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What is the role of catheter antibiotic prophylaxis for patients undergoing joint arthroplasty?

A prospective observational cohort study.

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Abstract:

Introduction: Antimicrobial prophylaxis at the time of urinary catheter insertion and removal is commonly administered in patients undergoing joint arthroplasty, despite the lack of evidence to support this practice. The rationale is the theoretical risk of prosthetic joint infection arising from bacterial seeding from the urinary tract at the time of catheterisation. In an era of antimicrobial stewardship further assessment is warranted.

Methods This study aimed; to investigate the incidence of catheter associated bacteriuria and bacteraemia in patients undergoing total joint arthroplasty and; to assess the antimicrobial susceptibility of any isolated microorganisms. This prospective observational study undertaken over a 6 month period (May-October 2014) included 99 patients undergoing elective primary hip and knee arthroplasty at St. Vincent's Hospital, Melbourne (SVHM). Urine specimens were collected at insertion and removal of urinary catheters along with blood cultures upon urinary catheter removal.

Results: Overall 98% of the cohort received catheter antimicrobial prophylaxis for urinary catheter insertion and removal; the majority of patients received gentamicin (94%). Bacteriuria on catheter insertion had an incidence of 4.4%. The incidence of catheter associated bacteriuria was 1.3%. All cultured organisms were sensitive to commonly used antibiotics including cephazolin. There were no cases of bacteraemia with urinary catheter removal. Increasing age, ASA status and female gender were associated with the development of bacteriuria.

Discussion: The incidence of catheter associated bacteriuria and bacteraemia with antimicrobial prophylaxis is low. This study provokes discussion about the requirement of catheter prophylaxis in this surgical context and the utility of pre-operative urine screening.

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Introduction

Over the past decade the number of primary total hip and knee replacements performed has increased by greater than 50% and 77% in Australia respectively.¹ Due to an ageing population it is estimated that there will be a two to six fold increase in joint replacements by 2030.² Prosthetic joint infection (PJI) is one of the most significant complications following joint arthroplasty and is associated with substantial patient morbidity.³ In addition, infection places a significant burden on the healthcare system: in Australia prosthetic joint infections were estimated to add a further \$101 million to annual arthroplasty costs in 2014.⁴ Therefore research and optimisation of prevention strategies for PJI is critical.

The administration of surgical antibiotic prophylaxis is a key practice for the prevention of PJI in patients undergoing joint arthroplasty. Guidelines currently recommend the use of cephalosporins as standard surgical prophylaxis, with the addition of antibiotic agents that cover the most frequently encountered organisms in the treating population.^{5,6} Surgical antibiotic prophylaxis is combined with additional antibiotic catheter prophylaxis in many orthopaedic centres across Victoria, Australia with the aim of reducing the risk of surgical site and urinary infections.^{7,8} In the era Antimicrobial Stewardship this, potentially unnecessary, use of antibiotics warrants justification.

Guidelines of The Infectious Diseases Society of America (IDSA) state the routine use of prophylactic antibiotics for urinary catheters should only occur if bacteriuria poses specific significant potential complications.⁹ The evidence of a link to urinary infection is contentious.¹⁰ Several case reports and small case series restricted to the 1970's-1980's demonstrated links between distant infection sites (including the urinary tract) and the development of PJI.¹¹⁻¹⁴ It was proposed that bacteriuria could result in bacteraemia and haematogenous seeding during catheter

manipulation (insertion, removal, post removal).¹⁵ A more recent cohort study reported an increased risk of PJI in patients with bacteriuria (OR 3.23 CI 1.67-6.27 p<0.05).¹⁶ Conversely two large case-control trials found there was no increase in the relative risk of PJI in patients with peri-operative bacteriuria.^{17,18} Thus, whilst the use of a urinary catheter increases the risk of bacteriuria (3-7% per day in situ)¹⁹, there is conflicting evidence regarding the risk bacteriuria poses to an implanted prosthesis.

