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Intraosseous Regional Prophylactic Antibiotics Decrease the Risk of Prosthetic Joint Infection in Primary TKA: A Multicenter Study

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Abstract

Background Recent studies have demonstrated that the administration of regional prophylactic antibiotics by intraosseous (IO) injection achieves tissue concentrations around the knee that are 10- to 15-fold higher than intravenous (IV) delivery of prophylactic antibiotics. It is currently unknown whether the use of regional prophylactic antibiotics for primary TKA would result in a lower risk of prosthetic joint infection (PJI).

Questions/purposes (1) Is IO injection of prophylactic antibiotics associated with a decreased risk of early (< 12 months) deep PJI compared with traditional IV prophylactic antibiotics? (2) What other patient factors are associated with an increased risk of early PJI after TKA, and do regional prophylactic antibiotics influence these risk factors? (3) Can IO antibiotics be administered to all patients, and what complications occurred from the delivery of IO prophylactic antibiotics?

Methods A retrospective comparative study of all primary TKAs (1909 TKAs) over a 5-year period (January 2013 to December 2017) was performed to determine the risk of early PJI. Three primary TKAs did not meet the study inclusion criteria and were excluded from the study, leaving a total of 1906 TKAs (725 IO, 1181 IV) for analysis at a minimum of 12 months after index procedure. Both cohorts exhibited similar ages, BMI, and American Society of Anesthesiologists (ASA) grades; however, a greater proportion of patients in the IO cohort were smokers (p = 0.01), while a greater proportion of patients were diabetic in the IV cohort (p = 0.006). The PJI risk between IO and IV delivery techniques was compared while adjusting for patient demographics and medical comorbidities. Complications related to IO delivery—inability to administer via IO technique, compartment syndrome, fat embolism, and red man syndrome with vancomycin use—were recorded.

Results The delivery of regional prophylactic antibiotics by the IO technique resulted in a lower PJI risk than IV prophylactic antibiotics (0.1% [1 of 725] compared with 1.4% [16 of 1181]; relative risk 0.10 [95% CI 0.01 to 0.77];

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Ethical approval for this study was obtained from Townsville Hospital and Health Service Human Research Ethics Committee (number HREC/17/QTHS/223).
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p = 0.03). BMI (β = -0.17; standard error = 0.08; p = 0.02), diabetes (β = -1.80; standard error = 0.75; p = 0.02), and renal failure (β = -2.37; standard error = 0.84; p = 0.01) were factors associated with of PJI, while smoking, sex, and ASA score were not contributing factors (p > 0.05). Although BMI, diabetes, and renal failure were identified as infection risk factors, the use of IO antibiotics in these patients did not result in a lower PJI risk compared with IV antibiotics (p > 0.05). IO antibiotics were able to be successfully administered to all patients in this cohort, and there were no complications related to the delivery of IO antibiotics.

Conclusion Surgeons should consider administering regional prophylactic antibiotics in primary TKA to reduce the risk of early PJI. Future randomized prospective clinical trials are needed to validate the efficacy of regional prophylactic antibiotics in reducing the PJI risk in primary TKA.

Level of Evidence Level III, therapeutic study.

Introduction

Background

Over the past two decades, extensive advances in our understanding of the risk factors and methods to minimize prosthetic joint infection (PJI) risk have been made [2, 19, 23]. Despite this, the incidence of early PJI has remained constant or even possibly increased, with an incidence between 1% and 2% [3, 14]. The delivery of prophylactic antibiotics is considered one of most important PJI risk-reduction interventions [1, 12]. To be effective, the antibiotic concentration in the serum, bone, and soft tissue must exceed the target bacteria's minimum inhibitory concentration [4]. Recent research has shown intravenous (IV) antibiotic prophylaxis administration is subtherapeutic for some patients [5, 30, 31]. Additionally, there has been an increase in bacterial antibiotic resistance, particularly for cefazolin-resistant coagulase-negative *Staphylococcus* [26, 28]. Studies have shown that more than 50% of cefazolin-resistant coagulase-negative *Staphylococcus* isolates from early PJIs are resistant to standard therapeutic levels of cefazolin, with a minimum inhibitory concentration$_{90}$ as high as 100 ug/mL [22, 28].

