Antibiotic prophylaxis for urinary catheter manipulation following arthroplasty: a systematic review.

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Abstract

Background: urinary catheter use in the peri- and post-operative phase following arthroplasty may be associated with urinary tract infection (UTI) and deep prosthetic joint infection (PJI). These can be catastrophic complications in joint arthroplasty. We performed a systematic review of the evidence on use of antibiotics for urinary catheter insertion and removal following arthroplasty.

Methods: Electronic databases were searched using the HDAS interface. Grey literature was searched. From 219 citations, 6 studies were deemed eligible for review. Due to study heterogeneity a narrative approach was adopted. Methodological quality of each study was assessed using the CASP appraisal tool.

Results: 4696 hip and knee arthroplasties were performed on 4578 participants across all studies. Of these 1475 (31%) were on men and 3189 (68%) on women. Mean age of study participants was 69 years. 3489 cases (74.3%) related to hip arthroplasty and 629 (13.4%) to knee arthroplasty. 578 (12.3%) were either hip or knee arthroplasty. 45 PJIs were reported across all studies (0.96%). Two studies found either no PJI or no statistical difference in the rate of PJI when no antibiotic prophylaxis was used for catheter manipulation. Another study found no statistical difference in PJI rates between patients with or without preoperative bacteriuria. Where studies report potential haematogenous spread from UTIs, this association can only be assumed. Increased duration of urinary catheterisation is positively associated with UTI.

Conclusion: It remains difficult to justify the use of prophylactic antibiotics for catheter manipulation in well patients. Their use is not recommended for this indication.

INTRODUCTION

Urinary catheter use in the peri-operative and post-operative phase following arthroplasty may be associated with increased risk of urinary tract infection (UTI) and deep prosthetic joint infection (PJI) [1,2]. Local trauma during catheter insertion and removal might lead to transient bacteraemia resulting in haematogenous spread of bacteria to a newly implanted joint. PJI is potentially catastrophic and carries a significant burden, both to the patient for mortality and morbidity and economically to health services [3]. Consequently, prophylactic antibiotics (often a single dose of an aminoglycoside such as gentamicin) are advocated by some prior to urinary catheter manipulation [4,5].

The use of antibiotics, in particular aminoglycosides, is not without risks. In addition to the known risk of ototoxicity, a recent systematic review reported that gentamicin use for surgical prophylaxis in orthopaedic patients is associated with increased risk of acute kidney injury [6]. Extended spectrum cephalosporins such as Ceftriaxone (another common prophylaxis for this indication) are associated with the development of *Clostridium difficile* [7].

The theory of haematogenous spread and prophylactic antibiotic can be seen in other surgical procedures, most notably following invasive dental work. Haematogenous seeding from routine dental work is however extremely uncommon and routine prophylactic antibiotics for dental work in this group of patients is now not recommended [8]. Furthermore, previous literature has suggested that bacteraemia secondary to catheter manipulation may be uncommon, transient and at very low concentration [9]. Whilst evidence exists to show a link between postoperative

urinary tract infection and subsequent deep joint infection [10,11], evidence linking PJI and urinary infections in asymptomatic patients remains uncertain [12].

The number of arthroplasty surgeries done is expected to rise over the coming years, with an increasingly ageing cohort of patients who might benefit from such surgery [13]. With such a cohort, not only are the risks of surgery magnified, but so too are any possible risks associated with inappropriate antibiotic use. No systematic review has specifically investigated the use of prophylactic antibiotics for catheter insertion or removal in arthroplasty patients. The purpose of this study was to address this limitation.

MATERIALS AND METHODS

The review was registered *a priori* through PROSPERO (CRD42019124582).

Search strategy:

The electronic databases: Embase and Medline via the Healthcare Databases Advanced Search (HDAS) interface, PubMed and Cochrane library. Grey literature resources: OpenGrey, Beilfield academic search engine (BASE), Opengrey.eu, British library, NTLTD and Greylit.com were searched. An example of the search strategy, adapted for each of the databases, is presented as ***Figure 1***. Finally, Google Scholar was searched using right hand truncation in combination with Boolean Operators. Additionally, reference lists from all eligible studies were screened to identify any studies which may have been omitted.

