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Increased Rate of Early Periprosthetic Joint Infection in Total Hip Arthroplasty With the Use of Alternatives to Cefazolin Despite Additional Gram-Negative Coverage

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ABSTRACT

Background: Periprosthetic joint infection (PJI) remains one of the most devastating complications following total joint arthroplasty. Appropriate prophylactic antimicrobial administration and antibiotic stewardship are major factors impacting the risk of PJI in total hip arthroplasty (THA). The purpose of our study was to evaluate whether cefazolin administration was superior to noncefazolin antibiotics in prevention of PJI after primary THA.

Material and methods: A review of 9910 patients undergoing primary THA from 2013 to 2019 at a single institution was conducted. The primary outcome was PJI within 90 days of surgery. The Musculoskeletal Infection Society definition of PJI was used for this analysis. Groups were those receiving cefazolin + expanded gram-negative antimicrobial prophylaxis (EGNAP) and those receiving an alternative to cefazolin + EGNAP. Chi-square tests were conducted to determine statistical significance. Multivariate logistic regression was performed to eliminate confounders.

Results: 9028 patients received cefazolin + EGNAP, and 882 patients received an alternative to cefazolin + EGNAP. PJI rate using the Musculoskeletal Infection Society criteria was 0.82% (81/9910). PJI rate in the cefazolin + EGNAP group was 0.75% (68/9028). In the group receiving an alternative to cefazolin + EGNAP, the PJI rate was 1.47% (13/882). This difference was statistically significant ($P = .023$). On multivariate analysis, the odds ratio for developing PJI when an alternative to cefazolin was used was 2.05 ($P = .022$). When comparing alternatives, there remained a statistically significant increased PJI rate when the alternative used was clindamycin (odds ratio 2.65, $P = .007$).

Conclusion: Our data demonstrate that in the presence of EGNAP in THA, there was a higher PJI rate when clindamycin was given as an alternative to cefazolin. The number of THA patients receiving alternatives to cefazolin must be minimized.

Level of Evidence: III, Retrospective Cohort Study.

Introduction

Periprosthetic joint infection (PJI) remains one of the most feared complications in arthroplasty surgery. As a result, a great deal of effort has been made to minimize the risk of infection in this patient population. Antibiotic stewardship is one of the major factors affecting the risk of PJI in total knee (TKA) and hip arthroplasty (THA) patients. Recently, Wyles et al. published data supporting an increased risk of PJI in a large series of THA and TKA patients receiving a perioperative antibiotic other than cefazolin, leading to the recommendation of routine allergy testing in patients with a reported penicillin allergy [1]. The 2019 American Academy of Orthopaedic Surgeons clinical practice guidelines on PJI state only that there is limited evidence regarding the choice of one

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antibiotic over another and do not cite any evidence regarding superiority of cefazolin over noncefazolin antibiotics [2].

At our institution, we instituted an expanded gram-negative antimicrobial prophylaxis (EGNAP) protocol for THA after discovering that approximately 30% of PJIs in hips were secondary to gram-negative infections [3]. This protocol reduced the rate of PJI in THA patients and is now the standard of care for all THA patients at our center. However, in light of emerging data demonstrating that cefazolin may be more effective at reducing the risk of PJI than noncefazolin alternatives (ie, vancomycin or clindamycin) [4], we sought to investigate whether this assertion held true in the setting of the addition of the EGNAP protocol.

The purpose of this study was to compare the rate of PJI in THA patients receiving cefazolin vs that in those receiving noncefazolin antibiotics in addition to EGNAP at a high-volume institution. We hypothesized that there would be no difference in infection rates with cefazolin and noncefazolin antibiotics.

Material and methods

A review of all patients undergoing primary THA from 2013 to 2019 at a single academic orthopedic hospital was conducted. All patients undergoing primary THA with 90-day follow-up were included. The primary outcome measure was PJI within 90 days of surgery. The Musculoskeletal Infection Society (MSIS) definition of PJI was utilized for this analysis [5]. Groups were divided into those receiving cefazolin plus EGNAP and those receiving an alternative to cefazolin plus EGNAP. Patients undergoing THA who did not receive EGNAP as part of the perioperative antibiotic regimen, THA as the primary treatment for femoral neck fracture, and revision THA were excluded from analysis.

