# Efficacy of A Single Dose of Cefazolin as a Prophylactic Antibiotic in Primary Arthroplasty

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**Abstract:** We analyzed the wound infection rate of 1,367 primary total hip and knee arthroplasties performed between 1991 and 1999. Two hundred and fifteen arthroplasties were performed with 3 doses (3 × 750 mg) of cefuroxime, and 1,152 arthroplasties were performed with a single preoperative dose (1 × 1 g) of cefazolin as antimicrobial prophylaxis. All wound infections that occurred within 2 years of the index surgery were analyzed. The deep wound infection rate of total hip arthroplasty was 1.1% (95% confidence interval [CI], 0%–3.3%) in the cefuroxime group and 1.1% (95% CI, 0%–2.2%) in the cefazolin group (Fisher's exact test, $P = 1.0$). The deep wound infection rate of total knee arthroplasty in the cefuroxime group (1.6%; 95% CI, 0%–3.8%) was not significantly different from the cefazolin group (1.0%; 95% CI, 0.3%–1.7%) (Fisher's exact test, $P = .63$). We concluded that a single dose (1 g) of cefazolin given at anesthetic induction offered similar protection to 3 doses (3 × 750 mg) of cefuroxime in preventing infection in primary total joint arthroplasty. **Key words:** antimicrobial prophylaxis, antibiotic, total joint arthroplasty, infection, prevention.


Although it is uncommon, periprosthetic infection is probably the most devastating and expensive complication in arthroplasty surgery. It has been estimated that the hospital cost for treating an infected arthroplasty was 3 to 6 times that of a primary arthroplasty [1,2]. Prophylactic antibiotic drugs have been proven to be an effective measure for prevention of postoperative wound infection in patients with prosthetic joint implantation [3–6]. Although it is generally accepted that cefazolin is the antibiotic of choice for antimicrobial prophylaxis in arthroplasty, there is no common consensus with regard to the optimal duration of prophylaxis. We performed a retrospective review of all the primary total joint arthroplasties performed in our center from January 1991 to December 1999. During this time, all the surgical wounds were routinely and systematically monitored by infection control nurses. Our goal was to report the superficial and deep wound infection rates of primary arthroplasty performed with a single preoperative dose of cefazolin as antimicrobial prophylaxis.

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## Patients and Methods

We reviewed all the primary total hip arthroplasties (THAs) and total knee arthroplasties (TKAs) performed in our hospital from January 1991 to December 1999. In January 1991, we launched a surgical wound infection surveillance program to

monitor all orthopedic surgeries, including total joint arthroplasty. A designated registered nurse from the hospital infection control unit regularly assessed all patients who underwent orthopedic procedures in the absence of the surgical team to record and report all wound complications. Wound infection was defined as the presence of erythema, tenderness, and increase in temperature at the wound together with purulent discharge from the wound. Wound infection was further classified as superficial or deep according to the involvement above or below the deep fascia. Wound swabs were taken from all infected wounds. After the patients were discharge from the hospital, clinical assessment was repeated at 3 months, 6 months, and 1 year after the surgery. We recorded all periprosthetic infections thereafter.

In line with the hospital infection control policy, we changed the prophylactic antibiotic regimen for all clean orthopedic surgeries from intravenous cefuroxime (1 preoperative and 2 postoperative doses every 8 hours; each dose 750 mg) to one single preoperative dose (1 g) of intravenous cefazolin in January 1993. The patients were grouped according to the regimen of antimicrobial prophylaxis they received. We excluded from this review patients with a known history of allergy to penicillin or cephalosporin groups of antibiotics and patients with inflammatory arthritis who required steroids for disease control at the time of the index surgery. We did not include revision arthroplasty because we cannot confidently exclude the presence of concomitant low-grade infection. For the same reason, we did not include conversion arthroplasty performed for failed hemiarthroplasty for femoral neck fracture as well as failed internal fixation for intertrochanteric fracture. The same prophylactic antibiotic regimen that we used for primary arthroplasty was used for revision and conversion arthroplasty.

All surgeries were performed in operating rooms equipped with vertical laminar air flow. The surgical team, including the scrub nurse, used a total body exhaust system in all primary TKA, but not in THA. The preoperative dose of antibiotic was given at anesthetic induction by the anesthetist. All TKAs were performed with a tourniquet. We ensured that the time interval between antibiotic administration and inflation of the tourniquet was not less than 20 minutes. The skin of the surgical field was not shaved, but was prepared with 10% povidone iodine solution twice before draping. The duration between the incision and wound closure was noted by the anesthetist. We used both cemented and cementless hip prostheses, but only cemented knee prostheses were used. No antibiotic-containing cement was used. Drainage tubes were routinely used in all cases. All surgeries were performed by surgeons with more than 5 years of orthopedic training.