Eligibility criteria:

Studies were included if they reported data on the primary and secondary outcome measures from patients of any age who received a urinary catheter peri-operatively, or in the immediate post-operative period for arthroplasty, with or without antibiotic prophylaxis. Review articles, letters and editorials were excluded. Studies done using animals were excluded. We included studies of any language or age of publication. Studies not published in English were translated prior to assessment.

Study Identification:

All titles and abstracts were assessed by one reviewer (TR). A second reviewer (CG) independently verified potential study eligibility. This process was repeated for the

assessment of full-text papers. Through this, full-text papers were deemed eligible by both reviewers (TR, CG).

Methodological appraisal:

The Critical Appraisal Skills Programme (CASP) tools were used to critically appraise eligible papers. Cohort studies were appraised using the CASP Cohort study tool whilst randomised controlled trials (RCTs) were appraised using the CASP RCT tool. All papers were reviewed by one reviewer (TR) and independently verified by a second reviewer (CG). Disagreements were resolved through discussion.

Data Analysis:

Data was synthesised under primary and secondary outcome measures. The primary outcome measure was presence of prosthetic joint infection, related to catheter use following arthroplasty. Secondary outcome measures included: presence of superficial infection, urinary tract infection, bacteriuria and acute kidney injury. The data were investigated for the ability to pool the data in a meta-analysis by observation of the data extraction tables. There was insufficient data for a specific outcome to be able to pool the data and a narrative analysis approach was therefore adopted.

RESEARCH

Search Results:

A summary of the search results (PRISMA flow diagram) is presented in ***Figure 2***. In total 219 citations were identified. After duplicates were removed, 154 titles and abstracts were assessed for eligibility. Thirty-seven full papers were obtained and assessed. Six papers were deemed to be eligible and were included in the final review.

Study demographics:

A summary of the characteristics of the participants is presented in ***Tables 1 and 2.*** A total of 4696 hip and knee arthroplasties were performed on 4578 participants across all studies. Of these 1475 (31%) were undertaken on men and 3189 (68%) on women. Gender information on the remaining 1% was not attributed to a subset of patients within one study [1]. Mean age of study participants was 69 years. Two studies (including 541 participants) were not included in this calculation as they either did not report mean age [1], or provided only median age of participants [14]. The majority of the data relates to hip arthroplasty: 3489 cases (74.3%). 629 of cases (13.4%) relate to knee arthroplasty. 578 cases (12.3%) only specify that either hip or knee arthroplasty was performed.

Methodological quality:

The appraisal results are presented in ***Tables 3 and 4.*** This demonstrated moderate to good methodological quality. All studies address a focused issue and in all cohort studies the study groups were recruited in an acceptable way. Exposure and outcome bias were largely controlled and results were applicable to other similar

study populations. Particular deficiencies were noted in a lack of appreciation for all possible confounding factors, both in the study design and analysis. The findings of these studies must be considered with this in mind.

Clinical Findings

Primary outcome measure: evidence of prosthetic joint infection

In total, 45 PJIs were reported across all studies (0.96%). Two of the included studies found either no PJI [15] or no statistical difference in the rate of PJI [16] when antibiotic prophylaxis was not used for catheter manipulation following arthroplasty. In the second of these, the authors found no cases of PJI in the prophylaxis group and only one PJI in the no-prophylaxis group. Rates of AKI were also unchanged. Use of a urinary catheter has also been found to make no statistical difference in the rate of PJI following arthroplasty [11].

Scarlato et al [14] reported rates of PJI in patients with positive urine samples (collected on catheter insertion and removal) and presence of bacteraemia following catheter removal. Two cases of PJI were found in patients with a positive preoperative urine culture versus one with a negative culture. This was not statistically significant. Bacteria cultured from infected joints were different from those cultured in preoperative urine samples. There were no cases of bacteraemia on catheter removal.

