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CEFAZOLIN PROPHYLACTIC EFFICACY ON PROSTHETIC JOINT INFECTION AFTER PRIMARY HIP ARTHROPLASTY

EFICÁCIA PROFILÁTICA DA CEFAZOLINA SOBRE A INFECÇÃO PROTÉTICA ARTICULAR APÓS ARTROPLASTIA PRIMÁRIA DE QUADRIL

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ABSTRACT

Objective: Perioperative deep prosthetic joint infection (PJI) is a serious postoperative complication of total hip arthroplasty (THA). We aimed to compare the efficacy of cefazolin administered within 24 and 48 h of primary THA for PJI prophylaxis. Methods: In this retrospective study, 720 patients were divided into two groups depending on whether cefazolin was administered as a single injection of 2 g twice daily within 24 (24-h group) or 48 h of surgery and the following day (48-h group). Sex, age at surgery, body mass index, co-existing diseases, blood test data, and PJI risk factors were evaluated. Results: The 24- and 48-h groups included 364 and 356 patients, respectively. Diabetes mellitus was the most common risk factor for PJI in both groups. The corresponding incidence of perioperative deep PJI following primary THA was 0.55% and 0.28% in the 24- and 48-h groups, respectively. There was no significant difference in patient background characteristics between the groups. Conclusions: Cefazolin administration within 24 h of primary THA may be appropriate for perioperative deep PJI. ***Level of Evidence II; Retrospective study.***

Keywords: Cefazolin. Surgical Wound Infection. Arthroplasty, Replacement, Hip. Antibiotic Prophylaxis.

RESUMO

*Objetivo: A infecção de prótese articular (IPA) perioperatória profunda é uma grave complicação pós-operatória da artroplastia total de quadril (ATQ). Este estudo buscou comparar a eficácia da cefazolina administrada dentro de 24 e 48 horas após ATQ para profilaxia de IPA. Métodos: Neste estudo retrospectivo, 720 pacientes foram divididos em dois grupos, que receberam cefazolina em uma injeção de 2g duas vezes por dia nas primeiras 24 e 48 horas (grupos de 24 e 48 horas), respectivamente. Foram avaliados sexo, idade na data da cirurgia, índice de massa corporal, comorbidades, testes sanguíneos e fatores de risco para IPA. Resultados: Os grupos de 24 e 48 horas incluíram, respectivamente, 364 e 356 pacientes. O fator de risco para IPA mais comum nos dois grupos foi o diabetes mellitus. A incidência de IPA perioperatória profunda após ATQ foi, respectivamente, de 0,55% e 0,28% nos grupos de 24 e 48 horas. Não houve diferença significativa nas características gerais dos pacientes entre os dois grupos. Conclusão: A administração de cefazolina dentro de 24 horas após ATQ primária pode ser adequada para IPA perioperatória profunda. **Nível de Evidência II; Estudo retrospectivo.***

Descritores: *Cefazolina. Infecção da Ferida Cirúrgica. Artroplastia de Quadril. Antibioticoprofilaxia.*

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INTRODUCTION

Prosthetic joint infection (PJI) is one of the most serious post-operative complications of total hip arthroplasty (THA), with an estimated incidence of 1.1% or less.[1] Cefazolin, a first-generation cephalosporin, is a first-line drug for PJI prophylaxis following THA.[2] In 2017, the United States Center for Disease Control and Prevention (CDC) recommended a single antibiotic dose to prevent postoperative infection.[3] However, the American Association of Hip and Knee Surgeons disagrees with this recommendation owing to a lack of evidence of a protective effect with a single antibiotic dose against PJI in case of artificial joint replacements. The current recommendation is prophylactic antibiotic dosing at 24 h postoperatively.[4] Thus, further research is needed to determine the most appropriate time for cefazolin administration and procure a more direct evidence of its effects. Therefore, we investigated the incidence of perioperative deep PJI in patients who underwent primary THA followed by cefazolin prophylaxis administration within 24 and 48 h.

All authors declare no potential conflict of interest related to this article.

