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Short Report

Effect of non-cephalosporin antibiotic prophylaxis on the risk of periprosthetic joint infection after total joint replacement surgery: a retrospective study with a 1-year follow-up

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SUMMARY

Background: Cephalosporins are recommended as first-line antibiotic prophylaxis in total joint replacement surgery. Studies have shown an increased risk for periprosthetic joint infection (PJI) when non-cephalosporin antibiotics have been used. This study examines the effect of non-cephalosporin antibiotic prophylaxis on the risk for PJI.

Methods: Patients with a primary hip or knee replacement performed from 2012 to 2020 were identified (27 220 joint replacements). The primary outcome was the occurrence of a PJI in a one-year follow-up. The association between perioperative antibiotic prophylaxis and the outcome was examined using logistic regression analysis.

Discussion: Cefuroxime was used as prophylaxis in 26,467 operations (97.2%), clindamycin in 654 (2.4%) and vancomycin in 72 (0.3%). The incidence of PJI was 0.86% (228/26,467) with cefuroxime and 0.80% (6/753) with other prophylactic antibiotics. There was no difference in the risk for PJI with different prophylactic antibiotics in the univariate (OR 1.06, 95% CI 0.47–2.39) or multivariable analysis (OR 1.02, 95% CI 0.45–2.30).

Conclusion: Non-cephalosporin antibiotic prophylaxis in primary total joint replacement surgery was not associated with an increased risk for PJI.

Introduction

Periprosthetic joint infection (PJI) is one of the most feared complications after prosthetic joint surgery and therefore it is essential to prevent them. Perioperative antibiotic prophylaxis has a well-established role in the prevention of surgical site infections (SSIs) related to prosthetic joint surgery. First- or second-generation cephalosporins are recommended as first-line prophylactic antibiotics. [1].

The most common reasons to use non-cephalosporin prophylactic antibiotics are reported penicillin allergy and carriage of methicillin resistant *Staphylococcus aureus* (MRSA) [1].

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The prevalence of a reported penicillin allergy among patients with prosthetic joint surgery has been between 2.5—17% [2—5]. Cephalosporins are often avoided and other prophylactic antibiotics, such as clindamycin or vancomycin, are given prior to joint replacement surgery to patients with a reported penicillin allergy [2,4].

Studies have shown an association between a reported penicillin or beta-lactam allergy and an increased risk of SSI after joint replacement surgery [5], even though this association has not been evident in all studies [2]. The increased risk for SSI associated with reported penicillin allergy is postulated to be due to the use of non-cephalosporin prophylactic antibiotics [6]. The risk for infection after prosthetic joint surgery has been shown to be higher when clindamycin has been compared with cloxacillin [7] and when vancomycin has been compared with cefazolin [4,8]. Wyles *et al*. showed that the risk for infection after prosthetic joint surgery was significantly higher when non-cefazolin prophylactic antibiotics were used [3].

Previous studies examining the risk for PJI with non-cephalosporin prophylactic antibiotics have focused on cefazolin, so far similar studies have not been performed for cefuroxime. The aim of this study is to examine if the use of non-cephalosporin i.e. non-cefuroxime prophylactic antibiotic in primary prosthetic joint surgery is associated with an increased risk for PJI.

Methods

This retrospective study was performed in the Coxa Hospital for Joint Replacement, Tampere, Finland. Patients with an elective primary hip or knee replacement operation between January 2012 and December 2020 were identified from the hospital's electronic joint replacement database. Information on prophylactic antibiotics (antibiotic used and the timing of infusion with respect to the operation), operated joint, body mass index (BMI), American Society for Anesthesiologists (ASA) score, duration of surgery and the use of antibiotic impregnated cement was also collected from the database. Multiple surgeries could have been performed on one patient and each operation was assessed separately, except simultaneous bilateral operations were considered as one operation. Patients with a missing information on prophylactic antibiotics (n=663) were excluded.

The primary outcome was the occurrence of a PJI. A secondary outcome was the occurrence of any SSI (superficial or deep incisional infection or PJI). The infections were identified from prospective post-discharge surveillance data collected according to the Centers for Disease Control and Prevention Criteria [9]. The follow-up period was one year for each joint replacement surgery.

During the study period, routine prophylactic antibiotics were administered perioperatively prior to incision in all joint replacement surgeries. A single dose of 3 grams of cefuroxime was the standard of care. If this was deemed to be contraindicated, then most commonly 900 milligrams of clindamycin or one gram of vancomycin was given, other antibiotics were rarely given. The prophylactic antibiotic was defined as adequately administered if the infusion was started within 30—60 minutes before incision for cephalosporins and clindamycin and within 60—120 minutes for vancomycin [1].

Statistical analysis

All data analyses and management were performed using the SPSS for Windows 27.0 statistical software package. Categorical variables were compared with χ^2 test and continuous variables with Student's independent-samples t-test (age, BMI) or Mann-Whitney U-test (duration of surgery). A P-value <0.05 was considered statistically significant.

The association between perioperative antibiotic prophylaxis and the outcome (PJIs and all infections separately) was first examined using univariate logistic regression analysis, and odds ratios and 95% confidence intervals (CI) were calculated. Cephalosporins (cefuroxime, ceftriaxone, cefadroxil) were grouped together for the analyses. In addition, the possible confounding effect of clinically relevant independent factors (age, ASA score, BMI, duration of surgery, operated joint, gender and use of cement in the surgery) was taken into account in a multivariable analysis.

