring the resistant bacteria by culturing rectal swabs prior to the biopsy. Previous studies investigating the prevalence of quinolone-resistant organisms by using rectal swabs or fecal specimens have mainly used solid media containing low levels of a fluoroquinolone (1, 9, 11). The aim of this study was to develop a laboratory method to identify patients undergoing a transrectal biopsy colonized with even small numbers of *E. coli* organisms resistant to the fluoroquinolones.

From January 2009 to March 2010, 136 male patients undergoing ultrasound-guided, transrectal prostate needle biopsy participated in the study. The patients underwent antibiotic prophylaxis prescribed by the performing physician, all of which included ciprofloxacin 500 mg, except for 3 participants (Table 1). In regards to bowel preparation, 88 (65%) of the patients used a single (Bisacodyl) suppository the morning of the biopsy, and 42 (31%) had an enema. Univariate analysis showed no statistical difference as to the rate of isolating fluoroquinolone-resistant organisms relative to the antibiotic regimen ($P = 0.381$) or bowel preparation ($P = 0.589$). The study group consisted of men over the age of 35 years, with a median age of 65 years. Of these, 103 men had undergone previous transrectal prostate biopsies (median of 3), which likely increases the exposure to fluoroquinolones. The study was carried out at three separate institutions, the University of California, Irvine, Long Beach Veterans Affairs Medical Center, and Kaiser Permanente Orange County, and these sites contributed 36 (26%), 61 (45%), and 39 (29%) patients, respectively. Institutional review board approval was obtained from all participating institutions, as was patient informed consent.

Patients were prepared for the biopsy, and a rectal swab was obtained by the physician immediately prior to the biopsy. Upon collection, swabs were placed into 5 ml of brain heart infusion (BHI) broth containing 10 μg/ml of ciprofloxacin (Hardy Diagnostics, Santa Maria, CA), transported at room temperature to the laboratory, and incubated overnight at 35°C in ambient air. Subsequently, the broth was subcultured to MacConkey agar and MacConkey and HardyCHROM ECC agars, both containing 10 μg/ml ciprofloxacin (Hardy Diagnostics). Plates were inoculated with 0.1 ml of the broth culture and incubated overnight at 35°C in ambient air. All organisms recovered were characterized on Vitek I or Vitek II using GNI, GN, AST-GN-140, and AST-GN-30 cards (bioMérieux, Durham, NC) for identification or susceptibility testing, respectively.

Of the 136 study patients, upon broth enhancement of the rectal swabs, 30 patients (22%) had positive cultures, and all but one showed a heavy growth of *E. coli*. A *Brevundimonas* species was recovered from one patient. Phenotypically, the cultures grown on the three plates were identical from an individual patient; therefore, different strains of *E. coli* from a given patient's sample were not apparent. MacConkey agar both with and without ciprofloxacin gave similar results in terms of the number of organisms present. All *E. coli* isolates recovered had MICs to ciprofloxacin and levofloxacin of ≥4 μg/ml and ≥8 μg/ml, respectively (Table 2).

In this sample set, there was no difference based on whether the solid media used to subculture the specimen contained ciprofloxacin, since all media yielded the same result. However, a future goal is to obtain rectal cultures prior to the administration of prophylactic antibiotics to avoid administering a fluoroquinolone to patients already colonized with fluoroquinolone-resistant organisms. Since normal stool flora may obscure fluoroquinolone-resistant organisms in patients not on prophylactic antibiotics, we wanted to determine if it was necessary to incorporate a fluoroquinolone into the solid media

* Corresponding author. Mailing address: Department of Pathology and Laboratory Medicine, University of California, Irvine, Medical Science Building, D-440, Irvine, CA 92697-4800. Phone: (949) 824-4169. Fax: (949) 824-2160. E-mail: epeterso@uci.edu.