The study was conducted at the Nissan Tamagawa Hospital, Tokyo, Japan.
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PATIENTS AND METHODS

This retrospective study involved patients who received a single cefazolin injection (2 g) twice daily, for deep PJI prevention following primary THA, within 48 h of surgery and on the following day (48-h group) from August 2018 to June 2019, and within 24 h of surgery (24-h group) from July 2019 to January 2020. Furthermore, it was approved by our institutional ethics committee. For the 48-h group, rapid administration was performed 30 min preoperatively to maximize the drug tissue concentration during the operation. The second administration was performed 2 h after the surgery (3 h after starting the surgery in case of bilateral hip arthroplasty), and in the morning and afternoon on the second day. Body exhaust system surgical suits were worn during the surgery. All surgeons wore double gloves to ensure aseptic operation. The affected limb was thoroughly wiped with 70% alcohol containing chlorhexidine, and then with 10% iodine solution. The operative field was covered with an iodine drape and opened. Cases of revision THA and THA with concurrent surgery were excluded.

The following data were analyzed: sex, age, body mass index, surgical site, PJI risk factors (such as diabetes mellitus),[5] and preoperative blood test values. PJI was defined based on the criteria established by Parvizi et al.[6] and evaluated along with magnetic resonance imaging (MRI) findings. The investigation period was 90 days after the surgery.[7] Cases of late infection (>90 days) were excluded. Statistical analysis was performed using Excel Statistics ver. 3.2 (Bell Curve). Nominal and continuous variables were compared using Fisher's exact test and Mann–Whitney *U* test, respectively. Results were considered statistically significant at P-value < 0.05. The ethics committee of Nissan-Kouseikai Institute of Medicine approved this study (approved number 2019-027).

RESULTS

There were 364 and 356 patients in the 24- and 48-h groups, respectively. The proportion of women was higher in both groups; the median ages were 66 and 65 years in the 24- and 48-h groups, respectively. There was no significant difference in the distribution of body weight or surgical sites, with more surgeries performed for the right hip joint than for the left and both hip joints. Diabetes mellitus was the most common risk factor in both groups. Intergroup differences in the other baseline patient characteristics were statistically insignificant. (Table 1)

Table 1. Characteristics of patients in the two groups.

	Cefazolin at 24 h after surgery (n = 364)	Cefazolin at 48 h after surgery (n = 356)	P-value
Male/Female, n (%)	42/322 (11.5/88.5)	54/302 (15.2/84.8)	0.0929
Age (years), median (range)	66 (21–91)	65 (42–92)	0.5709
Body weight (kg), n (%)			
<60	244 (67.0)	221 (62.1)	0.0948
60–120	120 (33.0)	135 (37.9)	0.0948
BMI (kg/m^2), median (range)	22.7 (16.4–41.4)	23.0 (16.0–38.8)	0.2448
Surgical site, n (%)			
Right hip	173 (47.5)	157 (44.1)	0.1983
Left hip	116 (31.9)	133 (37.4)	0.3058
Both hip	75 (20.6)	66 (18.5)	0.2730
Diabetes mellitus, n (%)	27 (7.4)	22 (6.2)	0.3049
Blood tests, median (range)			
WBC (/μL)	5,300 (2,300–11,100)	5,300 (2,700–10,500)	0.6281
Lymp (%)	27.5 (5.4–49.0)	27.2 (5.6–47.7)	0.5413
AST (IU/L)	20.0 (10.0–71.0)	20.0 (10.0–116.0)	0.8801
ALT (IU/L)	15.0 (4.0–129.0)	16.0 (5.0–143.0)	0.4793
sCr (mg/dL)	0.7 (0.4–1.3)	0.7 (0.4–1.4)	0.6543
eGFR (mL/min/1.73 m^2)	70.9 (33.8–143.4)	71.4 (38.9–126.7)	0.1128

Abbreviations: BMI: body mass index; WBC: white blood cell; Lymp: lymphocyte; AST: aspartate aminotransferase; ALT: alanine aminotransferase; sCr: serum creatinine; eGFR: estimated glomerular filtration rate.

