ESBL in the rectal flora of patients undergoing transrectal prostate biopsy – a study of the prevalence in a major metropolitan hospital.

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Abstract

Objectives:

To determine the prevalence of ESBL in a patient population undergoing transrectal prostate biopsy. To assess the incidence of postoperative sepsis. To correlate the development of sepsis with the presence of preoperative ESBL on rectal swabs. To assess the adequacy of prophylactic antibiotic guidelines in the context of local ESBL prevalence.

Methods:

Patients undergoing TRUS biopsy at Royal Melbourne Hospital between January 2012 and July 2016 had rectal swabs immediately prior to TRUS with specific cultures to identify the presence of ESBL. Prophylactic antibiotics were 500mg oral ciprofloxacin 1-hour pre-procedure. Data were collected prospectively, with retrospective review of all readmitted patient files and audit data to ensure complete capture of events.

Results:

There were 387 TRUS biopsy procedures performed. Rectal swabs were correctly collected in 352 (91%). Median age was 65. 25 (7%) positive ESBL swabs were identified. Most ESBL were E. Coli. 50% of ESBL were resistant to ciprofloxacin and all were sensitive to meropenem. A small increase in ESBL prevalence over time was not significant (R2=0.35). Four patients (1.1%) were readmitted with sepsis; one previously grew ESBL pseudomonas, but sepsis was due to non-ESBL E. Coli. One of the readmitted patients grew ESBL E. Coli, but had not grown ESBL preoperatively. There were no deaths or HDU/ICU admissions.

Conclusions:

This study represents the largest Australian series to investigate ESBL prevalence, and reveals a rate lower than that of many other nations. Our sepsis rate is lower than many international series, perhaps due to our low ESBL rate and strict antibiotic prophylaxis. Preoperative swab result did not predict postoperative sepsis, and was therefore not useful for guiding antibiotic therapy. In this population TRUS biopsy, with ciprofloxacin prophylaxis, remains a safe option for diagnostic prostate biopsy.

Introduction

Transrectal ultrasound-guided biopsy of the prostate (TRUS biopsy) is the most common diagnostic procedure for prostate cancer. Prostate cancer is the most commonly diagnosed cancer in men in Western countries, and is a leading cause of death in the Western world[1–3]. TRUS biopsy is commonly performed one or more times during the diagnostic workup for men with prostate cancer, and numbers being performed exceed 1 million per year in the US alone[4].

Sepsis following TRUS biopsy is a the most significant complication, with incidence as high as 9% being reported, and rates of 2-6% widely accepted[5–8]. As the procedure involves passing a needle through the rectal mucosa into the adjacent prostate 12 or more times, the common organisms causing sepsis following TRUS biopsy are faecal bacteria, in particular gram-negative organisms such as Escherichia coli (E. coli). Recently, there has been a concern about rising rates of antibiotic resistance amongst E. coli and other gram negative organisms. Plasmids encoding resistance DNA are often responsible for this, with the most well-known resistance plasmids encoding extended-spectrum beta-lactamases (ESBL). These confer resistance to both penicillins and cephalosporins, and are not subject to the effects of betalactamase-inhibitors such as clavulanic acid[9].

ESBL gram negative organisms are increasing in prevalence, particularly in countries without strict regulation of antibiotic use in healthcare and in agriculture. They have been listed as a "serious threat" by the Centers for Disease Control and Prevention (CDC)[10]. In countries such as Thailand and India, the ESBL rates are as high as 80%, and even in the US the rates have been as high as 25% in published studies[11,12]. ESBL and other resistant organisms are thought to be responsible for a rising rate of sepsis following TRUS biopsy, as well as for many other postoperative infections, as they are commonly resistant to the common perioperative prophylactic antibiotics[8].

In this study, our objective was to determine the rates of ESBL in our population at a large tertiary referral centre in Australia, by performing preoperative rectal swabs on all patients presenting for TRUS biopsy. We aimed to evaluate our post-TRUS sepsis rate as well as to correlate the organisms responsible for the sepsis with preoperative growth. We sought to identify the resistance profile of our ESBL organisms, particularly with reference to the commonly used prophylactic fluoroquinolones. Finally, we wished to determine whether our prophylactic antibiotic regimen was effective and safe for this procedure, by comparing our sepsis rates with other published studies.