The standard of care for all patients undergoing primary THA was to administer weight-based dose of cefazolin (1 g if under 80 kg, 2 g if over 80 kg, 3 g if over 120 kg) and gentamicin dosing of 3-5 mg/kg, dosed based on a combination of the patient's height and weight, infused over 60 minutes. Patients older than 75 years, those weighing >120 kg, or with myasthenia gravis were given 2 g of aztreonam instead of gentamycin. Patients with a reported penicillin allergy (reported in the patient's medical record) or who had Methicillin-resistant Staphylococcus Aureus (MRSA) nares colonization were given a weight-based dose of vancomycin. Allergy testing for patients who reported a penicillin allergy was not routinely performed. Patients with MRSA nares colonization were also treated with nasal mupirocin as part of the institutional decolonization protocol. This protocol is additionally described in detail in previous literature from our institution [3].

Institutional hospital protocols during the study time period were standardized for all patients undergoing THA regardless of approach being used. Patients were advised to use 2% chlorhexidine gluconate wipes for skin decolonization the night before surgery as well as in the perioperative holding area prior to entering the operating theater. Additionally, all patients underwent nasal cleansing in the holding area with povidone iodine. Prior to preparing the patient in the operating theater, hair was removed from the incision site using clippers. The skin was then prepared using 2% chlorhexidine gluconate in 70% isopropyl alcohol solution (ChloraPrep; Carefusion, San Diego, CA). Tranexamic acid 1 g IV was administered to all patients prior to incision. All procedures were performed at a high-volume arthroplasty institution in standard operating theaters with similar staffing, sterile surgical helmet systems, and body exhaust suits. Surgical approach was performed based on surgeon preference and included direct anterior (DA), posterior, northern, anterolateral, and direct lateral approaches.

During the study period, there was the addition of vancomycin povidone iodine (VIP) protocol in high-risk patients as described by Iorio et al. [6] for the period January 2014 to December 2016. From January 2016 through the end of the study period, VIP protocol was used for all primary THA patients at our institution. The protocol consists of a 3-minute lavage with 0.35% povidone iodine (17.5 mL in 500 mL saline) following final component implantation. Pulsed irrigation is then performed using 1 L of sterile saline. Subsequently during wound closure, 1 g of vancomycin powder is placed deep to the fascia, and 1 g is placed superficial to the fascia [7]. All postoperative wounds were covered with a silver impregnated dressing (Aquacel; ConvaTec Inc.) which was removed 7 days after the operation. Deep vein thrombosis prophylaxis was aspirin 81 mg twice daily for 4 weeks in all patients except for those at high risk of thromboembolic event.

Chi-square analysis was conducted to determine statistical significance for categorical data. Age and body mass index (BMI) were treated as categorical variables with cutoffs of 65 years of age and BMI $\geq$ 35 kg/m^2. Significance was set at $P < .05$. Multivariate logistic regression was performed to control for identified independent risk factors for PJI. Fisher exact test was performed to compare the incidence of individual organisms in each cohort. All statistical analyses were performed using SPSS Version 25 (IBM, Armonk, NY). This retrospective review fell under the category of quality improvement and, therefore, did not require institutional review board approval. There was no outside funding for this study.

Results

A total of 9910 patients were included in the final analysis. The average age was 63.3 years (SD 11.5). The average BMI was 29.0 kg/m^2 (SD 5.9). Women constituted 56% of the cohort. There were significantly more men in the group receiving cefazolin. In the group not receiving cefazolin, there were significantly more patients with rheumatoid arthritis, aged $\geq$65 years, and with BMI $\geq$35. Complete demographic data are included in Table 1.

Of the total, 9028 patients received cefazolin + EGNAP, and 882 patients received an alternative to cefazolin + EGNAP. Among the patients receiving alternatives to cefazolin, 489 patients received clindamycin, and 393 patients received vancomycin. PJI rate in the entire cohort was 0.82% (81/9910). There were 68 PJIs in the cohort receiving cefazolin + EGNAP for a rate of 0.75% (68/9028). The PJI rate in the noncefazolin + EGNAP group was 1.47% (13/882). This difference was statistically significant ($P = .023$). There were 4 PJI cases in the vancomycin + EGNAP group for a rate of 1%, and 9 PJIs in the clindamycin + EGNAP group for a rate of 1.8%. Risk factors for PJI using the MSIS criteria are outlined in Table 2.

Male gender, diabetes, history of rheumatologic disease, and BMI $\geq$ 35 kg/m^2 were identified as risk factors for PJI independent of antibiotic regimen.