Young et al. [30, 31] investigated the administration of prophylactic antibiotics via a regional technique using intraosseous (IO) circulation to deliver these antibiotics [5, 30–32]. The technique of IO regional administration creates a Biers block of antibiotic to the limb through injection of the prophylactic antibiotic into the proximal tibial metaphyseal bone, with an inflated tourniquet on the leg. The antibiotics from the tibial metaphyseal bone flow directly into the limb's venous system and fill the limb below the tourniquet within seconds. This provides high antibiotic concentrations to all the tissues of the entire limb. This technique has been shown to provide patients with tissue and bone concentrations of antibiotic around the knee that are 10- to 15-fold higher than those receiving conventional IV prophylactic antibiotics [30-32]. More importantly, all patients receiving IO prophylactic antibiotics had concentrations above the recommended minimum inhibitory concentration for coagulase-negative *Staphylococcus* and *S. aureus* [30, 31]. Administration of 1 g of IO cefazolin resulted in a mean subcutaneous fat tissue concentration of 186 ug/g compared with 10.6 ug/g for 2 g of IV cefazolin [31]. Low-dose (500 mg) IO vancomycin has also been shown to provide tissue concentrations of 44 ug/g compared with 3.2 ug/g for 1 g of IV vancomycin [30]. The use of IO vancomycin administration for higher risk populations has also been studied. In patients who were morbidly obese and those who underwent revision TKA, IO vancomycin achieved mean tissue concentrations of 41.1 ug/g and 49.3 ug/g, respectively [5, 32].

Rationale

The research of Young et al. [30, 31] has provided the proof of concept for regional prophylactic antibiotics, but there are currently no published data to show whether this technique effectively reduces PJI risk in clinical practice. The cohort of comorbid patients with diabetes, obesity, renal failure, and smoking have a higher PJI risk, and it would be interesting to determine whether regional prophylactic antibiotics could mitigate or reduce the increased PJI risk for these patients. Finally, it is important to establish if the IO delivery technique can be universally and safely administered to all patients undergoing primary TKA.

Research Questions

Therefore, we asked: (1) Is IO injection of prophylactic antibiotics associated with a decreased risk of early (< 12 months) deep PJI compared with traditional IV prophylactic antibiotics? (2) What other patient factors are associated with an increased risk of early PJI after TKA, and do regional prophylactic antibiotics influence these risk factors? (3) Can IO antibiotics be administered to all patients, and what complications occurred from the delivery of IO prophylactic antibiotics?

Patients and Methods

Study Design and Setting

All primary TKAs performed by five surgeons (BP, PM, MW, KH, JH) over a 5-year period (January 2013 to December 2017) were retrospectively reviewed for