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TABLE 1. Antibiotic prophylaxis of the 136 participants

Antibiotic prophylaxis regimen	No. of patients in group	No. of patients with positive screen culture for *E. coli*
Ciprofloxacin 1 dose prior (with gentamicin)	30	6
Ciprofloxacin 1 dose prior (without gentamicin)	8	0
Ciprofloxacin 3 doses prior	91	21
Trimethoprim-sulfamethoxazole	1	0
Piperacillin-tazobactam	1	1
Ciprofloxacin and clindamycin	1	0
Cefuroxime and gentamicin	1	1
Ciprofloxacin, gentamicin, and amoxicillin	2	0
Ciprofloxacin and metronidazole	1	0

TABLE 2. Antibiogram of 29 fluoroquinolone-resistant *E. coli* isolates

Antibiotic	No. of isolates		
	Susceptible	Intermediate	Resistant
Amikacin	29	0	0
Ampicillin	2	1	26
Ampicillin-sulbactam	6	17	6
Cefazolin	23	0	6
Cefepime	27	0	2
Ceftazidime	27	1	1
Ciprofloxacin	0	0	29
Gentamicin	19	0	10
Imipenem	29	0	0
Levofloxacin	0	0	29
Nitrofurantoin	29	0	0
Piperacillin-tazobactam	26	3	0
Tobramycin	15	8	6
Trimethoprim-sulfamethoxazole	18	0	11

used for the subculture of the selective broth. To address this question, fecal specimens from 9 stool samples from patients not currently on a fluoroquinolone were used to compare both approaches. Prior to broth selection, a sample of the specimen was plated onto MacConkey agar without antibiotic. The quantity of growth was evaluated from 1+ to 4+, light to heavy, respectively. Upon overnight incubation in BHI broth containing ciprofloxacin, 10 μg/ml, cultures were subcultured to MacConkey agar with and without 10 μg/ml ciprofloxacin. There was no breakthrough of normal flora in the 4 specimens that had 2+ or 3+ growth prior to broth selection. However, all 5 specimens with 4+ growth prior to broth selection had growth on MacConkey agar without ciprofloxacin, while there was no growth on MacConkey agar with ciprofloxacin. One *E. coli* phenotype from each of the specimens with breakthrough growth on the MacConkey agar was tested for ciprofloxacin susceptibility, and all were found to be susceptible. Therefore, use of both broth and solid media in which ciprofloxacin has been incorporated may provide the optimal conditions for the identification of ciprofloxacin-resistant organisms, especially from specimens with a heavy growth of normal stool flora, which may occur prior to prophylaxis with antibiotics. In addition, while a high concentration of ciprofloxacin incorporated into the broth, as used in this evaluation, may be necessary especially for those specimens with a heavy amount of normal flora, we may be able to decrease the concentration in the plates so as to detect isolates with MICs to ciprofloxacin between 4 μg/ml and 10 μg/ml. We did not find that incorporation of a chromogenic medium incorporating ciprofloxacin, such as the one used in this study, i.e., HardyCHROM ECC agar, added any value over MacConkey agar containing ciprofloxacin.

A transrectal prostate biopsy is one of the most common procedures performed by urologists and confirms the diagnosis of prostate cancer (4). Unfortunately, there is no current method to provide patient-specific directed prophylaxis prior to a transrectal prostate biopsy. The intestine/rectal flora is a likely source of the resistant organisms being introduced into the bloodstream at the time of the biopsy and is the logical site to isolate bacteria which may be a future offending organism. In this study, we used rectal swabs, since they have been shown by others to have comparable sensitivity and specificity to the gold standard, fecal specimens, for the detection of fluoroquinolone-resistant *E. coli* from the intestine (8). Many groups have monitored the prevalence of fluoroquinolone-resistant organisms by using rectal or fecal specimens (2, 7, 14). One recent study with 445 patients undergoing prostate biopsy reported a rate of 10.6% resistance to ciprofloxacin (1). Rectal specimens were plated directly to CLED agar without antibiotics (Oxoid, Basingstoke, United Kingdom). Two patients became septic with ciprofloxacin-resistant *E. coli* after the biopsy. Only one patient had a positive rectal culture prior to the biopsy. This brings into question whether the culture procedure, which did not incorporate a selective broth or plate, missed low numbers of this resistant organism. We have shown that even after a 24-h incubation in BHI broth with ciprofloxacin, normal flora were recovered on MacConkey agar without antibiotics. Therefore, the use of both broth enrichment and agar containing ciprofloxacin, thereby limiting growth of normal flora, may facilitate the isolation and identification of fluoroquinolone-resistant enteric bacteria.