The incidence rates of perioperative deep PJI following primary THA were 0.55% (2/364) and 0.28% (1/356) in the 24- and 48-h groups, respectively; the intergroup differences were statistically insignificant. The clinical background and courses of the three PJI cases are shown in Table 2. MRI showed a high-intensity area, akin to that associated with pus accumulation (Figure 1). The age range of the patients with PJI was 65–85 years; there were no other risk factors. However, the infection onset date was postoperative days 9–21. These three cases of PJI were treated with debridement; the patients were administered several antibiotics orally and parenterally and were discharged on postoperative days 37–57.

DISCUSSION

This study suggests that a suitable cefazolin prophylaxis period for preventing perioperative deep PJI following primary THA is within 24 h of surgery. The overall incidence of PJI in this study was 0.42% (3/720), which was within the range reported previously.[1] In this study, the detected coagulase-negative staphylococci (CNS) strain was methicillin-resistant; moreover, the strains detected in the three cases have been previously reported.[8,9] The main advantages of shortening the antibiotic administration period are suppression of the emergence of resistant bacteria; prevention of needle stick infections; and reduction of drug-induced adverse events, medical costs, and work burdens.

In this study, cefazolin was administered at a dose of 2 g intravenously to all patients; this is the recommended standard adult perioperative dose.[10] However, the current guidelines recommend a weight-based dosing protocol of 1, 2, and 3 g once for patients weighing <60, 60–120, and >120 kg, respectively.[11,12] None of the patients weighed >120 kg in the present study, and it seems that there was no case of cefazolin underdosing.

PJI incidence has been reported to be significantly higher in patients with artificial joint replacements who have diabetes mellitus than in those without diabetes.[5] In this study, the hemoglobin A1c level in the 24- and 48-h groups was 6.6% (6.0%–7.5%) and 6.7% (5.9%–7.8%) in patients with diabetes mellitus, respectively, with intergroup differences being statistically insignificant. There were 67 and 50 patients aged ≥75 years in the 24- and 48-h groups, respectively; the corresponding PJI incidence rates were 1.5% and 2.0%, which did not differ significantly. As the three PJI patients were aged between 65 and 85 years, PJI may have to be monitored more closely in elderly patients than in young patients.

The limitations of this study are that it was conducted in a single facility as a retrospective survey with a small sample number of patients. Furthermore, the year of cefazolin administration was different between the groups. However, this study revealed the appropriate time of cefazolin administration for perioperative deep PJI prophylaxis following primary THA.

CONCLUSION

Cefazolin administration within 24 h of primary THA may be appropriate for the prophylaxis of perioperative deep PJI.

Table 2. Clinical background of and courses followed in the three cases with deep PJI.

Patient no.	Cefazolin	Age/body weight	Sex	Surgical site	Infection onset date/symptoms	Bacterium detection date/bacterium (Specimen)	Readmission date	Treatment	Discharge date
1	24 h	65/89.2 kg	Female	Both hip	POD9 Exudate from the right wound	POD16 /Staphylococcus epidermidis MRCNS (Pus)	Continued hospitalization	Debridement Levofloxacin Vancomycin Clindamycin Minomycin Sulfamethoxazole-Trimethoprim	POD37
2	24 h	85/55.5 kg	Male	Right hip	POD21 Fever, redness	POD25 /Staphylococcus aureus (Excise tissue, pus)	POD23	Debridement Linezolid Rifampicin Sulfamethoxazole-Trimethoprim Tedizolid Clindamycin	POD57
3	48 h	75/47.9 kg	Female	Right hip	POD18 Fever, pain	POD19 /MRSA (Excise tissue, synovial fluid)	POD19	Debridement Levofloxacin Rifampicin Linezolid Clindamycin	POD38

Abbreviations: PJI: prosthetic joint infection; MRCNS: methicillin-resistant coagulase-negative staphylococci; MRSA: methicillin-resistant *Staphylococcus aureus*; POD: postoperative day.