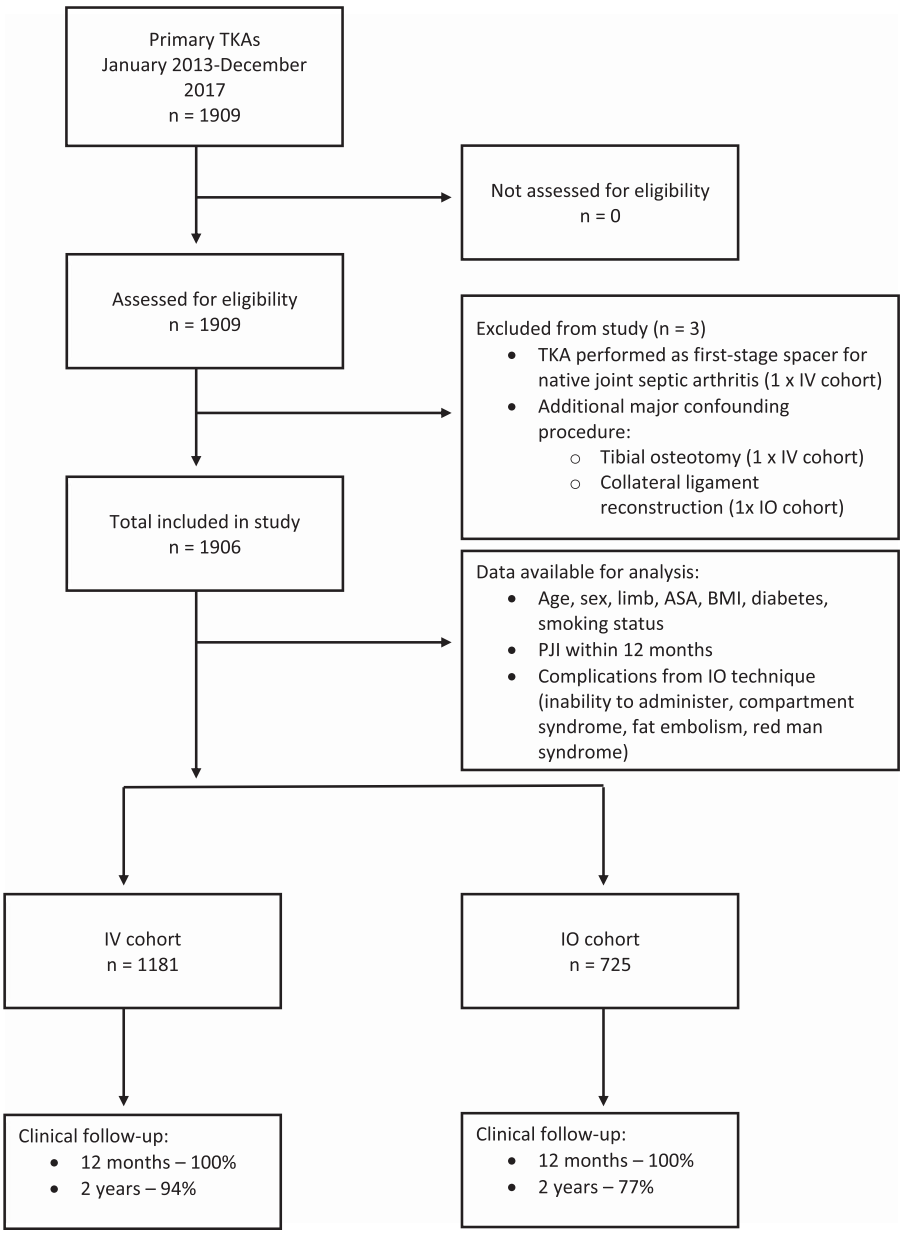

Fig. 1 STROBE flow diagram. IV = intravenous; IO = intraosseous; ASA = American Society of Anesthesiologists.

inclusion in this study. The procedures were performed across three Australian cities, in five separate hospitals. The facilities in this study were both public tertiary hospitals (two) and private elective surgery hospitals (three).

Participants

All 1909 primary TKAs performed during the study period were assessed for inclusion in this study (Fig. 1). Patient demographics and comorbidity data were collected for each patient: age, sex, limb, American Society of Anaesthesiologists (ASA) score, BMI, diabetic, and smoking status. The study exclusion criteria were: (1) TKA performed as a first-stage spacer for the treatment of native joint septic arthritis (one patient in IV cohort), (2) additional major confounding procedures such as tibial/femoral osteotomies (one patient in IV cohort), or concomitant collateral ligament reconstructions (one patient in IO cohort). All patients were followed with direct clinical review at 1 year, 2 years, and 5 years. For this study's primary outcome, a minimum of 12 months of follow-up was needed. Clinical assessment was achieved in 100% of

patients at 12 months and 88% of patients at 2 years. During the study period, each of the surgeons adopted IO regional administration of prophylactic antibiotics as their routine method for all primary TKAs. When surgeons made the change to IO delivery of prophylactic antibiotics, all patients received IO prophylactic antibiotics from that point onward so there was no selection bias to only use it in higher risk patients. The surgeons did not all switch from IV to IO prophylactic antibiotics at the same point. Surgeons made the change in their practice between May 2015 and August 2016.

Data Sources and Ethics

Data for all TKAs and patients were collected from each institution and surgeon's existing joint replacement databases. Individual surgeon's reports in the Australian Orthopaedic Association National Joint Replacement Registry were used as a secondary screening method for identifying additional PJI cases.

Ethical Approval

Ethical approval for the study was granted by the Townsville Hospital and Health Service Human Research and Ethics Committee (HREC/17/QTHS/223).

No funding was required for this study.

Patients and Controls: Descriptive Data

Patients Treated with IO Antibiotics (Treatment Group)

From May 2015 to December 2017, 726 primary TKAs were performed with IO regional antibiotic prophylaxis. One TKA procedure with a concomitant collateral ligament reconstruction was excluded from the study, leaving a total of 725 TKAs for analysis.

Patients Treated Without IO Antibiotics (Control Group)

From January 2013 to August 2016, 1183 primary TKAs were performed with IV prophylactic antibiotics (2g IV cefazolin). Two TKAs were excluded from the study as one procedure was performed as a first-stage spacer for native joint septic arthritis and the other TKA procedure was performed with a concomitant tibial osteotomy. This left 1181 TKAs for analysis.