Methods

In consultation with the Victorian Infectious Diseases Service at Royal Melbourne Hospital, we designed a protocol to screen for ESBL on rectal swabs from patients presenting for TRUS biopsy as a quality assurance (QA) activity. chromID® ESBL agar (bioMérieux, France) was chosen as a validated, commercially-available screening medium for the presence of ESBL[13]. Colony-forming organisms from the ESBL agar were further tested to identify resistance to specific antibiotics, in particular fluoroquinolones and carbapenems, as well as to confirm the ESBL production.

Patients presenting to Royal Melbourne Hospital for TRUS biopsy between January 2012 and July 2016 underwent rectal swab immediately prior to TRUS biopsy. All patients were given 500mg oral ciprofloxacin 1 hour preoperatively as the sole prophylactic antibiotic as per the Australian Therapeutic Guidelines[14]. TRUS biopsy was in most cases performed in the left lateral position under sedation, with a standard 12-core biopsy, with additional biopsies being taken if insufficient specimen was obtained or if clinically indicated (e.g. rising PSA and previous negative TRUS biopsy). The biopsy needle was dipped in povidone iodine then saline between each pass through the rectal mucosa.

Data were collected prospectively. All patients were reviewed in the outpatient clinic to discuss histopathology (at which time any complications of the procedure including sepsis were discussed), and quarterly audit data were retrospectively reviewed to identify re-presentations to other hospitals. The files of all patients who re-presented to hospital within 30 days of admission for TRUS biopsy were reviewed to identify any sepsis. Urinary tract infection (UTI) not requiring readmission to hospital was not recorded. Data were also collected regarding prostate-specific antigen (PSA) level, ICU/HDU admissions, and death.

Sepsis was defined according to the modified criteria for sepsis in the 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference[15].

Results

During the period between January 2012 and July 2016, 387 TRUS biopsy procedures were performed on 319 patients (Table 1). Rectal swabs were collected prior to 352 (91%) of these procedures, with the remainder either having not had a swab collected or having had the rectal swab sent for the incorrect test. Patients without rectal swabs were excluded from the study.

Median age of men in our study was 65 (41-86). PSA data was available for 71% of patients, with a median PSA of 7.2 (0.1-1321.9). The majority of TRUS biopsies were performed for investigation of elevated screening PSA, although TRUS biopsy performed for tissue confirmation of known metastatic prostate cancer, and for suspected post-radiotherapy recurrence, were also included in the study.

Cultures from the rectal swabs revealed 25 ESBL events (7% prevalence) in our population. Most ESBL were E. coli, although for 10 of the 25 ESBL, specific bacteria were not identified by the pathology service. Of the identified bacteria, 13 were E. coli, one was an Enterobacter species, and one was a Pseudomonas species. Half of the ESBL were resistant to ciprofloxacin, and all were sensitive to meropenem. There was a small but not statistically significant increase in ESBL prevalence over the three years of the study (linear regression R^2=0.35).

Four patients were readmitted with sepsis (1.1%). Three of these patients had previously had rectal swabs negative for ESBL, one grew ESBL Pseudomonas on the preoperative rectal swab. Blood cultures were available for all four septic patients; all four grew E. coli. Three patients grew non-ESBL E. coli (all of which were ciprofloxacin-sensitive), including the patient who had previously been positive for ESBL. One patient who had previously had a negative swab grew ESBL E. coli. No patients required ICU or HDU admission. Chi-squared contingency test revealed no statistically

significant difference between patients who preoperatively grew ESBL and those who did not with regards to development of postoperative sepsis (p=0.16).

Discussion

TRUS remains a commonly performed diagnostic procedure, despite newer techniques such as transperineal and in-bore MRI-guided biopsy becoming increasingly common. Recent large studies investigating the diagnostic role of prostatic MRI have continued to use TRUS biopsy for comparison and for localisation of lesions[16–18]. While published series of transperineal biopsies show low sepsis rates, the requirement for increased operating theatre time and specialist equipment have limited the procedure's widespread implementation, especially outside the public health system. Like some other Australian public hospitals, we are increasingly performing transperineal biopsies, however during the studied period the majority of our biopsies were performed transrectally. We continue to utilise the transrectal approach for some repeat biopsies, for tissue diagnosis in men with suspected metastatic prostate cancer, and for those in whom sedation is preferred to general anaesthesia. Registry data suggests selected octogenarians may benefit from prostate cancer treatment, which also raises the ongoing need to evaluate the safety of TRUS biopsy[19]. Our cohort represents the first Australian operative cohort to be tested for ESBL prevalence. This is particularly important as ESBL is often considered to be the organism responsible for rising post-TRUS sepsis rates at some institutions.