Results

The study population consisted of 27,220 primary joint replacement surgeries performed on 22,497 patients. Of these surgeries, 12,452 (46%) were hip replacements and 14 768 (54%) were knee replacements. In addition, 1450 (5%) of the joint replacement surgeries were bilateral.

vvCefuroxime was used as prophylaxis in 26,467 operations (97.2%), other antibiotics were used as follows: clindamycin 654 (2.4%), vancomycin 72 (0.3%) and other antibiotics in 27 (0.1%) operations. The proportion of women was higher, and patients were slightly younger, had a higher BMI and higher ASA scores among those receiving non-cefuroxime antibiotic prophylaxis than those receiving cefuroxime (Table I). Surgeries with non-cefuroxime antibiotic prophylaxis were longer in duration than those with cefuroxime prophylaxis (Table I).

In total, 379 SSIs were identified in the study population (1.4%). The overall incidence of PJI was 0.85% (234/27,220). The incidence of PJI was 0.86% (228/26,467) when cefuroxime was used and 0.80% (6/753) when other prophylactic antibiotics were given. Incidences of PJIs and superficial infections related to different prophylactic antibiotics are given in Table II. There was no difference in the risk for PJI when cephalosporin or non-cephalosporin antibiotic prophylaxis was used in the univariate analysis (OR 1.06, 95% CI 0.47—2.39) or multivariable analysis (OR 1.02, 95% CI 0.45—2.30). The results are similar when all SSIs are considered (OR 1.15, 95% CI 0.59—2.23 and OR 1.11, 95% 0.5—2.17 for univariate and multivariable analysis respectively).

Discussion

The results of this study show that the use of non-cephalosporin antibiotic prophylaxis before primary total joint arthroplasty was not associated with an increased risk for PJI. This is the first study to specifically assess the effect of cefuroxime prophylaxis. Clindamycin was the most used non-cephalosporin prophylaxis. The use of non-cephalosporin prophylaxis was more common in women, in obese patients and in patients with co-morbidities.

There was no difference in the incidence of PJI when the use of cephalosporins and non-cephalosporin antibiotics was

Table I
Comparison of prosthetic joint surgeries with perioperative cefuroxime and non-cefuroxime antibiotic prophylaxis

Variable	Surgeries with cefuroxime antibiotic prophylaxis (n=26,467)		Surgeries with non-cefuroxime antibiotic prophylaxis (n= 753)		*P*
	n	%	n	%	
Male gender	10,612	40	192	25	<0.001
Age, years, mean (SD)	68	(10)	67	(10)	0.01
Knee replacement	14,328	54	440	58	0.02
BMI, kg/m^2, mean (SD)	30	(5.5)	31	(6.2)	<0.001
American Society for Anesthesiologists score					0.01
1	3259	12	77	10	
2	13,070	49	339	45	
3	9,642	36	320	42	
4	467	1.8	17	2.3	
5	15	0.1	0	0	
6	14	0.1	0	0	
Duration of surgery, minutes, median (IQR)	68	(33)	71	(33)	0.002
Use of antibiotic impregnated cement	20,016	76	584	78	0.22

Table II
Incidence of periprosthetic joint infections (PJI) and superficial wound infections with different perioperative prophylactic antibiotics

Antibiotic	Number of operations		Incidence of PJIs		Incidence of superficial infections	
	n (N=27,220)	%	n (N=234)	%	n (N=145)	%
Cefuroxime	26,467	97.2	228	0.86	142	0.54
Clindamycin	654	2.4	6	0.92	3	0.46
Vancomycin	72	0.3	0	0	0	0
Other[a]	27	0.1	0	0	0	0

[a] Ceftriaxone, meropenem, levofloxacin, cefadroxil.

compared. Interestingly, in a similar study by Wyles *et al.*, but where cefazolin was the preferred cephalosporin, the results were opposite [3]. Perhaps the higher incidence of PJI in the study by Wyles *et al.* [3] explains this discrepancy. To support this, in a smaller study by Stone *et al.*, the reported PJI incidence was lower than in the current study, and they found no difference in PJI incidences when different prophylactic antibiotic regimens were compared [2]. If the incidence of PJI is already very low with the use of other preventive measures, the effect of different antibiotic groups may not be so significant.

The results of this study also show that the use of non-cephalosporin antibiotic prophylaxis was associated with female gender, a higher BMI and more co-morbidities. Similar results have been found by Seidelman *et al.*, who reported that penicillin or cephalosporin allergy in surgical patients was associated with female gender and more co-morbidities and was in fact found to be a risk factor for SSI independent of the given antibiotic prophylaxis [10]. It is possible that patients receiving non-cephalosporin prophylactic antibiotics have an increased risk for PJI at least partly due to higher BMI or multiple co-morbidities. It must be noted though that Wyles *et al.* reported the non-cephalosporin prophylaxis to be an independent risk factor for PJI despite its association with a higher BMI and higher ASA scores [3].

A few limitations to this study must be acknowledged. First, the power of the study may not have been sufficient to show a true difference between different antibiotic groups, as the incidence of PJI was very low, making the required sample size unfeasible in a single-centre study. On the other hand, previous studies assessing prophylactic antibiotics and risk for PJI have had similar sample sizes. Secondly, the retrospective nature of the study posed some limitations related to data acquisition, e.g. information on reported penicillin allergies was not available, and thus their association with the given antibiotic prophylaxis could not be evaluated.

In conclusion, this study found no association between the use of non-cephalosporin antibiotic prophylaxis and the risk for PJI, even though previous studies have suggested otherwise. On the other hand, the use of non-cephalosporin prophylaxis was very uncommon and the incidence of PJI was very low. Nevertheless, cephalosporins should be used as first-line prophylactic antibiotics before prosthetic joint replacement surgery, but perhaps the effect of different antibiotic groups on PJI risk may not be so significant, when the incidence of infection is already low.

Conflicts of interest

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CRediT author statement

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