The combination of standard surgical prophylaxis and catheter prophylaxis results in patients receiving broad spectrum antibiotics in the peri-procedural period. In particular the use of gentamicin for catheter prophylaxis, which has been associated with ototoxicity²⁰, nephrotoxicity²¹ and increasing levels of resistance²² and therefore requires caution. Currently there is limited evidence to inform current practice. This prospective observational cohort study aimed to identify the incidence of bacteriuria and urinary tract associated bacteraemia in catheterised patients receiving antibiotic catheter prophylaxis in the setting of joint arthroplasty. A secondary aim was to assess the susceptibility of any isolated organisms to standard surgical prophylaxis regimens.

Methods

A prospective observational cohort study of patients undergoing elective primary total hip or knee arthroplasty aged 18 years or older at St. Vincent's Hospital, Melbourne (SVHM) was conducted over a 6 month period (May – October 2014). SVHM orthopaedic department consisting of 15 orthopaedic surgeons is a state referral centre that conducted 692 total hip or knee arthroplasties in 2014. Patients were excluded if they did not have a urine specimen collected on the day of surgery, including if the patient did not receive a urinary catheter. The project was approved by the SVHM HREC-A committee (LRR: 152/13).

All patients undergoing joint arthroplasty at SVHM are screened for asymptomatic bacteriuria at pre-admission clinic as part of routine care. Patients with bacteriuria or urinary tract infection on pre-admission assessment are reviewed by their treating doctor for consideration for antibiotic therapy, if indicated. At the time of arthroplasty, Foley catheters are inserted pre-operatively (in the operating room or anaesthetic bay), by trained clinical personnel using aseptic technique and connected to a closed-drainage system. The catheter was routinely removed on day 2 as part of the clinical care pathway.⁸

In this current study, two urine specimens and a single blood culture were collected from consented participants. The urine specimens were collected immediately upon insertion and at the time of removal of indwelling Foleys catheter, using aseptic technique. Immediately subsequent to urinary catheter removal, blood cultures were also obtained by venepuncture to determine the incidence of associated bacteraemia. Specimens were cultured using standard microbiological techniques to a) identify if any organisms are present and b) assess antimicrobial susceptibilities. Significant bacteriuria was defined if urine cultures isolated a microorganism with a concentration greater than 10^5 CFU/mL.¹⁹ Catheter associated (CA) bacteriuria was defined as bacteriuria isolated from a patient that is currently, or has been within the last 48 hours, catheterised.

The medical records of each patient were examined by a single researcher (RS). A study database was created to record the use of antibiotic prophylaxis (surgical and catheter specific), demographics, pre-admission and admission data.

The choice of agent for surgical antibiotic prophylaxis including antibiotic catheter prophylaxis was in keeping with the local hospital antibiotic prophylaxis guideline, modified from the Therapeutic Guidelines:Antibiotic (Version 14) recommendations.⁵ The exact prophylactic agent/s selected was at the discretion of the treating surgeon.

Descriptive statistics were used to summarise and report the data. Descriptive statistics for continuous variables were reported in medians and interquartile ranges (IQR) and for categorical variables percentages and frequencies were used. Comparisons were made between subjects with and without a recorded episode of bacteriuria. Univariate analysis was used to identify factors associated with bacteriuria. Continuous variables were assessed using parametric (unpaired student t-tests) or non-parametric tests (Mann Whitney U-test) depending on the normal distribution of the data. Categorical variables were assessed using Fisher's exact test. All reported p values were two-tailed and for each analysis $p < 0.05$ was considered statistically significant. All analyses were performed using Stata 12.0 software (StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX: StataCorp LP.).

Results

Over the study period 99 subjects had a first urine specimen collected on catheter insertion and were included in the study (see Flowchart Supplementary Figure 1). 79 subjects had a second urine specimen and blood culture taken on catheter removal. In addition, a mid-stream urine collection for urinalysis and culture as part of pre-admission screening was performed on 98 included subjects. The cohort had a median age of 67 years (IQR 60-74 years) with a slight female predominance (57%) and median BMI of 32 (IQR 27-36) with 56% of patients categorised as obese (BMI >30). A total of 48% of patients had an ASA score of 3 or 4. The median day of catheter removal was day 2 post operation (IQR, 2 to 3 days). Demographic, procedure and admission characteristics of the cohort are outlined in Table 1.