The rates of PJI were 6.2% and 1.1% were reported in Wroblewski [2] and Donovan [1] respectively. In the former, the majority of hip infections were caused by *S.*

aureus (4 cases) or the bacterium was unknown (4 cases). Two patients with *S. aureus* PJI died in the perioperative period. In one case Proteus was isolated in both the CSU and subsequent hip samples. Direct correlation or causation between urethral instrumentation and development of PJI could only be assumed. In the latter, one acute PJI in a patient that had been catheterised post-operatively was reported, which the authors attribute to a Pseudomonas urinary infection. It is worth noting that the patient had rheumatoid arthritis, was on steroid therapy and had a history of recent urinary infection. Four cases of delayed PJI were also diagnosed, however the organisms involved were Staphylococcus, enterococci, Pseudomonas and *Escherichia coli* (from biliary sepsis). It is not known if these correlated with preoperative urine samples.

Secondary outcome measures - bacteriuria, UTI, superficial infection and AKI

Rates of bacteriuria varied greatly across the studies and changed depending on when the sample was taken and the gender of patient. For example bacteriuria in preoperative urine samples were found to be as low as 2% in men and 6.6% in women [1], and as high as 20% [16]. CSU cultures on catheter removal also varied greatly, with rates between 1.3% [14] and 56.3% [2] being reported. This difference may reflect the cohort of patients studied or possibly the duration of catheterisation – although this is not known. In women, antibiotic prophylaxis has been shown to significantly reduce the incidence of bacteriuria on catheter removal, but without affecting rates of UTI [15]. Higher ASA grade and increased age have also been found to increase the incidence of bacteriuria on catheter removal ($p<0.05$) [14].

In Donovan et al's [1] study, 22% of catheterised patients had positive postoperative cultures versus 2.6% of non-catheterised patients in the retrospective arm. This differs from the prospective arm in which 20% of catheterised patients and 19.3% of non-catheterised patients had positive cultures. This difference might be accounted for by the fact that urine samples in the retrospective study were only taken for patients with urinary symptoms, whereas multiple samples were taken postoperatively for each patient in the prospective arm. This could also explain the difference in treatment of UTI in the retrospective study - 20% of catheterised patients and 1% of the non-catheterised patients - versus 10% of the catheterised and 3.5% of the non-catheterised patients in the prospective part of the study. The authors do not comment on whether this was statistically significant.

Duration of catheterisation is reported to have a significant effect on the rate of UTI, with incidence increasing to 48% after the catheter remained in situ for 3 days [11]. Post-op UTI was also significantly increased in women (17%) compared with men (7%). Post-operative patients with a UTI were described as being at an increased risk of developing PJI. The bacterium isolated from hip and urine only matched in one case however, and the authors conclude that positive postoperative urine cultures and the subsequent development of PJI is not causally related.

In Bond et al's study rates of treated UTI were not statistically significant (44% vs 29%, p=0.24). There was one superficial infection in the prophylaxis group versus none in the non-prophylaxis group (p=0.45). The only other study to report on superficial infection was Wroblewski [2] who report nine cases (4.6%). Two AKIs

were reported by Bond et al. in the prophylaxis group versus one in the non-prophylaxis group. This was not statistically significant (p=0.35).

DISCUSSION

Urinary catheters are a known risk factor for development of asymptomatic bacteriuria and UTI [17,18,19]. Within orthopaedics the long-held concern is that bacteria from the urinary tract might seed to a newly implanted joint resulting in deep infection. The assumed mechanism is through local or minor trauma during urinary catheter insertion or removal, which causes transient bacteraemia and subsequent seeding of a prosthetic joint [20]. Urinary tract infection has previously been reported as a risk factor for development of PJI [10]; however this is disputed by others [21]. Accordingly, the question of preoperative screening of urine has also been raised, with some arguing that routine screen for asymptomatic bacteriuria in arthroplasty patients is futile [20,22].