Our ESBL prevalence is quite low when compared with neighbouring countries[13]. A recent study from Finland with also discovered much higher rates of resistant organisms[20]. It has previously been shown that ESBL rates vary widely between countries. In part this is thought to be related to antibiotic use in healthcare and agriculture; this is highly regulated in Australia, and may account for the low prevalence. However, our hospital services a culturally and ethnically diverse population, many of whom spend significant amounts of time in countries with higher prevalence of ESBL. Further opportunity exists for research comparing the rate of ESBL in our general patient population to those undergoing TRUS biopsy; perhaps the older age and the diagnostic nature of the procedure selects a group of patients who are more likely to be permanently based in Australia.

Although ESBL rates are rising worldwide, our rates remained stable through the three years of our study, with only a small increase that was not statistically significant. As we continue to collect data and to perform swabs, we will continue to assess this trend. It seems likely that given the global trend towards an increase in prevalence, this will also be seen in our population. Data should continue to be prospectively collected to identify these changing rates and to determine whether sepsis rates correlate with a change in resistance patterns. It would also be interesting to obtain

travel history of all patients prospectively to determine whether this influences ESBL prevalence in our cohort.

Many institutions have reported high rates of sepsis following TRUS biopsy. However, our rate is low (1.1%), in line with a previous population study from Victoria, Australia showing a rate of 1.7%[21] This may be related to multiple factors, including our low prevalence of multi-resistant organisms such as ESBL. Having a consistent and evidence-based approach to antibiotic prophylaxis is likely an important factor, especially given the procedures were performed by several different surgeons and trainees. Patient compliance with preoperative ciprofloxacin in hospital is likely to be better than compliance with preoperative antibiotics taken at home. The patient demographics were typical of those undergoing TRUS biopsy in a public hospital, although future opportunities exist for more detailed analysis of patient comorbidities such as diabetes and immunocompromise. Our low rate of ESBL may mean that the antibiotic regimen we use for prophylaxis is less appropriate in areas with a higher ESBL rate.

Given the concerns regarding ESBL and post-TRUS sepsis, correlation between preoperative rectal swabs and the organism responsible for postoperative sepsis merits consideration. One previous study attempted culture-directed prophylaxis, and although a trend towards a lower infection rate was found in the rectal swab group, it did not reach statistical significance[12]. In our study, none of the patients who had grown ESBL on rectal swabs taken immediately before passage of the biopsy needle through the rectum subsequently developed sepsis from the same organism. One patient who grew ESBL developed non-ESBL sepsis, and one who was clear of ESBL on his preoperative swabs became septic with an ESBL organism. As sepsis was so rare in our cohort, much larger numbers would be required to draw firm conclusions regarding these results. However, this strongly suggests that altering routine prophylaxis based upon a rectal swab performed in the time leading up to surgery would not be useful.

In our cohort, none of the patients who developed postoperative sepsis required Intensive Care or High Dependency Unit admission (at our hospital all patient who require invasive monitoring or vasopressor support require ICU/HDU). There were no deaths. This is a reassuring finding and suggests that TRUS biopsy is a relatively safe procedure at our institution.

In conclusion, transrectal prostate biopsy is a common diagnostic procedure for men with suspected prostate cancer, which has come under increasing scrutiny for high reported rates of postoperative sepsis. Many have correlated this with rising rates of ESBL organisms in much of the world. We present the first Australian cohort of men to undergo routine preoperative screening for ESBL. At our institution, ESBL prevalence was 7%, which is much lower than many international

rates. Our postoperative sepsis incidence was low, at 1.1%, with no ICU/HDU admissions or deaths. We do not recommend routine preoperative screening for ESBL to guide antibiotic prophylaxis.

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Tables

Table 1: Patient demographics and outcomes

Demographic	
Total patients, n	387
Age, median (range)	65 (41-86)
PSA, median (range)	7.2 (0.1-1321.9)
Swab performed, n (%)	352 (91%)
ESBL, n (%)	25 (7%)
Sepsis, n (%)	4 (1.1%)
ICU/HDU admissions, n (%)	0 (0%)
Deaths, n (%)	0 (0%)

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