The most common antibiotic chosen for surgical prophylaxis at the time of index arthroplasty was cephazolin (65%). Nine patients (9%) received cephazolin *plus* vancomycin,

seventeen patients received vancomycin (17%), and seven patients received ceftriaxone (7%). Specific prophylaxis for urinary catheter insertion was administered in 39 patients (39%) including gentamicin in 21 patients (21%) and ceftriaxone in 18 patients (18%). The majority of patients (98%) received an 80mg stat dose of parenteral gentamicin prior to catheter removal.

As demonstrated in Table 2 the incidence of bacteriuria was highest on pre-admission urine analysis (14%) compared with catheter insertion (4%). The incidence of catheter associated (CA) bacteriuria on catheter removal was 1.3% (n, 1). The incidence of leucocyturia ($>10 \times 10^6$ /L) was highest on catheter removal (40%). There were no episodes of bacteraemia on catheter removal. The most common organism isolated in urine pre-operatively was *Escherichia coli*; 36% of pre-admission isolates and 75% of cultures at catheter insertion. The only organism isolated on catheter removal was *Morganella morganii* with a leucocyte count $<10 \times 10^6$ /L. All organisms isolated on catheter insertion were sensitive to cephazolin yet 30% of organisms isolated on pre-admission urine analysis and the single case of *Morganella morganii* isolated on catheter removal were resistant.

As shown in Table 3, a total of 17 patients had a recorded episode of bacteriuria cultured either at pre admission, catheter insertion or catheter removal. Female gender, increased age and higher ASA score was associated with increased risk bacteriuria ($p < 0.05$).

It was shown that at one month follow up post joint replacement a total of three patients had developed PJI. Of the seventeen patients with documented bacteriuria, two (2/17: 12%) developed a PJI compared with one of the 82 patients (1/82: 1%) with no documented bacteriuria ($p = 0.075$).

Two patients had bacteriuria on both pre-admission urine screening and catheter insertion yet the organisms isolated were different on each occasion. In reference to Table 4 (supporting information), a total of three PJI were recorded in this cohort. Two PJI had occurred in patients that

had returned a positive urine sample, however the same organisms were not isolated in the urine and the joint in either case. The organisms isolated from PJI include; Gram-positive cocci (staphylococcal spp including coagulase negative staphylococci and *Enterococcus faecalis*) and Gram-negative species (*Escherichia coli* and *Proteus mirabilis*).

Discussion

This descriptive study of patients undergoing joint arthroplasty receiving both standard surgical and specific catheter prophylaxis demonstrates that the incidence of CA bacteriuria is low, 1.4%. This study is the first to investigate a patient cohort receiving specific catheter prophylaxis in this surgical context. Previous studies have demonstrated CA bacteriuria to have an incidence ranging from 4% to 28% in patients receiving surgical prophylaxis yet no specific antimicrobial catheter prophylaxis.²³⁻²⁵ In our study there was an incidence of bacteriuria of 14% at pre admission and 4% on catheter insertion. A recent study (n, 2500) reported the prevalence of pre-operative bacteriuria as 12.1%, however these results were from mid-stream urine specimens in patients who had not undergone pre-admission urine testing.¹⁶ Comparatively in a study (n, 500) of patients undergoing joint arthroplasty, without a urinary catheter in situ, the incidence of bacteriuria pre operatively was 36% and 3 days post operatively was 41%.²⁶ The incidence of both, pre-operative bacteriuria and CA bacteriuria, was lower in this study than previous studies. This may reflect the concurrent administration of surgical antibiotic prophylaxis, different urine sampling technique (mid-stream versus in-dwelling catheter) or the potential effect of pre admission urine screening.

There were no cases of bacteraemia upon catheter removal in this study. Previous studies have reported an incidence of bacteraemia on urinary catheter removal or replacement ranging from 4% to 10% however these studies investigated patients with long term catheters in situ.^{9,27,28} As

there have been no documented studies of the risk of bacteraemia on catheter removal in the context of short term catheterisation there is no data to support the postulated mechanism that catheter manipulation may result in bacteraemia in this clinical context.