There were no differences in the patient demographics between the IO and IV cohorts in terms of age (IO: 67 ± 9 years, IV: 67 ± 8 years; p = 0.76), BMI (IO: 31.5 ± 5.5 kg/m^2, IV: 31.3 ± 5.3 kg/m^2; p = 0.46), and ASA status (p = 0.76) (Table 1). However, a greater proportion of patients in the IO cohort were smokers (p = 0.01), while a greater proportion of patients were diabetic in the IV cohort (p = 0.006).

Treatments

IO Antibiotics

Either 1g of cefazolin or 500 mg of vancomycin was administered via the IO technique (of 725 TKAs, 334 received IO cefazolin and 391 received IO vancomycin). In the IO cohort, 232 patients received only prophylactic antibiotics via the IO route (no additional IV antibiotics), and the remaining 493 received both IO and IV prophylactic antibiotics. The surgeons who continued to administer IV antibiotics in addition to the IO dose were required to do so to remain compliant with the local hospitals' antibiotic prophylaxis guidelines. From previous studies by Young et al. [30, 31], the addition of IV antibiotics provides less than a 10% increase in the end-tissue antibiotic concentration compared with the IO delivery route. Additionally, separating the IO and IO + IV cohorts would limit the ability for statistical analysis and increase the chance of statistical error. Due to these reasons, all patients who received IO +/- IV prophylactic antibiotics were grouped together and compared with the cohort who received the traditional IV-only prophylactic antibiotics. The technique for IO regional administration of antibiotics was based on the description by Young et al. [31]; after the limb was prepared and draped with an inflated tourniquet, 1g cefazolin or 500 mg vancomycin was added to 100 mL to 200 mL of saline (volume as per individual surgeon preference), which was injected into the proximal tibial metaphyseal bone using a 14-gauge Dieckmann IO needle. The IO antibiotics were injected immediately before making the skin incision for the procedure. Intraosseous antibiotic dosing was not adjusted in patients with obesity. The use of either cefazolin or vancomycin for IO antibiotics was based on surgeon preference. The minimum tourniquet time after administration of the IO dose was 30 minutes.

Control Group

For IV prophylactic antibiotic dosing, patients routinely received 2 g of IV cefazolin (3g of cefazolin if their weight was greater than 120 kg) unless they were a known carrier of methicillin-resistant *S. aureus* or had an allergy requiring IV vancomycin.

Primary and Secondary Study Outcomes

The primary study goal was to compare the risk of early PJI between the IO and IV cohorts. Early PJI was defined as a deep PJI within 12 months of the primary procedure, as per the MusculoSkeletal Infection Society (MSIS) [20]. The treating surgeons identified all PJI cases during routine

Table 1. Patient demographics of study cohorts

Factor	Intraosseous	Intravenous	Mean difference	p value
Sample, % female	52% (379 of 725)	49% (573 of 1181)		0.11
Age in years	67 ± 9 (66-68)	67 ± 8 (66-67)	0.3	0.76
BMI in kg/m^2	31.5 ± 5.5 (31.1-31.9)	31.3 ± 5.3 (31.0-31.6)	0.2	0.46
ASA				0.76
Healthy	5% (37 of 724)[b]	4% (49 of 1181)		
Mild disease	72% (520 of 724)[b]	72% (844 of 1181)		
Severe disease	23% (165 of 724)[b]	24% (284 of 1181)		
Life-threatening	0.3% (2 of 724)[b]	0.3% (4 of 1181)		
Smoking	4% (30 of 725)[a]	2% (26 of 1181)		0.01
Diabetes	9% (66 of 725)[a]	14% (81 of 582)		0.006

The mean ± SD (95% CI), mean difference, effect size, and proportions of the demographics for the intraosseous and intravenous groups.
[a]Difference between intraosseous and intravenous cohorts ($p < 0.05$).
[b]Missing data point of one patient from the intraosseous cohort

postoperative clinical care. We selected 12 months as the timepoint to define early PJI based on the following factors: (1) PJI within 12 months is secondary to intraoperative bacterial contamination in most cases, and prophylactic antibiotics offer the greatest risk reduction against this [25]. (2) Twelve months allows enough time for the identification of lower-virulence PJI cases due to bacteria such as coagulase-negative *Staphylococcus*, which are known to cause a large percentage of early PJIs [17, 22]. (3) Theoretically, IO antibiotics will have the greatest effect on preventing coagulase-negative *Staphylococcus* PJIs as prior studies have shown more than 50% of these infections are resistant to standard IV cefazolin antibiotic levels [17, 22, 28]. (4) Acute hematogenous PJIs could occur between 30 days to 1 year, and they would be falsely classified as early PJI, but this potential confounder applies equally to both cohorts.