Fisher's exact test was used to evaluate the statistical differences of categorical data because the frequency in at least one of the cells was below 5. Continuous data were compared using student's *t*-test. All calculations were performed using the software SPSS (SPSS, Chicago, IL). Type I error was set at the value of 0.05. The odds ratio and type II error were also calculated.

## Results

From January 1991 to December 1999, we performed a total of 1,377 primary THAs and primary TKAs in 897 patients. Four patients were excluded because they were allergic to penicillins or cephalosporins, and 6 additional patients were excluded because they required steroid treatment for inflammatory arthritis. Therefore, 1,367 arthroplasties in 887 patients were available for review. Of these 1,367 arthroplasties, 215 were in the cefuroxime group and 1,152 were in the cefazolin group. The demographic characteristics of these 887 patients were summarized in Table 1.

The 2 groups did not show significant difference in age and gender. No patient was lost to follow-up or died within the 2-year period after the index surgery, and all patients were followed up for at least 2 years. All surgeries were completed within 4 hours, and therefore, no intraoperative antibiotic was given [7].

The overall deep wound infection rate in the cefuroxime group was 1.4% (95% confident interval [CI], 0%–2.96%) and 1.0% (95% CI, 0.5%–1.6%) in the cefazolin group (Fisher's exact test, $P = .72$). The deep wound infection rate of THA was 1.1% (95% CI, 0%–3.3%) in the cefuroxime group and 1.1% (95% CI, 0%–2.2%) in the cefazolin group (Fisher's exact test, $P = 1.0$). The deep wound infection rate of TKA in the cefuroxime group (1.6%; 95% CI, 0%–3.8%) was not significantly different from the cefazolin group (1.0%; 95% CI, 0.3%–1.7%) (Fisher's exact test, $P = .63$). The primary diagnosis and bacteriology of the infected cases were summarized in Table 2. The interval between the index surgery and the diagnosis of infection was 6.7 months in the cefuroxime group and 7.0 months in the cefazolin group (student's *t*-test, $P = .89$).

The overall superficial wound infection rates of the cefuroxime group and the cefazolin group were

**Table 1.** Epidemiology and Number of Wound Infections in Patients Receiving Cefuroxime and Cefazolin as Antimicrobial Prophylaxis

| | | Cefuroxime Group (n = 215) | Cefazolin Group (n = 1152) | *P* Value |
|---|---|---|---|---|
| Gender (F:M ratio) | | 155F:60M | 852F:300M | .32 |
| Age (years ± SD) | THA | 52.4 ± 14.3 | 55.2 ± 12.5 | >0.05 |
| | TKA | 70.8 ± 13.6 | 72.3 ± 10.6 | >0.10 |
| Procedures (n) | THA | 90 | 360 | — |
| | TKA | 125 | 792 | — |
| Superficial wound infections (n) | Overall | 6 | 19 | 0.26 |
| | THA | 4 | 8 | 0.27 |
| | TKA | 2 | 11 | 0.69 |
| Deep wound infections (n) | Overall | 3 | 12 | 0.72 |
| | THA | 1 | 4 | 1.00 |
| | TKA | 2 | 8 | 0.63 |

Abbreviations: THA, total hip arthroplasty; TKA, total knee arthroplasty, SD = standard deviation.

2.8%, (95% CI, 0.6%–5.0%) and 1.6% (95% CI, 0.9%–2.4%) (Fisher's exact test, $P = .26$), respectively. With the given sample size, the odds ratio was 0.7 and the type II error was 0.61.

## Discussion

Cefazolin is a broad-spectrum, first-generation cephalosporin. It is currently the most popular antimicrobial prophylaxis in a wide range of "clean" surgeries, including cardiac and vascular surgery [8] as well as orthopedic procedures [4,9–13]. Although the pharmacokinetics aspects [7,9,14–18] and the efficacy of cefazolin in bringing down the infection rate of arthroplasty to around 1% were well studied and documented [5,9–13], there is still no consensus on the optimum duration of giving the antibiotic as prophylaxis [4,11].

