A Prospective Randomized Trial of Povidone-Iodine Prophylactic Cleansing of the Rectum Before Transrectal Ultrasound Guided Prostate Biopsy

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Abbreviations and Acronyms

DRE = digital rectal examination
ICU = intensive care unit
PSA = prostate specific antigen
TRUSBx = transrectal ultrasound guided prostate biopsy
UTI = urinary tract infection

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Purpose: Transrectal ultrasound guided prostate biopsy can lead to urinary tract infections in 3% to 11% and sepsis in 0.1% to 5% of patients. We investigated the efficacy of rectal cleansing with povidone-iodine before transrectal ultrasound guided prostate biopsy to reduce infectious complications.
Materials and Methods: Between 2009 and 2011, 865 men were prospectively randomized to rectal cleansing (421) or no cleansing (444) before transrectal ultrasound guided prostate biopsy. Patients received ciprofloxacin prophylaxis and rectal swab cultures were obtained before transrectal ultrasound guided prostate biopsy. Patients completed a telephone interview 7 days after undergoing the biopsy. The primary end point was the rate of infectious complications, a composite end point of 1 or more of 1) fever greater than 38.0C, 2) urinary tract infection or 3) sepsis (standardized definition). Chi-square significance testing was performed for differences between groups and a multivariate analysis was performed to assess risk factors for infectious complications.
Results: Infectious complications were observed in 31 (3.5%) patients, including 11 (2.6%) treated and 20 (4.5%) control patients ($p = 0.15$). Sepsis was observed in 4 (1.0%) treated and 7 (1.6%) control patients ($p = 0.55$). On multivariate analysis resistance to ciprofloxacin in the rectal swab culture ($p = 0.002$) and a history of taking ciprofloxacin in the 3 months preceding transrectal ultrasound guided prostate biopsy ($p = 0.009$) predicted infectious complications.
Conclusions: Rectal cleansing with povidone-iodine before transrectal ultrasound guided prostate biopsy was safe, but the 42% relative risk reduction of infectious complications was not statistically significant. Patients who have received ciprofloxacin within 3 months of transrectal ultrasound guided prostate biopsy should be considered for alternate prophylaxis or possibly a delay of biopsy beyond 3 months.

Key Words: prostate, biopsy, prostatic neoplasms, sepsis, urinary tract infections

Infectious complications associated with transrectal ultrasound guided prostate biopsies are a growing concern. More frequent complications are being observed[1,2] and the rate of resistance to commonly used antibiotics is increasing.[3,4] Infectious complications related to TRUSBx range from transient fever to UTI, sepsis and possible death. The rate of sepsis

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after TRUSBx is estimated to be between 0.1% to 5%, while UTIs occur in 3% to 11% of patients.[1–3,5–8] With more than 1 million transrectal ultrasound guided prostate biopsies performed annually in North America, every effort must be made to minimize the risks associated with this increasingly dangerous procedure. The harm incurred by TRUSBx is part of the justification for the recent recommendation of the U.S. Preventive Services Task Force against prostate cancer screening. The complications of TRUSBx are also a barrier to the adoption of active surveillance for prostate cancer. Therefore, it is important that we look at novel ways to reduce the occurrence of infectious complications after TRUSBx.

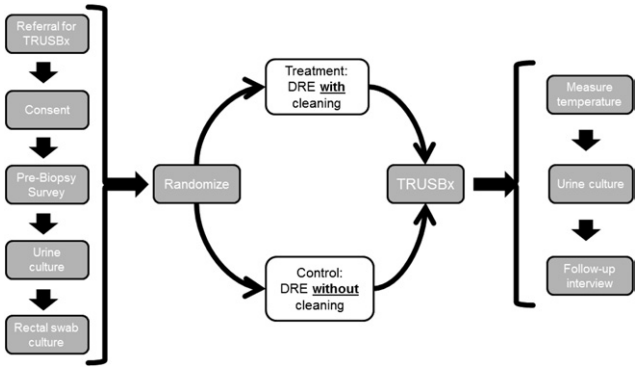
Efforts to reduce the risk of post-biopsy infectious complications have focused mostly on improving antibiotic prophylaxis. We propose that cleaning the rectum with povidone-iodine before insertion of the ultrasound probe will reduce the incidence of UTI and sepsis. Povidone-iodine is an inexpensive and widely available antiseptic appropriate for procedures performed through the rectum. Rectal cleansing with povidone-iodine has been demonstrated to be safe and effective in decreasing rectal flora counts preceding colorectal surgery[9] and transrectal natural orifice surgery,[10] and there is some evidence of efficacy before TRUSBx.[8,11] We hypothesized that povidone-iodine prophylactic cleansing of the rectum before TRUSBx would decrease the rate of infectious complications.