Table 2. Summary of TKA PJI cases (n = 17)

Age	Gender	AB route	AB type	Time to infection	Organism
66	M	IV	Cefazolin	3 weeks	Methicillin-sensitive *Staphylococcus aureus*
69	M	IV	Cefazolin	3 weeks	*Serratia marcescens*
71	F	IV	Cefazolin	3 weeks	*S. marcescens*
66	M	IV	Cefazolin	4 weeks	*S. vitulinus; Cutibacterium acnes*
69	M	IV	Cefazolin	4 weeks	MSSA
80	M	IV	Cefazolin	4 weeks	*S. aureus; Escherichia coli*
80	F	IV	Cefazolin	2 months	*Streptococcus viridans*
61	M	IV	Cefazolin	3 months	*S. warneri*
59	M	IV	Cefazolin	4 months	Methicillin-sensitive *S. aureus*
79	F	IV	Cefazolin	4 months	No growth[a]
81	F	IV	Cefazolin	6 months	MSSA
70	M	IV	Cefazolin	8 months	*S. caprae*
65	M	IV	Cefazolin	9 months	*S. caprae*
53	M	IV	Cefazolin	10 months	No growth[a]
67	F	IV	Cefazolin	10 months	*S. agalactiae*
77	F	IV	Cefazolin	10 months	Methicillin-sensitive *S. aureus*
71	F	IO + IV	Vancomycin/cefazolin	6 months	*S. lugdensis*

[a]Pathology results indicated negative culture/no growth for bacteria.
AB = antibiotic; MSSA = methacillin-susceptible *S. aureus*.

All clinically identified deep PJI cases within the first 12 months were recorded. A total of 17 PJIs occurred within 12 months of the primary procedure (16 in the IV cohort, 1 in the IO cohort) (Table 2). The infection within the IO cohort occurred in a patient who received both IO and IV prophylactic antibiotics; there were no infections within the cases who received only IO prophylactic antibiotics.

The secondary study goals were to define the patient factors that increased the PJI risk and then determine whether IO prophylactic antibiotics decreased the PJI risk in those patients. Additionally, we recorded complications thought to be related to the IO technique (compartment syndrome, fat embolism, inability to administer via IO technique, and red man syndrome with vancomycin use).

Bias

There was no selection bias for patients who received IO antibiotics because all surgeons switched to this technique as their routine method of administering prophylactic antibiotics. There is a potential bias for the type of prophylactic antibiotic administered between cohorts. Within the IO cohort, 54% of cases were administered IO vancomycin. All surgeons routinely administered IV cefazolin for the IV cohort; however, when the change to IO antibiotics occurred, some surgeons switched to routinely using IO vancomycin. The surgeons' rationale for the routine use of IO vancomycin was because of the potential improved coverage against methicillin-resistant *S. aureus* and coagulase-negative *Staphylococcus*. This rationale for routine use of vancomycin may not be clinically relevant as IO cefazolin achieves tissue concentrations higher than the reported resistance levels of coagulase-negative *Staphylococcus* [9, 28]. We acknowledge the potential bias that may exist in the IO cohort with the use of vancomycin; however, it is unlikely to be clinically relevant as both IO cefazolin and IO vancomycin would provide adequate antibiotic levels to cover resistant *Staphylococcus* species.

During the study period, all primary TKAs performed by the five surgeons (BP, PM, MW, KH, JH) were included for analysis. Only three procedures that did not meet the inclusion criteria were excluded. Importantly, direct clinical follow-up of all procedures at the study's primary endpoint of PJI within 12 months was achieved. The diagnosis of deep PJI was defined by the MSIS criteria [20]. To ensure no cases of PJI were missed, a secondary review of individual surgeons' national joint replacement registry data was undertaken to identify any additional cases of revision for PJI. No additional cases of PJI were found from this database. The potential complications of the IO delivery technique were easily monitored because they would be clinically apparent within hours of the procedure.