In our study it was shown that female gender, increasing age and higher ASA score was associated with the development of bacteriuria ($p < 0.05$). Such associations were consistent with a recent cohort study by Sousa et al¹⁶ who also demonstrated that bacteriuria (OR 3.23; 95% CI 1.67-6.27; $p = 0.001$) and post-operative UTI (OR 6.64, 95% CI= 1.24-35.64) increased the risk of prosthetic joint infection on multivariate analysis.¹⁶ Our study similarly demonstrated an increased proportion of PJI at one month follow up in the bacteriuria group compared with non bacteriuria group (12% vs 1.2%; $p = 0.075$), however this was not statistically significant. This must be interpreted in light of limited follow up time and a small sample in our cohort. These associations may highlight patients at higher risk of developing infection in the general sense. Importantly in our study and the study by Sousa and colleagues, there was no correlation between the organisms isolated from the urine and from subsequent prosthetic joint infections¹⁶. Sousa and colleagues¹⁶ similarly propose that urinary infection may act as a surrogate marker for the overall tendency of a patient to develop infection. From this it can be suggested that there may be other modifiable factors increasing the risk of infection, the significance of which are yet to be recognised such as immobility, hygiene, relative immunosuppression and general debility. Further investigations with larger cohorts are required to adequately assess the underlying pathological mechanisms for this observed association with PJI in more depth.

Patients on the waiting list for elective joint replacement at St. Vincent's Hospital, Melbourne undergo pre-admission assessment including urine screening and treatment of urinary tract infection, as part of clinical practice. It was demonstrated in this study that 70% of organisms

isolated in pre-admission screening were sensitive to standard surgical prophylaxis with cephazolin. Furthermore, all cases of detected bacteriuria at the time of catheter insertion were susceptible to the antibiotics administered at the time of surgical antibiotic prophylaxis. Screening for asymptomatic bacteriuria is commonly performed at many centres, however, the benefit and cost-utility of this practice has not been established and warrants further investigation. A recent randomised control trial demonstrated that there was no significant difference in the development of post-operative urinary tract infection if bacteriuria on pre admission is treated. Of note, however this study was undertaken in a cohort of patients that did not undergo insertion of urinary catheters at the time of arthroplasty.¹⁶ It has been estimated that, given the risk of PJI from a urinary focus is rare, in order to prevent one PJI originating from the urinary tract 25 000 patients with asymptomatic bacteriuria would need to be treated with specific antibiotics.²⁹ In terms of direct health care cost, a 500 fold cost reduction has been estimated when comparing the treatment of PJIs attributable to the urinary tract and the cost of routine screening for all.³⁰ However, as discussed above, Sousa and colleagues¹⁶ highlighted that patients with asymptomatic bacteriuria were at increased risk of PJI within the first post-operative year and hence pre-operative screening may assist in identifying patients at higher risk of infection. It was also shown by Sousa and colleagues¹⁶ that there was no significant difference in the rate of PJI in patients with asymptomatic bacteriuria that were treated or untreated (OR= 0.82, 95% CI= 0.27- 2.51, P=0.78). The topic of pre-operative urine screening and treatment remains one of clinical debate, highlighted further in the current study. The most recent edition of Therapeutic Guidelines: Antibiotics (Version 15) released at the completion of this study concluded there was no need for treatment of pre-operative asymptomatic bacteriuria and explicitly stated that in the Prevention of infection: surgical prophylaxis section that catheter prophylaxis was not recommended in this surgical context.⁵

The results of the study must be interpreted in light of its limitations. This study had a small sample size (n, 99) which may have resulted in comparatively lower incidence of bacteriuria and bacteraemia as they are relatively infrequent occurrences. Although in light of the limited current literature assessing this clinical practice the study provides the largest sample of clinically relevant data. In this observational study, there were a number of surgical prophylaxis regimens provided, which may have altered the incidence of infective complications such as bacteriuria and bacteraemia relative to the antibiotic combinations used. Similarly the timing of antibiotic administration in relation to the collection of urine samples and the exact time between urinary catheter removal and collection of the blood culture specimen were not identified. Due to logistical complications 20% (n, 20) of patients who had first urine specimens taken on catheter insertion did not have urine or blood specimens taken on catheter removal, potentially underestimating the incidence of complications such as bacteraemia and bacteriuria.