MATERIALS AND METHODS

All men referred for TRUSBx at Vancouver General Hospital between December 2009 and April 2011 were invited to participate in the trial. The study was approved by the human ethics committee of the University of British Columbia and registered at ClinicalTrials.gov (NCT00999427). All patients signed an informed consent before participating in the study.

Indications for biopsy included an increased PSA and/or abnormal DRE, as well as being on active surveillance and undergoing repeat biopsy. Men were excluded from study if they were unable to provide informed consent, or if they had an allergy to ciprofloxacin or iodine. At the start of the study period men were also excluded if they had received ciprofloxacin for another reason within 3 months preceding TRUSBx, if they had a history of bladder or prostate infection within 3 months preceding TRUSBx, or if they had a history of UTI or sepsis after TRUSBx. These last 3 exclusion criteria were implemented to ensure a homogenous patient population, but were later removed after enrolling the first 450 patients when it was noted that the infection rate was lower than anticipated.

The study design is summarized in the figure. All patients were asked to supply a urine sample for routine culture at the time the biopsy was scheduled (before starting antibiotic prophylaxis). Patients received extended release ciprofloxacin (1,000 mg) orally for 3 days starting the day before the biopsy. They were also instructed to instill a Fleet® enema at home approximately 2 hours before the biopsy. Immediately before the biopsy, a rectal swab was taken and sent for routine culture.



Study design

Patients were randomized into 2 groups. In the treatment group the anterior rectal wall over the prostate was cleansed using a thin layer of gauze soaked in povidone-iodine. The examiner used his/her index finger to wipe across the prostate at least 5 times from one lateral margin to the other. Two minutes were allowed to pass between this cleansing and the start of the biopsy. The control group underwent DRE without cleansing. There was no blinding. All prostate biopsies were performed transrectally using an 18 gauge Tru-Cut® needle under ultrasound guidance after local infiltration of bupivacaine. A variable number of cores was taken depending on prostate volume as determined on ultrasound, with 12 cores for prostate volume larger than 50 ml, 10 cores for 35 to 50 ml and 8 cores for less than 35 ml. All patients were discharged home after the biopsy with instructions to record oral temperature every 6 hours for 48 hours and to deliver a post-biopsy urine sample for culture after 48 hours. A structured telephone interview was conducted 7 days after the biopsy to ascertain whether any infectious or noninfectious complications had occurred. If a patient received medical attention in the intervening 7 days, the medical records were obtained and reviewed.

The primary end point of this study was the rate of infectious complications, which was defined as a composite of 1 or more of fever, UTI and sepsis. Fever was defined as oral temperature 38.0C or greater within 48 hours after biopsy. UTI was defined as more than 100 million cfu/L in urine culture obtained 48 hours after biopsy, associated with any clinical symptoms of UTI. Sepsis was defined by the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference as positive urine or blood culture plus 2 or more of the following criteria within 1 week of biopsy, that is temperature 38.0C or greater, or less than 36.0C; heart rate greater than 90 beats per minute; respiratory rate greater than 20 breaths per minute; white blood cell count greater than 12.0 or less than 4.0×10^9/L, or more than 0.10 immature forms.[12]

This composite end point was chosen because the sample size required to demonstrate a significant difference in the