Cases of haematogenous seeding of a prosthesis have been documented in the literature [23,24,25]. In most cases the aetiology is that of a significant primary infection (for example sepsis secondary to a parotid gland abscess [23]), or concomitant comorbidities resulting in immunosuppression (such as rheumatoid arthritis). Spontaneous seeding of a prosthetic joint is uncommon. This was shown by Ainscow and Denham, who followed 1112 joint replacements prospectively for an average of six years, concluding that transient bacteraemia (from events such as dental work or minor surgical procedures) is not likely to infect an implanted joint in an otherwise healthy individual [26].

The papers presented in this review show low rates of PJI following arthroplasty, which is line with other literature. Whilst it may be historically tempting to follow the logical progression that urinary catheters lead to UTIs and UTIs lead to PJI (and in doing so self-validate the argument for prophylactic antibiotic use), evidence for increased risk of PJI through catheter use is not supported. Other studies agree, with a recent observational study of elderly patients suffering neck of femur fractures (all of whom were catheterised on admission) finding no difference in the rates of perioperative wound infection between patients diagnosed with a UTI or not [27]. Bond et al. were the only group to look at rates of AKI and found no difference between groups given gentamicin or not. It is worth noting however that doses used for surgical prophylaxis are typically greater than those used for catheter removal and the findings by Bond et al. may reflect this difference.

To conclude, it remains difficult to justify the routine use of prophylactic antibiotics for catheter manipulation in well patients and we therefore do not recommend their use for this indication. Greater work should however continue to take place to investigate the risk factors surrounding development of PJI in arthroplasty patients. In particular investigation into how asymptomatic bacteriuria and PJI are related would be of great benefit to the orthopaedic community. When catheters are used, these should be left in situ for the shortest duration possible.

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FIGURE AND TABLE LEGENDS

Figure 1: MEDBASE search strategy using MeSH terms or truncation and asterisks

Figure 2: PRISMA flow diagram of search results

Table 1: Patient demographics and summary of results

Table 2: Patient demographics and summary of results

Table 3: Summary of critical appraisal scores – cohort studies (full papers only)

Table 4: Summary of critical appraisal scores – randomised controlled trials (full papers only)

Figure 1: MEDBASE search strategy using MeSH terms or truncation and asterisks

((((ORTHOPEDICS/ OR exp "JOINT PROSTHESIS"/ OR exp "ARTHROPLASTY, REPLACEMENT"/ OR ARTHROPLASTY/ OR REOPERATION/) AND ("SURGICAL WOUND INFECTION"/ OR "WOUND INFECTION"/ OR "POSTOPERATIVE COMPLICATIONS"/ OR exp "URINARY TRACT INFECTIONS"/)) AND (exp "URINARY CATHETERIZATION"/ OR exp CATHETERS/ OR exp "CATHETERS, INDWELLING"/)) AND (exp "ANTI-BACTERIAL AGENTS"/ OR exp GENTAMICINS/ OR exp "ANTIBIOTIC PROPHYLAXIS"/)) [Humans]"

(((orthopedi* OR "joint prothesis" OR arthroplast* OR reoperati*).ti,ab AND ("surgical wound infect*" OR "wound infect*" OR "postoperative complicat*" OR uti OR "urinary tract infect*" OR BACTERIURIA).ti,ab) AND ("indwelling catheter*" OR catheter* OR "urinary catheter*").ti,ab) AND (gentamicin OR gentamycin OR antibacterial agent* OR prophyla*).ti,ab