As the data for this study were collated retrospectively from multiple institutions, the BMI, diabetes, and renal failure comorbidity data were incomplete/unknown for a subset of patients, which has limited the sample size available for statistical comparison of these individual comorbidity risk factors between IO and IV cohorts (Table 3). Future studies with larger cohort sizes will be required to determine whether IO antibiotics can reduce the PJI risk for high-risk patients with these comorbidities.

Statistical Analysis

The central tendency and dispersion are reported as the mean ± SD. The Shapiro-Wilk test indicated that the continuous parameters departed from the norm, and thus the main effect of route (IV and IO) and infection risk on age and BMI were analyzed using the Mann-Whitney U test. We used chi-square tests to examine the association between infection risk, route method (IV versus IO), diabetes status, smoking status, sex, and ASA grade. A multivariate analysis of variance was conducted to compare age and BMI between the IO and IV cohorts. The relative risk of sustaining an infection between the IO and IV cohorts was also calculated, with associated 95% confidence intervals and p values. Finally, we used a stepwise binary logistic regression analysis to determine factors associated with infection risk, with the infection risk treated as the dependent variable and diabetes, BMI, renal failure, smoking, sex, and ASA status as explanatory variables. All data were analyzed using SPSS Statistics for Windows, Version 25.0 (IBM Corp), with the alpha level set at 0.05 for all statistical analyses.

Results

Comparison of PJI Risk Between IO and Traditional IV Antibiotic Administration

IO regional antibiotic delivery was associated with a lower risk of infection within 12 months (0.1% [1 of 725]) compared with the risk after traditional IV administration (1.4% [16 of 1181], relative risk 0.10 [95% CI 0.01 to 0.77]; p = 0.03).

Other PJI Risk Factors

When accounting for other patient factors, BMI (β = -0.17; standard error = 0.08; p = 0.02), diabetes (β = -1.80; standard error = 0.75; p = 0.02), and renal failure (β = -2.37; standard error = 0.84; p = 0.01) were factors associated with infection risk. Other factors (smoking status, sex, and ASA grade) were not associated with the risk (p >

Table 3. Infection rate between the intraosseous and intravenous groups by BMI, diabetic status, and renal failure

Parameter	Intraosseous	Intravenous	Relative risk (95% CI)	p value
BMI				
> 35 kg/m^2	0.6% (1 of 166)	1.7% (4 of 238)	0.36 (0.05-3.21)	0.36
< 35 kg/m^2	0% (0 of 504)	1.4% (12 of 857)	0.07 (0.004-1.16)	0.06
Diabetic status				
With diabetes	1.5% (1 of 65)	6.6% (5 of 76)	0.25 (0.03-2.05)	0.20
Without diabetes	0% (0 of 659)	1.0% (5 of 496)	0.07 (0.004-1.25)	0.07
Renal failure				
With renal failure	0% (0 of 9)	23.1% (3 of 13)	0.24 (0.01-4.23)	0.33
Without renal failure	0% (0 of 478)	1.3% (6 of 457)	0.07 (0.004-1.32)	0.08

0.05). Although BMI, diabetes, and renal failure were identified as infection risk factors, when stratifying IO and IV administration by patients with these factors, there were no differences between the IV and IO cohorts (Table 3).

Complications Associated with IO Administration of Antibiotics

IO antibiotics were successfully administered to all patients in this cohort, and there were no complications secondary to the delivery of IO antibiotics.

Discussion

IO regional administration of prophylactic antibiotics has previously been shown to provide tissue antibiotic concentrations 10- to 15-fold higher than the traditional IV route [30-32]. With the increasing rates of cefazolin antibiotic resistance among *Staphylococcal* species, the IO technique provides adequate tissue concentrations of antibiotics for coverage of these bacteria [17, 22, 28]. To date, there have not been any clinical studies to determine whether the IO technique would reduce the PJI risk in comparison to traditional IV prophylactic antibiotics. This study has shown the risk of early PJI was lower with IO regional antibiotics compared with traditional IV prophylactic antibiotics. However, in the cohort of higher risk patients with diabetes, renal failure, and obesity, IO antibiotics did not offer a lower PJI risk compared with traditional IV antibiotics. Importantly, all patients were able to be administered IO antibiotics, and there were no complications related to the IO delivery technique.

