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Gentamicin and norfloxacin prophylaxis for transrectal ultrasound-guided prostate biopsy

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Abstract. ***Background*:** Transrectal ultrasound guided prostate biopsy (TRUSPB) is the mainstay of diagnosis for prostate cancer. Clinical trials have established that antibiotic prophylaxis is effective in reducing infective complications, but breakthrough bacteraemia has been described with multiresistant organisms. We reviewed the rate of bacteraemia and re-admission in patients undergoing TRUSPB.

***Methods*:** The Alfred Hospital is a tertiary referral hospital in Melbourne, Australia. The routine antibiotic prophylactic regimen is gentamicin and norfloxacin. Patients undergoing TRUSPB at the Alfred Hospital were linked to databases of blood and urine cultures, and to admissions with infective complications within 14 days.

***Results*:** Between June 2007 and July 2010, 459 patients underwent TRUSPB at the Alfred Hospital. No patient (95% CI: 0, 0.8%) had a positive blood culture, and one patient had a positive urine culture (95% CI: 0.04, 1.2%) within 14 days of the procedure. There were two readmissions: a 66 year old man with systemic culture-negative sepsis, and a 54 year old man with a urinary tract infection. In 50 randomly selected patients, all patients received norfloxacin but only 80% of patients received gentamicin. Between 2007 and 2010, 6.0% of isolates were non-susceptible to norfloxacin, 5.8% were non-susceptible to gentamicin and 3.2% were non-susceptible to both gentamicin and norfloxacin.

***Conclusions*:** Recent reports of breakthrough bacteraemia suggest that effectiveness of single agent fluoroquinolone or gentamicin prophylaxis may be compromised by increasing rates of resistance. Combination prophylaxis with gentamicin and norfloxacin is associated with a low rate of infective complications.

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Introduction

Transrectal ultrasound guided prostate biopsy (TRUSPB) is the definitive method used for the evaluation and diagnosis of prostate cancer in those with either an abnormal digital rectal examination or elevated prostate-specific antigen (PSA). The procedure is considered relatively safe; however, associated infective complications include fever, asymptomatic bacteriuria, urinary tract infection, bacteraemia and sepsis. Several measures have been shown to reduce rates of such complications.

Increasing the number of biopsies from 6 to 12 allows optimal cancer detection rates without a corresponding rise in infective complications; however, additional biopsies are accompanied by an increased infective risk.[1–3] Bowel preparation with pre-procedure enemas appears to reduce the risk of complications and is generally recommended.[2,4]

Without the use of antibiotic prophylaxis, infectious complications may occur in up to 25–36% of patients.[5,6] More conservative estimates quote rates of bacteriuria at 8%, clinical urinary tract infections (UTIs) in 5% and

Implications

- Reports of breakthrough infective complications of transrectal ultrasound guided prostate biopsy due to multiresistant organisms are increasing.
- Combination gentamicin + norfloxacin prophylaxis is associated with low infective complication rates.
- Combined gentamicin + norfloxacin prophylaxis may be a suitable alternative to carbapenems where there is a high rate of individual (but not dual) aminoglycoside or fluoroquinolone resistance.

hospitalisation rates of 2%.[7] There is good evidence that antimicrobial prophylaxis reduces the rate of infectious complications, although the optimal antibiotic regimen is unclear, and individual practices vary.[5,6,8–10] Original studies using carbenicillin for 24 hours peri-procedure demonstrated a reduction in positive urine cultures from 36% to 8.6% at 48 hours.[6] Subsequent prospective placebo-controlled randomised studies using ciprofloxacin and tinidazole reduced rates of infective complications from 25% to 9.0%.[5] Extended courses, compared with single doses of ciprofloxacin, may be associated with further reductions in infectious complications, although differences did not reach statistical significance.[11] Oral ciprofloxacin has also been shown to be at least comparable with intravenous prophylactic antibiotic regimens.[8,12] Australian guidelines recommend the use of single dose prophylaxis with ciprofloxacin.[13]