Figure 2: PRISMA flow diagram of search results

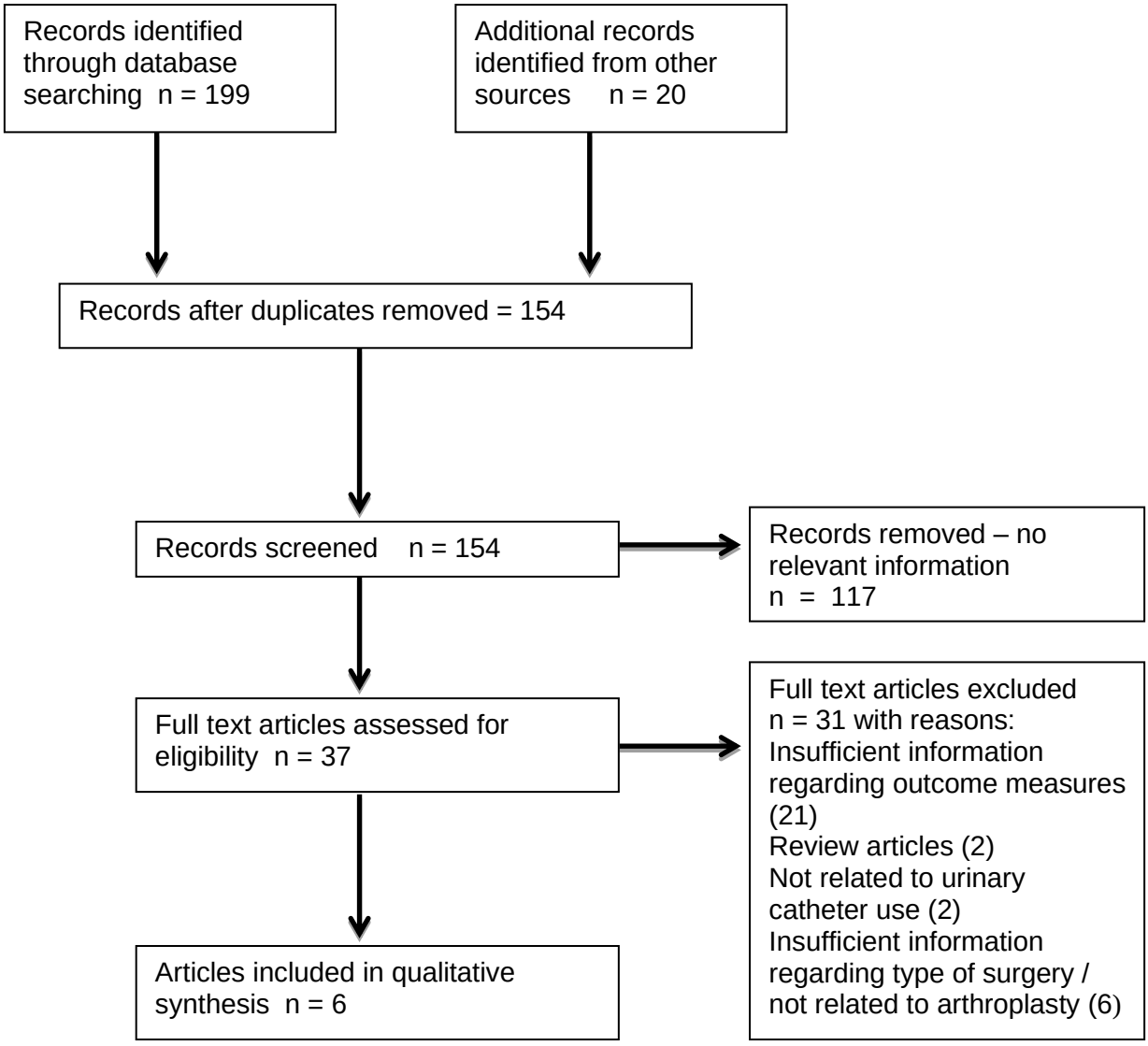

Table 1: Patient demographics and summary of results

Study	Subsection within study	Type of study	No. of participants	Mean age	Arthroplasty performed	% patients Catheterised	Mean duration of catheter in days	Surgical prophylaxis	Catheter prophylaxis	Follow up period	Evidence of deep infection
Dejmek et al.	A	Cohort	478	68 (38-89)	Hip and Knee	NA	NA	NA	NA	NA	NA
	B	RCT	100	Women: 73 (52-87) Men: 70 (47-89)	Hip and Knee	100%	4 (3 - 5)	1g cefazolin	960mg oral co-trimoxazole, 2 doses	20-32 months	No
Donovan et al.	Retrospective	Cohort	359 (386 hips)	*	Hip	13.92	*	IV cephalosporin for 5-7 days	NA	4 years	1 acute infection attributed to pseudomonas urinary infection. 4 latent PJI: staph aureus, enterococci, pseudomonas and e. Coli (secondary to biliary sepsis)
	Prospective	Cohort	67	*	Hip	14.93	*	IV cephalosporin for 5-7 days	NA	10 months	
Scarlato et al.		Cohort	99	67 (IQR 60-74)	Hip and Knee	100	2 (IQR 2-3)	IV cefazolin 56% (+/- vancomycin 9%), Vancomycin (17%) or ceftriaxone (7%)	Gentamicin 80mg OR Ceftriaxone	1 month	3 PJIs. 2 in pts with positive urine preadmission, 1 in a patient with a negative culture (p=0.75)