Theoretically, the ideal length for antimicrobial prophylaxis should be as short as possible to prevent the emergence of resistant organisms, to reduce the chance of developing adverse reactions, to improve adherence, and to reduce drug costs and personnel requirements. It has been shown that antimicrobial prophylaxis started more than a few hours before or several hours after skin incision is ineffective [11,19,20]. Burke [19] had suggested that the most suitable time for antimicrobial prophylaxis administration was just before the skin incision. Moreover, prophylactic antibiotics contin-

**Table 2.** Characteristics and Bacteriology of Arthroplasties Complicated by Deep Wound Infection

| Arthroplasty | Primary Diagnosis* | Antimicrobial Prophylaxis Received | Bacteriology | Time Interval Between Operation and Infection (mo) |
|---|---|---|---|---|
| THA | AVN | Cefuroxime | MRSA | 6 |
| THA | AVN | Cefazolin | MRSA | 3 |
| THA | AVN | Cefazolin | MRSA | 10 |
| THA | AVN | Cefazolin | MRSA | 13 |
| THA | AS | Cefazolin | *Staphylococcus epidermidis* | 5 |
| TKA | OA | Cefuroxime | MRSA | 10 |
| TKA | OA | Cefuroxime | MRSA | 4 |
| TKA | ON | Cefazolin | Group G *Streptococcus* | 12 |
| TKA | OA | Cefazolin | MRSA | 11 |
| TKA | OA | Cefazolin | MRSA | 4 |
| TKA | OA | Cefazolin | MRSA | 3 |
| TKA | ON | Cefazolin | MRSA | 1 |
| TKA | OA | Cefazolin | *Staphylococcus epidermidis* | 5 |
| TKA | OA | Cefazolin | *Streptococcus pyogenes* | 8 |
| TKA | OA | Cefazolin | *Pseudomonas aeruginosa* | 9 |

Abbreviations: AVN, avascular necrosis: AS, ankylosing spondylitis: OA, osteoarthritis; ON, osteonecrosis; MRSA, methicillin-resistant *Staphylococcus aureus.*

ued for more than 24 hours has also been shown to be ineffective in clean orthopedic procedures [11,21,22]. Therefore, a number of expert panels suggested an antimicrobial prophylaxis regimen consisting of one preoperative dose of antibiotics followed by 2 to 3 postoperative doses [4,13,23–25].

A number of reports have documented the efficacy of using 3 or more doses of cefazolin as antimicrobial prophylaxis in clean orthopedic procedures [9–13]. The efficacy of using just one single preoperative dose of cefazolin has only been reported once [11]. Heydemann and Nelson [11] reported no deep infection in a group of 103 patients receiving a single preoperative dose of 1 g of either cefazolin or nafcillin. We have further confirmed in our study, with a larger sample size, that a single 1 g dose of cefazolin given at anesthetic induction was as effective as 3 doses of cefuroxime. We arbitrarily included infections that occurred within 2 years after the index arthroplasty because we believed that infection that occurs after that period may not be related to the prophylactic measures given perioperatively. No patient was lost to follow-up evaluation during this relatively short study period. The 1.1% and 1.0% deep wound infection rates in our THA and TKA patients are within the range reported in other large series using various prophylactic antibiotic regimens (THA, 0.25%–1.67% [26–30]; TKA, 0.63%–2.0% [27,31–33]).

Furthermore, it has been shown that even in the standard of living in 1986, the saving in drug costs of using just one dose of antibiotic instead of a 48-hour regimen would be $7,700,000 per 100,000 patients [11]. We concluded that a single dose (1 g) of cefazolin given at anesthetic induction provided the same protection in our primary total joint arthroplasty patients as 3 doses (3 × 750 mg) of cefuroxime. However, because of the small difference in infection rates of using various antibiotic regimes, the sample size of our study did not have a very strong power to reject the null hypothesis that there is no difference in the infection rates with the 2 antibiotic regimes. We propose that a prospective study with a larger sample size should be performed to confirm our findings. Nevertheless, this study provided a basis for further prospective investigations using a single dose of antibiotic as antimicrobial prophylaxis in primary total joint arthroplasty.

The bacteriology of the present series is similar to others that reported periprosthetic infection complicating knee [34–36] and hip arthroplasty [34,37]. *Staphylococcus aureus* remains the most commonly encountered organism. One might comment that the present series has a higher prevalence for methicillin-resistant *S. aureus* infection than the others. A similar higher prevalence of resistant *S. aureus* has not been previously reported in other series that use cefazolin as the prophylactic antibiotic [11,38]. As more periprosthetic infections are caused by resistant organisms, including *S. aureus* and other coagulase negative staphylococci [34,36,39–42], we postulate that this may explain the bacteriology pattern reported in the present series.

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