In conclusion this descriptive study demonstrates that in a cohort of arthroplasty patients receiving surgical and catheter prophylaxis the rate of CA bacteriuria and bacteraemia is low. Older female patients with a higher ASA score were more likely to have documented bacteriuria. This study provokes discussion about the role of catheter prophylaxis in this cohort of patients. Furthermore, the potential association between asymptomatic bacteriuria and prosthetic joint infection is intriguing and both questions warrant further investigation.

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Table 1: Demographic and procedure characteristics of the cohort.

Variable	No. (%) of patients (n=99)
Median age (IQR)	67 (60-74)
Female	57 (57)
Median body mass index (IQR)	32 (27-36)
American Society of Anaesthesiologist score (ASA)	
1	3 (3)

2	48 (50)
3	43 (44)
4	2 (2)
Comorbidity	
Diabetes Mellitus	19 (19)
Recurrent UTI	6 (6)
Pre-existing antibiotic therapy	7 (7)
Index arthroplasty site	
Hip	46 (46)
Knee	53 (53)
Indication for index arthroplasty	
Osteoarthritis	95 (96)
Rheumatoid Arthritis	2 (2)
Inflammatory Arthritis	1 (1)
Post- traumatic	1 (1)
Anaesthetic Type	
Neuraxial	83 (85)
General anaesthetic	7 (7)
Neuraxial and General anaesthetic	8 (8)
Median duration (mins) of procedure (IQR)	109 (92-124)
Median post-operative day of catheter removal (IQR)	2 (2-3)
Median length of stay in days (IQR)	4 (4-5)

Table 2: Pre-admission and peri-operative urine and blood microscopy and culture results.

	Pre admission urine analysis (n=99) (n,%)	Catheter insertion (n=99) (n,%)	Catheter removal (n=79) (n,%)
Leucocyturia §	24 (26)	14 (14)	32 (40)
Bacteriuria ¶	14 (14)	4 (4)	1 (1.3)
Leucocyturia and bacteriuria	11 (11)	4 (4)	0 (0)
Bacteraemia	N/A	N/A	0 (0)
Organism detected (n,%)	n= 14	n= 4	n= 1
<i>Escherichia coli</i>	5 (36)	3 (75)	0 (0)
<i>Streptococcus agalactiae</i>	1 (7)	1 (25)	0 (0)
<i>Morganella morganii</i>	0 (0)	0 (0)	1 (100)
<i>Mixed organisms</i>	5 (36)	0 (0)	0 (0)
<i>Enterococcus faecalis</i>	1 (10)	0 (0)	0 (0)
<i>Klebsiella pneumoniae</i>	1(10)	0 (0)	0 (0)
<i>Salmonella spp.</i>	1 (10)	0 (0)	0 (0)
Covered by cephazolin	10 (71)	4 (100)	0 (0)

§ (>10x10⁶)

¶ (>10⁵ CFU/mL)

Table 3: Factors of association with bacteriuria on univariate analysis.

Variable	Bacteriuria (n=17) (n,%)	No bacteriuria (n=82) (n,%)	p Value
Median Age (IQR)	74 (68-77)	67 (59-73)	0.014*
Female	15 (88)	42 (51)	0.006*
Median body mass index (IQR)	35 (29-38)	30 (27-35)	0.247
Obese (BMI>30; obese)	11 (64)	45 (55)	0.593
Median ASA (IQR)	3 (2-3)	2 (2-3)	0.030*
ASA >2	11 (64)	37 (45)	0.185
Diabetes Mellitus	4 (23)	15 (18)	0.735

* p <0.05= statistically significant

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