In the present study, the sample size is relatively small, 136 patients, and we selected only organisms with a high level of resistance to the quinolones, owing to the concentration of ciprofloxacin incorporated into the media. However, we propose that the protocol outlined here be used in further investigations of a larger patient population to evaluate the utility, cost, and benefit of this screening test. Our long-term goal is to provide appropriate prophylactic antibiotic coverage to prevent sepsis following a transrectal procedure. Therefore, identification of patients colonized with these isolates means that a culture be obtained at least 48 h prior to the prostate biopsy to afford the opportunity to tailor the antibiotic(s) administered prior to the procedure.

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REFERENCES

1. **Batura, D., G. G. Rao, and P. B. Nielsen.** 2010. Prevalence of antimicrobial resistance in intestinal flora of patients undergoing prostatic biopsy: implications for prophylaxis and treatment of infections after biopsy. BJU Int. **106:**1017–1020.
2. **Carratala, J., A. Fernandez-Sevilla, F. Tubau, M. A. Dominguez, and F.**

Gudiol. 1996. Emergence of fluoroquinolone-resistant *Escherichia coli* in fecal flora of cancer patients receiving norfloxacin prophylaxis. Antimicrob. Agents Chemother. **40:**503–505.
3. **Feliciano, J., et al.** 2008. The incidence of fluoroquinolone resistant infections after prostate biopsy—are fluoroquinolones still effective prophylaxis? J. Urol. **179:**952–955; discussion, 955.
4. **Hodge, K. K., J. E. McNeal, and T. A. Stamey.** 1989. Ultrasound guided transrectal core biopsies of the palpably abnormal prostate. J. Urol. **142:**66–70.
5. **Horcajada, J. P., et al.** 2009. High prevalence of extended-spectrum beta-lactamase-producing enterobacteriaceae in bacteremia after transrectal ultrasound-guided prostate biopsy: a need for changing preventive protocol. Urology **74:**1195–1199.
6. **Lange, D., et al.** 2009. Bacterial sepsis after prostate biopsy—a new perspective. Urology **74:**1200–1205.
7. **Lautenbach, E., et al.** 2006. Phenotypic and genotypic characterization of fecal *Escherichia coli* isolates with decreased susceptibility to fluoroquinolones: results from a large hospital-based surveillance initiative. J. Infect. Dis. **194:**79–85.
8. **Lautenbach, E., et al.** 2005. Test characteristics of perirectal and rectal swab compared to stool sample for detection of fluoroquinolone-resistant *Escherichia coli* in the gastrointestinal tract. Antimicrob. Agents Chemother. **49:**798–800.
9. **Maslow, J. N., E. Lautenbach, T. Glaze, W. Bilker, and J. R. Johnson.** 2004. Colonization with extraintestinal pathogenic *Escherichia coli* among nursing home residents and its relationship to fluoroquinolone resistance. Antimicrob. Agents Chemother. **48:**3618–3620.
10. **Nam, R. K., et al.** 2010. Increasing hospital admission rates for urological complications after transrectal ultrasound guided prostate biopsy. J. Urol. **183:**963–968.
11. **Nys, S., et al.** 2004. Antibiotic resistance of faecal *Escherichia coli* from healthy volunteers from eight developing countries. J. Antimicrob. Chemother. **54:**952–955.
12. **Tal, R., P. M. Livne, D. M. Lask, and J. Baniel.** 2003. Empirical management of urinary tract infections complicating transrectal ultrasound guided prostate biopsy. J. Urol. **169:**1762–1765.
13. **Wolf, J. S., Jr., et al.** 2008. Best practice policy statement on urologic surgery antimicrobial prophylaxis. J. Urol. **179:**1379–1390.
14. **Yagci, D., F. Yoruk, A. Azap, and O. Memikoglu.** 2009. Prevalence and risk factors for selection of quinolone-resistant *Escherichia coli* strains in fecal flora of patients receiving quinolone therapy. Antimicrob. Agents Chemother. **53:**1287–1289.
15. **Young, J. L., M. A. Liss, and R. J. Szabo.** 2009. Sepsis due to fluoroquinolone-resistant *Escherichia coli* after transrectal ultrasound-guided prostate needle biopsy. Urology **74:**332–338.