Multivariate logistic regression controlling for potentially confounding variables from Tables 1 and 2 showed the odds ratio of PJI to be 2.05 when an alternative to cefazolin was used ($P = .02$, 95% CI 1.1-3.7), which was statistically significant (Table 3). When directly comparing EGNAP + cefazolin to EGNAP + clindamycin in the multivariate model, there was an adjusted OR of 2.65 for PJI when using clindamycin compared with using cefazolin. This difference was statistically significant ($P = .007$). Given the issue of multiple comparisons in comparing the different alternatives to cefazolin (clindamycin and vancomycin), the Bonferroni correction was applied to compare cefazolin + EGNAP to vancomycin + EGNAP. In this model, there was no statistically significant difference in PJI rate between these 2 groups.

Organism profiles in each of the groups were also investigated. This was calculated as the incidence of each organism occurring in each patient cohort (Table 4). The incidence of gram-negative isolates was higher in the noncefazolin group (0.45%) than that in the

Table 1
Demographics of EGNAP therapy patients on cefazolin vs noncefazolin group.

Risk factors assessed for association with administration EGNAP with cefazolin intraoperatively						Risk factors assessed for association with administration EGNAP with cefazolin compared with clindamycin			
Risk factor	Total N (%)	EGNAP w/ cefazolin, n (%)	EGNAP w/o cefazolin, n (%)	EGNAP w/ clindamycin (%)	*P* value	Total N (%)	EGNAP w/ cefazolin, n (%)	EGNAP w/ clindamycin (%)	*P* value
Patients	9910	9028	393	489	N/A	9517	9028	489	N/A
Male	4365 (44)	4071 (45.1)	136 (34.6)	**158 (32.3)**	**<.0001**[a] χ^2	**4229**	**4071 (45.1)**	**158 (32.3)**	**<.0001**[a] χ^2
Female	5545 (56)	4957 (54.9)	257 (65.4)	331 (67.7)		5288	4957 (54.9)	331 (67.7)	
Diabetes mellitus	543 (5.5)	486 (5.4)	28 (7.1)	29 (5.9)	.300 χ^2	515	486 (5.4)	29 (5.9)	.602 χ^2
Rheumatologic history	379	337 (3.7)	23 (5.9)	19 (3.9)	.100 χ^2	356	337 (3.7)	19 (3.9)	.862 χ^2
Rheumatoid arthritis	258	226 (2.5)	19 (4.8)	**13 (2.7)**	**.018**[a] χ^2	239	226 (2.5)	13 (2.7)	.831 χ^2
Smoking	924	851 (9.4)	34 (8.7)	39 (8.0)	.503 χ^2	890	851 (9.4)	39 (8.0)	.283 χ^2
Age ≥65	4811	4353 (48.2)	213 (54.2)	**245 (50.1)**	**.053**[a] χ^2	4598	4353 (48.2)	245 (50.1)	.416 χ^2
BMI ≥35	1490	1329 (14.7)	75 (19.1)	**86 (17.6)**	**.016**[a] χ^2	1415	1329 (14.7)	86 (17.6)	.083 χ^2
MSIS PJI	81	68 (0.8)	4 (1.0)	**9 (1.8)**	**.031**[a] χ^2	**77**	**68 (0.8)**	**9 (1.8)**	**.009**[a] χ^2
Anterior approach	3854	3528 (39.1)	137 (34.9)	189 (38.7)	.243 χ^2	3717	3528 (39.1)	189 (38.7)	.850 χ^2

CI, confidence interval; N/A, not applicable; OR, odds ratio.
χ^2, Chi-square test.
Corresponding values for statistically significant comparisons are in bold.
[a] Statistically significant.

cefazolin group (0.14%); this finding approached but did not achieve statistical significance ($P = .058$).

When examining the different time periods when VIP was implemented, we found a trend in all 3 periods of higher rates of PJI in patients receiving alternatives to cefazolin. This was not significant for any individual time period. Additionally, there was a trend toward lower rate of PJI over time as VIP became the standard protocol for all primary THAs at our institution. The results of the sub-analysis and multivariate regression models demonstrating the effect of alternatives to cefazolin on PJI during the 3 time periods over which VIP was implemented are summarized in Table 5.

Discussion

The search for modifiable risk factors to lower the rate of PJI constitutes one of the most consistent efforts in arthroplasty practice. The discussion regarding the use of prophylactic antibiotics has evolved considerably over the years, with recommendations continuing to be refined. The 2019 American Academy of Orthopaedic Surgeons clinical practice guideline on the diagnosis and prevention of PJI cites limited evidence regarding the superiority of one antibiotic over another [2]. We found superiority of cefazolin to alternatives, with patients not receiving cefazolin at approximately twice the risk of developing early PJI when controlling for independent risk factors.

