Comparative Effectiveness of Targeted vs Empirical Antibiotic Prophylaxis to Prevent Sepsis from Transrectal Prostate Biopsy: A Retrospective Analysis

Michael A. Liss, William Kim, Dena Moskowitz and Richard J. Szabo*

From the Departments of Urology, University of Texas Health Science Center San Antonio (MAL), San Antonio, Texas, and University of California-Irvine (WK, DM) and Department of Urology, Southern California Kaiser Permanente, Orange County (RJS), Irvine, California

Purpose: We compared the effectiveness of targeted prophylaxis to the effectiveness of empirical prophylaxis for preventing sepsis after transrectal prostate biopsy using a retrospective multicenter quality improvement study.

Materials and Methods: A total of 13 Kaiser Permanente urology departments participated in a 1-year retrospective analysis of a quality improvement study. In the targeted prophylaxis group rectal cultures were performed before transrectal prostate biopsy and antibiotic sensitivities of Escherichia coli were used to guide the selection of a single agent antibiotic for prophylaxis. Cultures were plated on 10 μg/ml ciprofloxacin infused MacConkey agar at a central laboratory. Urologists using empirical prophylaxis continued the usual regimen of ciprofloxacin monotherapy prophylaxis but sometimes added an additional prophylactic antibiotic. The primary outcome of post-biopsy sepsis was compiled by a search of the electronic medical record for the appropriate ICD-9 codes.

Results: A total of 5,355 prostate biopsy procedures were performed between May 1, 2013 and April 30, 2014. Targeted prophylaxis was used in 1,802 procedures (34%) and empirical prophylaxis was used in 3,553 (66%). The overall incidence of post-biopsy sepsis was 0.52% (28 of 5,355 cases). The incidence of sepsis was 0.44% (8 of 1,802 cases) in the targeted prophylaxis group and 0.56% (20 of 3,553) in the empirical prophylaxis group ($p = 0.568$). The prevalence of ciprofloxacin resistant E. coli on rectal culture was 25% (444 of 1,802 cases). Seven of the 8 patients (88%) on targeted prophylaxis in whom sepsis developed used a prophylactic antibiotic to which the bacteria causing post-biopsy sepsis were sensitive.

Conclusions: The targeted prophylaxis protocol enabled physicians to avoid using more than 1 broad-spectrum empirical antibiotic while simultaneously achieving an overall rate of sepsis similar to the rate seen with empirical prophylaxis.

Key Words: prostate; biopsy; antibiotic prophylaxis; fluoroquinolones; drug resistance, bacterial

Abbreviations and Acronyms

EP = empirical prophylaxis
FQ-R = fluoroquinolone resistant
TP = targeted prophylaxis
TRPB = transrectal prostate biopsy

Accepted for publication March 16, 2015.
Study received institutional review board approval.

* Correspondence: Department of Urology, Orange County, Southern California Permanente Medical Group, 6600 Alton Pkwy., Irvine, California 92618 (e-mail: Richard.Szabo@kp.org).

See Editorial on page 282.

For another article on a related topic see page 563.

Editor's Note: This article is the third of 5 published in this issue for which category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 602 and 603.

More than 1 million TRPBs are performed in Europe and the United States each year to determine whether patients have prostate cancer.[1–3] A significant proportion of complications of prostate biopsy include infections such as prostatitis, epididymitis and sepsis.[4,5]

0022-5347/15/1942-0397/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2015.03.110
Vol. 194, 397-402, August 2015
Printed in U.S.A.

Post-biopsy sepsis, most commonly due to FQ-R Escherichia coli, develops in 1% to 3% of procedures and this incidence is rising rapidly.[2,3,5–7] This has led to increased use of multiple broad-spectrum antibiotics for prophylaxis and this practice may accelerate the development of resistant bacteria.[8,9] In addition, there is a sevenfold increase in the risk of post-biopsy infection in patients who are found to have FQ-R organisms in the rectal flora.[10] Therefore, at some centers TP is used in an effort to reduce post-biopsy sepsis.

TP uses a preprocedure rectal swab culture using specialized media to detect any FQ-R E. coli present to guide prophylaxis based on sensitivity analysis.[11–13] Success with this regimen has only been described to date in small, single center studies with relatively few patients. We report rates of post-biopsy sepsis and patterns of antibiotic use among centers using TP and EP in a multicenter quality improvement initiative.