Recently there have been reports of increasing infective complications after TRUSBP.[10,14–20] It is thought that emerging antibiotic resistance to fluoroquinolones in Enterobacteriaceae, and thus failure of prophylaxis, has been responsible for the increase. Antibiotic resistance in Enterobacteriaceae appears highest in developing countries and has significant geographic variability.[21–25] In countries such as Australia where resistance rates of Enterobacteriaceae are relatively low, an association with travel to areas with higher resistance rates and failure of prophylaxis has been noted.[26] Presumably this relates to a change in host flora associated with travel.

Fluoroquinolone resistance is often associated with resistance to aminoglycosides, penicillins, cephalosporins and cotrimoxazole, and thus the question of the most appropriate prophylactic antibiotic regimen has been raised.[23,25] At our hospital, we have not adhered to national guidelines recommending single dose ciprofloxacin because of reports of breakthrough bacteraemia; we report on our experience with combination norfloxacin + gentamicin antibiotic prophylaxis for TRUSBP.

Methods

The Alfred Hospital is a tertiary referral hospital in Melbourne, Australia. The recommended antibiotic prophylactic regimen is gentamicin (3 mg kg^{-1} IV before procedure) and norfloxacin (400 mg orally, twice daily for 3 days starting 1 day before the procedure), with associated rectal enema. In the majority of instances, 12 prostatic biopsies are taken.

We obtained a list of patients with TRUSPB at the Alfred Hospital, including elective and inpatient procedures. We linked this to databases of positive blood and urine cultures taken within 14 days of the procedure. We reviewed all admissions with infective complications (ICD-10 codes A40-41, T81.42, N39.0, N41.0-9, R50.8 R50.9, T81.1) within 14 days. Post-operative bacteraemia and bacteriuria was defined as a positive culture from blood or urine respectively within 14 days. Post-operative sepsis was defined as an admission with sepsis or urinary tract infection under any of the urology, general medicine or infectious diseases units within 14 days of TRUSBP.

Compliance with hospital guidelines was assessed in 50 randomly selected patients and was defined as receipt of both gentamicin and a fluoroqinolone (norfloxacin or ciprofloxacin). Antibiotic resistance rates were reviewed in a similar demographic group. The susceptibility test results of Enterobacteriaeceae isolated from urine specimens in males aged >50 years presenting to the emergency department were reviewed between 2001 and 2010.

Confidence intervals were calculated using exact binomial methods. Statistical procedures were performed using Stata 9.0 (College Station, Texas). As this was a quality audit not involving patient contact, ethical review was not deemed necessary for this study.

Results

Between June 2007 and July 2010, 459 patients underwent TRUSBP at the Alfred Hospital.

Rates of infective complications

No patient had a positive blood culture or positive urine culture collected at the Alfred hospital within 14 days of the procedure, but one patient (case 2 below) had a positive culture 2 days following the procedure performed at another laboratory. Two patients (0.44%; 95% CI: 0.1%, 1.6%) were readmitted within 14 days of the procedure with infective complications.

Details of cases

One patient, a 66 year old man, was readmitted with sepsis 2 days following the procedure. Twelve biopsies were taken and prophylaxis consisted of gentamicin 80 mg (1.2 mg kg^{-1}) at the beginning of the procedure and norfloxacin 400 mg twice daily for 5 days starting 1 day before the procedure. Urine microscopy after antibiotics showed $<10 \times 10^6$ leucocytes L^{-1} and $>1000 \times 10^6$ erythrocytes L^{-1}, but culture was negative. Blood cultures taken after antibiotic administration were also negative. White cell count was 20.40×10^9 L^{-1} with neutrophilia of 18.6×10^9 L^{-1} and CRP was 219 mg L^{-1}. Ultrasound did not show any evidence of a collection. The patient required admission to the Intensive Care Unit for 36 hours for inotropic support, and was