Several other recent studies have emerged concurring with the findings of lower PJI rates when administering cefazolin than with noncefazolin prophylaxis. Wyles et al. has reported an increase in PJI risk with the use of alternatives to cefazolin for antibiotic prophylaxis in total joint arthroplasty [1]. They recommended allergy testing for all patients with a reported penicillin allergy. Pagani et al. reported that allergy testing for patients reporting either a penicillin or cephalosporin allergy was cost-effective in reducing the burden of PJI [8]. While allergy testing is one way to provide reassurance, with the cross-reactivity of penicillin and cephalosporin being much lower than what was previously thought [9,10], it may or may not be necessary. Our institutional protocol has been modified such that patients are now only given an alternative to cephalosporins if there is a patient-reported or documented severe (ie, angioedema, anaphylaxis) allergy to penicillin. Patients with reported mild symptoms (hives, itching, gastrointestinal distress, unknown/historically reported allergy) are given cefazolin per standard institutional protocol.

Tan et al. had previously reported that TJA patients receiving vancomycin as the sole antibiotic prophylaxis were not associated

Table 2
Risk factors assessed for association with prosthetic joint infection (PJI) by MSIS.

Risk factors assessed for association with prosthetic joint infection (PJI) by MSIS of EGNAP population with Ancef vs non-Ancef					Risk factors assessed for association with prosthetic joint infection (PJI) by MSIS of EGNAP population with Ancef vs clindamycin			
Risk factor	Total N (%)	PJI, n (%)	No PJI, n (%)	*P* value	Total N (%)	PJI, n (%)	No PJI, n (%)	*P* value
Patients	9910	81	9829	N/A	9517	77	9440	N/A
Male (higher risk)	4365 (44.0)	49 (60.5)	4316 (43.9)	**.003**[a] χ^2	**4229**	**48 (62.3)**	**4181 (44.3)**	**.002**[a] χ^2
Female	5545 (56.0)	32 (39.5)	5513 (56.1)		5288	29 (37.7)	5259 (55.7)	
Diabetes mellitus	543	12 (14.8)	531 (5.4)	**<.0001**[a] χ^2	**515**	**10 (13.0)**	**505 (5.3)**	**.003**[a] χ^2
Rheumatologic history	379	9 (11.1)	370 (3.8)	**.001**[a] χ^2	**356**	**8 (10.4)**	**348 (3.7)**	**.002**[a] χ^2
Rheumatoid arthritis	258	3 (3.7)	255 (2.6)	.532 χ^2	239	2 (2.6)	237 (2.5)	.961 χ^2
Smoking	924	11 (13.6)	913 (9.3)	.186 χ^2	890	11 (14.3)	879 (9.3)	.135 χ^2
Age ≥ 65	4811	34 (42)	4777 (48.6)	.235 χ^2	4598	30 (39.0)	4568 (48.4)	.099 χ^2
BMI ≥ 35	1490	27 (33.3)	1463 (14.9)	**<.0001**[a] χ^2	**1415**	**24 (31.2)**	**1391 (14.7)**	**<.0001**[a] χ^2
Anterior approach	3854	39 (48.1)	3815 (38.8)	.086	3717	36 (46.8)	3681 (39.0)	.165 χ^2

χ^2, Chi-square test.
CI, confidence interval; N/A, not applicable; OR, odds ratio.
Corresponding values for statistically significant comparisons are in bold.
[a] Statistically significant.

Table 3
Multivariate logistic regression cefazolin vs clindamycin.

EGNAP group	OR for PJI (95% CI)	*P* value
EGNAP group w/o cefazolin (MSIS) unadjusted	1.97 (1.1 to 3.6)	**.026**[a]
EGNAP group w/o cefazolin (MSIS): adjusted	2.05 (1.1 to 3.7)	**.020**[a,b]
EGNAP group on Clindamycin (MSIS) unadjusted	2.47 (1.2 to 5.0)	**.011**[a]
EGNAP group on Clindamycin (MSIS): Adjusted	2.65(1.3 to 5.4)	**.007**[a,b]

CI, confidence interval; OR, odds ratio.
Cefazolin: adjusted for male gender, BMI $\geq$ 35, age $\geq$ 65, diabetes mellitus, rheumatologic history, rheumatoid arthritis. Clindamycin: Adjusted for male gender, BMI $\geq$ 35, diabetes mellitus, and rheumatologic history.
Corresponding values for statistically significant comparisons are in bold.
[a] Statistically significant.
[b] Multivariate logistic regression.