METHODS

Study Population

Kaiser Permanente Southern California is an integrated health care network of 13 medical centers serving 3.7 million members. Between May 1, 2013 and April 30, 2014 departments of urology at 5 centers participated in a 1-year quality improvement initiative using TP prior to TRPB while another 8 departments continued usual care with EP before TRPB. Decisions at the individual department level to participate in the TP protocol were made by a consensus of the urologists in each of those departments. However, physicians still had autonomy to practice their preferences. Institutional review board No. 10356 approval was obtained for a retrospective data analysis of an ICD-9 code generated data set.

Microbiology

The ESwab™ liquid based culture and transport system was used to sample stool from the anal canal or the tip of a glove used for digital rectal examination approximately 2 weeks prior to TRPB.[14] This was transported to the Kaiser Permanente Regional Reference Laboratory, where it was inoculated on MacConkey agar containing 10 μg/ml ciprofloxacin (Hardy Diagnostics, Santa Maria, California).[15] As a control the sample was also inoculated on blood, chocolate, CNA and regular MacConkey agar to ensure that enteric bacteria were indeed on the swab. If after the 24-hour incubation there was no growth on the ciprofloxacin infused MacConkey agar but there was growth of normal flora on the other agars, the rectal flora was assumed to be ciprofloxacin sensitive. Conversely any growth of gram-negative rods on the ciprofloxacin infused MacConkey agar was presumed to be ciprofloxacin resistant. A representative of each distinct colony morphotype was then run through the Vitek® 2 analyzer for identification by GN (gram-negative) cards and for sensitivity testing by AST (antibiotic susceptibility test) cards using Clinical and Laboratory Standards Institute Interpretive Criteria.[16]

Antibiotic Selection

Patients with negative cultures for ciprofloxacin resistant E. coli were instructed to take 500 mg ciprofloxacin orally 1 hour before biopsy and 12 hours later. For TP cultures identifying a ciprofloxacin resistant organism the urologist consulted the sensitivity profile and selected an appropriate antibiotic from a list derived from the AUA Best Practice Statement on Urologic Surgery Antimicrobial Prophylaxis and from the Northwestern Department of Urology targeted prophylaxis protocol (table 1).[17]

Urologists in the EP group did not use rectal swab cultures. They simply continued the usual practice of oral ciprofloxacin prophylaxis (monotherapy prophylaxis) with or without an additional, usually parenteral antibiotic (augmented prophylaxis). All patients in the 2 groups performed a Fleet® sodium phosphate enema the morning of prostate biopsy. Patients underwent standard 12-core prostate needle biopsy at all centers except at 1 TP center where 16-core biopsies were the norm. On occasion there were minor deviations from the TP or EP protocol by individual urologists regardless of the protocol chosen by the department.

Study Outcomes and Definitions

The primary outcome was the incidence of post-prostate biopsy sepsis within 30 days of prostate biopsy. The criteria for sepsis were guided by the 2001 International Sepsis Definitions Conference.[18] Septic outcomes were collated by querying the Kaiser Permanente multicenter HealthConnect® electronic medical records system for ICD-9 codes 995.91 and 995.92. Additionally, the charts of all patients hospitalized within 30 days of prostate biopsy were reviewed to avoid missing cases of sepsis due to incorrect coding or mistaken initial coding if sepsis was coded later during hospitalization. Each case of sepsis was scrutinized for accuracy by chart review. The secondary outcome was the choice of prophylactic antibiotic(s). The primary predictor variables were TP vs EP. Secondary predictor variables were medical center, patient age and race.

Statistical Analysis

Treatment groups were compared based on the actual EP or TP regimen regardless of the department decision on whether to participate in the TP quality improvement

Table 1. *Alternative medication list in TP group*

Medication Alternative	Dose	Schedule
Oral trimethoprim-sulfamethoxazole	Double strength	1 Tablet 1 hr before biopsy + 1 tablet 12 hrs after first tablet
Intramuscular:		Once 1 hr before biopsy
Ceftriaxone (mg)	500	
Gentamicin (mg/kg)	2	
Amikacin (mg/kg)	5	
Aztreonam (mg)	500	
Imipenem (mg)	500	
Intravenous:		Once 1 hr before biopsy
Ceftriaxone (mg)	2,000	
Gentamicin (mg/kg)	2	
Amikacin (mg/kg)	5	
Aztreonam (mg)	2,000	
Imipenem (mg)	1,000	