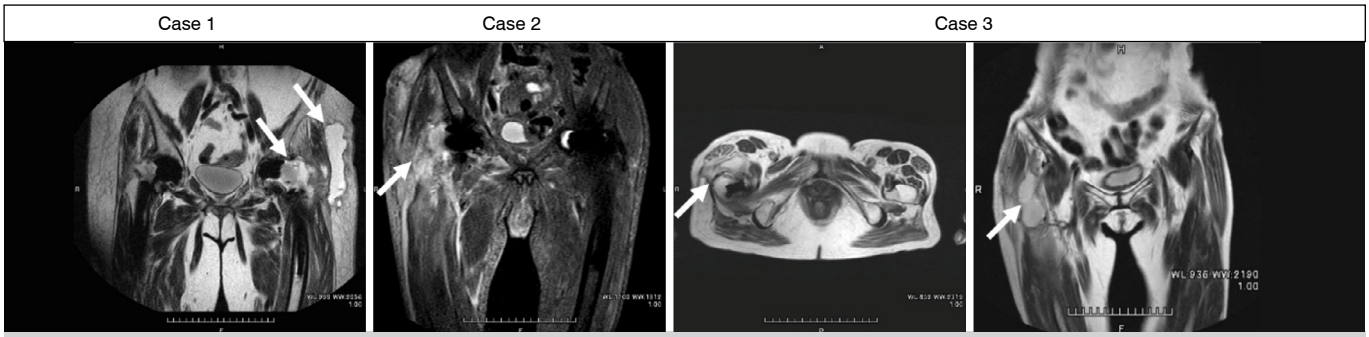

Figure 1. Magnetic resonance imaging findings in the three cases with deep prosthetic joint infection (PJI). Arrows indicate parts with deep PJI. Case 1: T2 coronal image, Case 2: fat-suppressed coronal image, Case 3: (left) T2 axial image, (right) T2 coronal image.

AUTHORS' CONTRIBUTION: This manuscript, which is a multi-institutional study has six authors. Each author contributed individually and significantly to the development of the manuscript: KS: Substantial contribution to the conception and design of the study, and acquisition, analysis, interpretation of the study data. Writing of the work and final approval of the version of the manuscript to be published; YT, ST, TO, AK and MM: Writing of the work and final approval of the version of the manuscript to be published.

REFERENCES

1. Tang WM, Chiu KY, Ng TP, Yau WP, Ching PTY, Seto WH. Efficacy of a single dose of cefazolin as a prophylactic antibiotic in primary arthroplasty. J Arthroplasty. 2003;(18):714-18.
2. Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm. 2013;(70):195-283.
3. Berríos-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, et al. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. JAMA Surg. 2017;152(8):784-91.
4. Yates AJ Jr. American Association of Hip and Knee Surgeons Evidence-Based Medicine Committee. Postoperative prophylactic antibiotics in total joint arthroplasty. Arthroplast Today. 2018;4(1):130-1.
5. Martin ET, Kaye KS, Knott C, Nguyen H, Santarossa M, Evans R, et al. Diabetes and risk of surgical site infection: a systematic review and meta-analysis. Infect Control Hosp Epidemiol. 2016;37(1):88-99.
6. Parvizi J, Tan TL, Goswami K, Higuera C, Della Valle C, Chen AF, et al. The 2018 definition of periprosthetic hip and knee infection: an evidence-based and validated criteria. J Arthroplasty. 2018;33(5):1309-14.e2.
7. Castella A, Argentero PA, Farina EC, Charrier L, Del Prever EMB, Zotti CM, et al. Incidence of surgical-site infections in orthopaedic surgery: a northern Italian experience. Epidemiol Infect. 2011;139(5):777-82.
8. Ammon P, Stockley I. Allograft bone in two-stage revision of the hip for infection. Is it safe?. J Bone Joint Surg Br. 2004;86(7):962-5.
9. Rafiq I, Gambhir AK, Wroblewski BM, Kay PR. The microbiology of infected hip arthroplasty. Int Orthop. 2006;30(6):532-5.
10. Ho VP, Nicolau DP, Dakin GF, Pomp A, Rich BS, Towe CW, et al. Cefazolin dosing for surgical prophylaxis in morbidly obese patients. Surg Infect (Larchmt). 2012;13(31):33-7.
11. Hansen E, Belden K, Silibovsky R, Vogt M, Arnold WV, Bicanic G, et al. Perioperative antibiotics. J Arthroplasty. 2014;29(Suppl 2):29-48.
12. Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt). 2013;(14):73-156.