with an increased risk of PJI [11]. However, Kheir et al. reported that there are concerns with underdosing of vancomycin and potential increased rate of PJI compared with cefazolin [12]. More recent data identified vancomycin alone as associated with increased risk of PJI in both THA and TKA [13]. Our data only showed a statistically significant increased rate of PJI when clindamycin was the chosen alternative. This is partly due to the confounding effect of performing multiple direct comparisons and the low number of actual PJI cases in the individual cohorts receiving either clindamycin or vancomycin. Our results are consistent with the data reported by Wyles et al., who reported on both THA and TKA patients from 2004 to 2017 with respect to the fact that there is an increased rate of PJI if an alternative to cefazolin is given [1]. However, this is the first report to confirm these findings even in the presence of expanded gram-negative prophylaxis, which all THA patients have been receiving at our institution since July 2012, and the VIP protocol, which all THA patients have been receiving since 2016. Additionally, our data reflect a contemporary cohort of patients that received a treatment protocol that included interventions that have become the standard of care for modern arthroplasty practice. These include the addition of tranexamic acid, the increasing trend toward aspirin for primary deep vein thrombosis prophylaxis, multimodal pain regimens, rapid recovery/discharge protocols, and silver-impregnated dressings, which have been independently shown to have a positive impact on PJI rates [14]. This enhances the generalizability of our findings as they can be applied to most modern arthroplasty practices. The use of the MSIS criteria for PJI in our cohort is also a strength as there was decreased variability in the diagnostic criteria, which may have impacted reported PJI rates in cohorts that included patients from the pre-MSIS period. Additionally, including only 90-day infection rate reduces the likelihood of infections unrelated to the surgical procedure being inadvertently counted as PJI. We have studied the effect of the other protocols such as VIP on organism profile at our institution and found no difference in overall profiles with or without the use of the VIP in TJA [15]. However, organism profile has been found to differ by approach, with a greater proportion of gram-negative PJI in DA approach THA [16].

Surgical approach may play a role and influence PJI rates as shown by Aggarwal et al., who reported a higher rate of PJI in DA approaches vs non-DA approaches [17]. However, in our cohort, despite a trend toward higher PJI rates in DA approach patients, there was no statistically significant difference in PJI rates between DA and non-DA approach.

The dosing of perioperative antibiotics may also be a factor to consider when examining PJI rates. In the past, most cefazolin administration protocols called for 1 g in most patients with an increase to 2 g in heavier patients. More recent guidelines recommend giving 2 g as the minimum dose with 3 g for patients weighing >120 kg [18,19]. Rondon et al. demonstrated that patients weighing >120 kg were frequently underdosed with cefazolin and thus at a higher risk of PJI [20]. In our cohort, BMI $\geq$ 35 was found to be an independent risk factor for PJI. Further investigation is warranted to determine the relationship between dosing of cefazolin and PJI rates in obese patients. With vancomycin, underdosing, especially in obese patients, has been demonstrated to be a

Table 4
Organism profile for PJI in each group.

Organism	N = 9028 Ancef	Organism/Ancef population (%)	N = 882 without Ancef	Organism/non-Ancef population (%)	*P* value
Gram positive					
Methicillin-Sensitive Staphylococcus Aureus	36	0.40	4	0.45	.778
Methicillin Resistant Staphylococcus Aureus	8	0.09	2	0.23	.222
Methicillin-Sensitive Staphylococcus Epidermidis	2	0.02	0	0.00	1.000
Methicillin-Resistant Staphylococcus Epidermidis	2	0.02	1	0.11	.244
Corynebacterium species	3	0.03	0	0.00	1.000
Serratia marcescens	1	0.01	0	0.00	1.000
Staphylococcus caprae	1	0.01	0	0.00	1.000
Staph. lugdunensis	3	0.03	0	0.00	1.000
Streptococcus agalactiae	9	0.10	1	0.11	.606
Strep. mitis	1	0.01	0	0.00	1.000
Strep. sanguinis	1	0.01	0	0.00	1.000
Cutibacterium acnes	1	0.01	1	0.11	.170
Peptostreptococcus asaccharolyticus	1	0.01	0	0.00	1.000
Finegoldia magna	1	0.01	0	0.00	1.000
Propionibacterium granulosum	0	0.00	1	0.11	.089
Total	70	0.78	10	1.13	.238
Gram negative					
Pseudomonas aeruginosa	4	0.04	1	0.11	.373
Enterococcus faecalis	3	0.03	1	0.11	.311
Enterobacter cloacae	3	0.03	1	0.11	.311
Enterococcus gallinarum	1	0.01	0	0.00	1.000
Klebsiella aerogenes	1	0.01	0	0.00	1.000
Citrobacter koseri	0	0.00	1	0.11	.089
Providencia stuartii	1	0.01	0	0.00	1.000
Total	13	0.14	4	0.45	.058

Table 5
Effect of noncefazolin antibiotics on PJI during various VIP time periods.

