

Fluoroquinolone Resistance in the Rectal Carriage of Men in an Active Surveillance Cohort: Longitudinal Analysis

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Abbreviations and Acronyms

AS = active surveillance
AUA = American Urological Association
FQ = fluoroquinolone
JHH = Johns Hopkins Hospital
TRUSB = transrectal ultrasound guided prostate biopsy

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Purpose: Rectal swabs can identify men with fluoroquinolone resistant bacteria and decrease the infection rate after transrectal ultrasound guided prostate biopsy by targeted antimicrobial prophylaxis. We evaluated the rate of fluoroquinolone resistance in an active surveillance cohort with attention to factors associated with resistance and changes in resistance with time.

Materials and Methods: We evaluated 416 men with prostate cancer on active surveillance who underwent rectal swabs to assess the rate of fluoroquinolone resistance compared to that in men undergoing diagnostic transrectal ultrasound guided prostate biopsy. The chi-square test and Student t-test were used to compare categorical and continuous variables, respectively. Poisson regression analysis was used for multivariate analysis.

Results: On the initial swab fluoroquinolone resistance was found in 95 of 416 men (22.8%) on active surveillance compared to 54 of 221 (24.4%) in the diagnostic biopsy cohort ($p = 0.675$). Diabetes was found in 4.0% of the fluoroquinolone sensitive group vs 14.7% of the resistant group ($p < 0.001$). Biopsy history was not associated with resistance. Of those with a resistant first swab 62.9% had a resistant second swab and 88.9% of those with 2 resistant swabs showed resistance on the third swab. Of men with a sensitive first swab 10.6% showed resistance on the second swab and 10.6% of those with 2 sensitive swabs had resistant third swabs.

Conclusions: One of 4 men who present for surveillance and diagnostic transrectal ultrasound guided prostate biopsy have rectal flora resistant to fluoroquinolone. Resistance is significantly associated with diabetes but the number of prior biopsies is not. Men with fluoroquinolone resistant flora tend to remain resistant with time.

Key Words: prostatic neoplasms; biopsy; fluoroquinolones; drug resistance, bacterial; diabetes mellitus

ONE of the major complications of TRUSB is infection in the genitourinary system and sepsis. Rectal flora most likely enter the genitourinary tract or bloodstream through perforation of the bowel mucosa during the procedure.¹ Antibiotic prophylaxis has become an important measure to

prevent these complications with FQ used to prevent infectious complications.^{2,3} The 2008 AUA Best Practice Policy Statement recommends FQ prophylaxis before TRUSB along with preferred second line agents.⁴ Despite this recommendation there have been increasing rates of infection related

complications after TRUSB.^{5,6} The increase is thought to be due to FQ resistant organisms in the rectal carriage.^{5,7}

Previous studies demonstrated that rectal swabs and resistance profiles of the rectal flora are effective for preventing post-procedure infectious complications, mainly by identifying FQ resistant bacteria.^{1,8} These findings led some groups to adopt rectal culture and directed prophylactic therapy before TRUSB. FQ resistance in the rectal carriage was reported in 10% to 22% of men who undergo TRUSB. FQ resistance is associated with previous heart valve replacement, diabetes and FQ use in the prior 3 months.^{8,9} However, to our knowledge no longitudinal study has been done to assess trends in resistance patterns in individuals with time.

We evaluated the rate of FQ resistance, the factors associated with resistance and the trends in resistance with time in a well characterized AS program. The resistance rate was compared to that in men not on AS who were undergoing diagnostic TRUSB.

METHODS

Study Cohort

The AS program at JHH is an institutional review board approved, open enrollment, longitudinal study consisting of men with very low to low risk prostate cancer who elect close followup as an alternative to curative intervention after a diagnosis of prostate cancer.¹⁰ A total of 1,297 men were enrolled in the AS cohort as of February 2014. Starting in July 2012 rectal swabs were performed in all men at JHH undergoing diagnostic and surveillance TRUSB in an effort to decrease post-TRUSB infectious complications. In the AS cohort a total of 717 swabs had been performed in 416 men as of May 2014.

We queried the AS database and the electronic medical records for FQ resistance (specifically ciprofloxacin resistance) in individual swabs, antibiotic resistance profiles, medical history, demographic data and biopsy history. Infection rates were not included in this study because this outcome was not prospectively included in our cohort. Information such as previous antibiotic use and hospitalizations in the last 6 months was also not available.

As a comparison cohort we determined the FQ resistance rate in 221 men who presented to JHH for diagnostic biopsy during the period when rectal swabs were done in the AS cohort (February 2013 to February 2014). Men who underwent diagnostic swabs at JHH under the same protocol as the AS cohort served as controls to determine whether the resistance rate in the AS cohort differed from that in men who presented for prostate biopsy without a prostate cancer diagnosis. Additional data such as medical and biopsy history were not available and these men did not serve as controls in the remaining analysis.

Rectal Swabs

Rectal swabs were performed in clinician office about 2 to 4 weeks before TRUSB. The swabs were incubated in

broth containing ciprofloxacin for 24 hours at 35C. If there was evidence of bacterial growth in the broth, it was transferred to a MacConkey agar plate, a MacConkey agar plate with 10 µg/ml ciprofloxacin plate and 5% sheep blood agar plate. Gram staining was done to confirm gram-negative rods. The plates were incubated for 24 hours at 35C. If there was growth on the ciprofloxacin containing plate, organism identification and antimicrobial susceptibility testing were done on isolates from the nonselective plates using the BD Phoenix™ Automated Microbial System. If there was no evidence of growth in the broth containing ciprofloxacin, it was incubated an additional 24 hours before the swab was reported as negative for FQ resistant gram-negative rods.

The targeted prophylaxis approach was used. Patients with sensitive swabs received ciprofloxacin prophylaxis based on the standard empirical prophylaxis protocol described in the 2008 AUA Best Practice Policy Statement.⁴ Those with resistant swabs received alternative prophylaxis based on the swab resistance profile, which is standard practice at JHH.¹¹

All men were advised to discontinue medication interfering with platelet function 10 days before biopsy and to administer an enema on the morning of biopsy.

Statistical Analysis

The chi-square test and Student t-test were used to compare categorical and continuous variables, respectively. Multivariate Poisson regression analysis was done to calculate the RR of potential independent risk factors associated with FQ resistant flora in the AS cohort. The results of rectal swabs of men with a rectal swab history were compared to those of men who underwent an initial swab. The demographic and antibiotic resistance status of men not on AS who underwent rectal swabs and TRUSB at JHH served as controls.

Potential risk factors used in analysis included diabetes, increased cholesterol, hypertension and heart disease (congestive heart failure, coronary artery disease or a history of myocardial infarction). Presence of a risk factor was determined by the problem list in the electronic medical record.

RESULTS

FQ Resistance Rates in AS Cohort vs Controls

During the study period 416 men on AS and 221 controls underwent rectal swabs. There was no statistically significant difference in age between the 2 groups. Of the AS group 91% were white compared to 72% of controls (chi-square test $p < 0.001$). Of 416 men in the AS cohort with a rectal swab 95 (22.8%) had FQ resistance on the first swab compared to 54 of 221 (24.4%) with rectal swabs in the control group (chi-square test $p = 0.675$).

FQ Resistance Trends

Resistance rates were determined for other widely used antibiotics in swabs reported to be FQ resistant. Resistance was found for ampicillin in 79% of

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