Table 2: Patient demographics and summary of results

Study	Subsection within study	Type of study	No. of participants	Mean age	Arthroplasty performed	% patients Catheterised	Mean duration of catheter in days	Surgical prophylaxis	Catheter prophylaxis	Follow up period	Evidence of deep infection
Bond et al.	Retrospective	Cohort	137	72 (40-91)	Hip and Knee	100	*	Cefazoline +/- vancomycin	gentamicin 80-240mg	6 months	0 PJI (p=0.59) 1 superficial SSI (p=0.45)
	Prospective	Cohort	205	72 (35-87)	Hip and Knee	100	*	Cefazoline +/- vancomycin	NA	12 months	1 PJI (p=0.59) 0 superficial SSI (p=0.45)
Wroblewski et al.	Retrospective	Cohort	195	67.3 (42-89)	Hip	64 received catheter only	*	Varied	NA	Mean 2.1 years	12 PJI Staph aureus (4), Organism unknown (4), E. coli (2), Proteus (1), Caog negative staph. (1)
Wymenga et al.		RCT	2892 (2631 hips & 362 knees)	69.1 (hips) 70.9 (knees)	Hip and Knee	52 Hip 37.6 Knee	Variable	1.5g cefuroxime +/- two further doses at 750mg	NA	Mean 13 months for hip, 12 months for knee	Hip: 0.75% with catheter vs 0.45% without catheter (p=0.23) Knee 1.5% with catheter vs 3.1% without catheter (p=0.8)

Table 3: Summary of critical appraisal scores – cohort studies (full papers only)

CASP question	1	2	3	4	5a	5b	6a	6b	9	10	11
Donovan et al [1]	Y	Y	Y	N	N	N	N	Y	N	Y	Y
Scarlato et al. [14]	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y
Bond et al [16]	Y	Y	Y	Y	N	N	Y	N	Y	Y	Y
Wroblewski et al. [2]	Y	Y	Y	Y	N	N	Y	Y	N	Y	Y

Y = Yes, N = No

1. Did the study address a clearly focussed issue?
2. Was the cohort recruited in an acceptable way?
3. Was the exposure accurately measured to minimise bias?
4. Was the outcome accurately measured to minimise bias?
5.
    a. Have the authors identified all important confounding factors?
    b. Have they taken account of the confounding factors in the design/analysis?
6.
    a. Was the follow up of subjects complete enough?
    b. Was the follow up of subjects long enough?
9. Do you believe the results?
10. Can the results be applied to the local population?
11. Do the results of this study fit with other available evidence?

Table 4: Summary of critical appraisal scores – randomised controlled trials (full papers only)

CASP question	1	2	3	4	5	6	9	10	11
Dejmek at al [15]	Y	Y	Y	N	Y	Y	Y	Y	Y
Wymenga et al [11]	Y	Y	Y	N	Y	Y	Y	Y	Y

Y = Yes, N = No

1. Did the trial address a clearly focused issue?
2. Was the assignment of patient to treatments randomised?
3. Were all of the patients who entered the trial properly accounted for at its conclusion?
4. Were patients, health workers and study personnel 'blind' to treatment?
5. Were the groups similar at the start of the trial?
6. Aside from the experimental intervention, were the groups treated equally?
9. Can the results be applied to the local population, or in your context?
10. Were all clinically important outcomes considered?
11. Are the benefits worth the harms and costs?