VIP intervention on EGNAP with cefazolin	OR (95% CI)	*P* value	OR (95% CI)[a]	*P* value[a]
January 2013 to December 2013(pre-VIP)	3.197 (.82 to 12.51)	.095	2.536 (.63 to 10.29)	.193
January 2014 to December 2015 (high-risk VIP)	1.651 (.62 to 4.39)	.315	1.883 (.69 to 5.14)	.216
January 2016 to September 2019 (all-risk VIP)	1.698 (.67 to 4.33)	.267	1.819 (.71 to 4.69)	.215

CI, confidence interval; OR, odds ratio.
Adjusted for Male gender, BMI $\geq$ 35, age $\geq$ 65, diabetes mellitus, rheumatoid arthritis, and rheumatologic history.
[a] Multivariate logistic regression.

common phenomenon [12], which may also potentially be a contributing factor to the increased rate of PJI in out cohort. Recommendation for vancomycin dosing is 15 mg/kg [21]. While our institutional protocol follows this guideline, patients heavier than 100 kg receive 2 g as the maximum dose. This dosing is adequate for patients weighing up to 133 kg based on the 15-mg/kg guideline. However, patients who weigh more than 133 kg are at risk of being underdosed. With the prevalence of obesity in Americans aged 60 years and older being over 40% as of 2018 [22], this is likely to become an increasing concern among arthroplasty patients, especially given concerns for nephrotoxicity [23], which is much less of a concern with cefazolin [24]. The combination of obesity as an independent risk factor for PJI and the increased likelihood of obese patients to be underdosed with perioperative antibiotics is a topic that warrants further investigation.

Limitations of this study include the retrospective design. Patients in the cohort receiving alternatives to cefazolin may have received either clindamycin or vancomycin. An additional subgroup analysis was not performed to directly compare PJI rates in patients receiving clindamycin vs vancomycin due to small numbers in each antibiotic group. While only including those infections that occurred within 90 days of surgery can be viewed as a limitation, we thought that the impact of a modifiable risk factor such as prophylactic antibiotic administration would manifest itself in the early postoperative period. Another limitation is that EGNAP is not the sole additional intervention that was undertaken at our institution during the study period. Our institutional protocol has evolved to include the addition of betadine irrigation/topical vancomycin powder (VIP). Published literature from our institution has demonstrated a decrease in PJI rates in TKA and high-risk THA and TKA patients with the use of VIP [6,25]. However, even in the presence of these changes, there still appears to be an additional protective effect of receiving cefazolin vs noncefazolin antibiotics in the early postoperative period, with the rate of PJI approximately twice that of those receiving cefazolin plus EGNAP. This study adds to the growing body of evidence that cefazolin is strongly preferred over noncefazolin antibiotics to minimize the risk of PJI.

Conclusion

Our data demonstrate that in the presence of expanded gram-negative antibiotic prophylaxis in THA, there was a higher PJI rate when clindamycin was given as an alternative to cefazolin. The number of THA patients receiving alternatives to cefazolin for antibiotic prophylaxis must be minimized.

Conflicts of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

D. Ortiz has stock holdings in ROM3 Technologies, Inc.; is on the editorial board of *Journal of Arthroplasty* and *Arthroscopy Journal*; and is a member of the Knee Program Committee of AAOS. W. J. Long received royalties from Ortho Development, Microport, and J&J; is in the speakers' bureau of or gave paid presentations for Convatec, THINK Surgical, and Pacira; is a paid consultant for TJO, DePuy, Ortho Development, Microport, J&J, THINK Surgical, Convatec, and Pacira; receives research support as a principal investigator from THINK Surgical and KCI; receives financial or material support from Elsevier; is on the editorial or governing board of *Journal of Arthroplasty* and *The Knee*; and is a member of AAOS ICL Hip.

For full disclosure statements refer to https://doi.org/10.1016/j.artd.2022.02.019.

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