Limitations

This study has limitations. First, patients were not randomized to either antibiotic prophylaxis technique. Instead, we reported on the infection risk after the surgeons adopted IO regional administration as their routine prophylactic antibiotic delivery method. Importantly, the cohorts of patients did not differ in age, BMI, or ASA grade. Second, other PJI reduction methods could have been introduced to the surgeons' practices during the study period, which may have influenced the results. To our knowledge, there were no other major changes to the surgeons' routine TKA practices, but this is a potential bias for which we cannot account. Third, the IO cohort included patients who received only IO prophylactic antibiotics and those who received both IV and IO antibiotics. We intentionally grouped these patients as the primary outcome measure of this study was to investigate the influence of the higher IO prophylactic antibiotic concentrations on PJI risk. The addition of IV antibiotics contributes less than a 10% increase to the total antibiotic concentration of the already extremely high tissue levels provided by the IO antibiotics. Interestingly, the infection within the IO cohort occurred in a patient who received both IV and IO antibiotics, with no infections occurring in those who received only IO antibiotics. Fourth, several surgeons elected to give IO vancomycin routinely to all their patients, while the remaining surgeons administered IO cefazolin unless there was a clinical indication to use vancomycin. The routine use of IO vancomycin was chosen for the potential improved coverage against methicillin-resistant *S. aureus* and coagulase-negative *Staphylococcus*; however, this rationale may not be clinically relevant as IO cefazolin achieves tissue concentrations higher than the reported resistance levels of coagulase-negative *Staphylococcus* [9, 28]. Additionally, the use of vancomycin for antibiotic prophylaxis has been shown to increase PJI risk in primary TKA [27].

Comparison of PJI Risk Between IO and Traditional IV Antibiotic Administration

The first clinical report on using regional prophylactic antibiotics (via limb intravenous cannulation) in TKA patients was by de Lalla et al. [7]. They performed 205 TKAs and reported no deep PJIs in this cohort. A more recent study

reported no early PJIs in a cohort of 331 patients who underwent primary TKAs and who received IO vancomycin [13]. The effectiveness of higher tissue antibiotic concentrations against *S. aureus* has also been studied in a mouse model to compare IV and IO regional administration of cefazolin and vancomycin [29]. In this study, mice were implanted with intraarticular knee prostheses inoculated with *S. aureus*; the mice were then randomized to one of six different antibiotic prophylaxis protocols. After 4 days, the bacterial load in the knee prostheses was quantified to compare each prophylactic regimen. Mice who received IO prophylactic antibiotics had a lower bacterial burden compared with mice receiving the same-dose IV prophylactic antibiotics for both cefazolin and vancomycin. We suggest that the ability of IO regional antibiotics to achieve tissue concentrations many times higher than bacterial minimum inhibitory concentrations is the mechanism responsible for reducing the PJI risk.

Other PJI Risk Factors

Diabetes, BMI, and renal failure were found to be PJI risk factors. This finding is consistent with previous studies that have shown a higher PJI risk in these patients [11, 15, 16, 23]. However, for the patients with these risk factors, the use of IO antibiotics did not result in a lower risk of infection (Table 3). Future studies with a larger sample size are needed to determine whether IO prophylactic antibiotics can reduce the PJI risk in patients with these risk factors.

Complications Associated with IO Administration of Antibiotics

All surgeons in this study found the technique of IO regional administration of antibiotics to the proximal tibial metaphyseal bone was found to be simple and straightforward. There were no cases where the prophylactic antibiotics could not be delivered by the IO route. Importantly in this series, there were no technique-related complications. The potential risks of the IO technique include compartment syndrome from incorrect needle placement and fat emboli syndrome [8, 18, 21]. Previous animal studies on IO fluid resuscitation have reported the subclinical occurrence of fat emboli, but this finding was also seen in the cases with IV fluid resuscitation [8, 10, 18]. Reassuringly, our study did not have any cases of clinically evident fat emboli syndrome. Red man syndrome is not an uncommon clinical occurrence when administering IV vancomycin [6, 24]. We found no instances of red man syndrome after IO vancomycin administration; another recent study has also reported no cases of red man syndrome in 331 patients who received 500 mg of IO vancomycin [13].

Conclusion

Regional IO prophylactic antibiotics in primary TKA results in a lower risk of early PJI compared with the traditional IV prophylactic antibiotics. This finding has clinical relevance as the volume of PJIs is increasing across the globe. Further randomized, prospective clinical trials are needed to validate the efficacy of regional prophylactic antibiotics in reducing PJI risk in primary TKA.

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