

Perioperative Cefazolin for Surgical Prophylaxis in Total Joint Replacement Patients with a Self-Reported Penicillin Allergy: Is It Safe?

Brandon Robert Bukowski¹, Ricardo Torres², Daniel Kevin Devine, Alberto V Carli², Daniel Maalouf, Enrique Goytizolo, Andy Miller, Jose A Rodriguez²

¹Hospital for Special Surgery, ²Hospital For Special Surgery

INTRODUCTION: Cefazolin is the standard of care for perioperative antibiotic prophylaxis in total joint replacement patients in the United States. The potential allergic cross-reactivity between cefazolin and penicillin due to their beta-lactam molecular structure causes uncertainty regarding optimal antibiotic choice in patients with a reported penicillin allergy (PCNA) and frequently results in alternative antibiotic prophylaxis that is less efficacious. However, current evidence suggests that the rate of clinically-relevant reactions to cephalosporins among patients with penicillin allergy is <1%. The purpose of this study was to determine the safety of perioperative prophylaxis with cefazolin in PCNA patients undergoing total joint replacement.

METHODS: We identified all patients (n=49,842) undergoing total hip arthroplasty (n=25,659) or primary total knee arthroplasty (n=24,183) at a single institution from 2016-2022 who received perioperative intravenous antibiotic prophylaxis. Patients with a PCNA (n=5,508) who received cefazolin (n=4,938, 89.7%) were compared to PCNA patients who did not (n=570, 10.3%) and to patients with no allergy history (n=43,359). The primary outcome was the rate of allergic reactions within 72 hours postoperatively based on allergy status and the antibiotic administered. Secondary outcomes included the rates of superficial infections, deep infections, and *Clostridium difficile* infections within 90 days postoperatively.

RESULTS: The rate of allergic reactions was 0.1% (n=5) in PCNA patients who received cefazolin compared to 0.2% (n=1) in PCNA patients who did not (p=0.61) and 0.02% (n=11) in patients with no allergy history (p=0.005). Allergic reactions were mild in all 5 PCNA patients and were characterized by cutaneous symptoms (n=4) or dyspnea in the absence of respiratory distress (n=1) that resolved promptly with antibiotic discontinuation and administration of antihistamines and/or corticosteroids. There were no differences in the rates of superficial infections (0.1% vs. 0.2%, p=0.84), periprosthetic joint infection (0.3% vs. 0.4%, p=0.77), or *Clostridium difficile* infections (0.04% vs. 0%, p=0.631) within 90 days in PCNA patients who received cefazolin versus alternative perioperative antibiotics.

DISCUSSION AND CONCLUSION: In this series of over 5,500 patients with PCNA undergoing total joint replacement, perioperative surgical prophylaxis with cefazolin resulted in a 0.1% incidence of allergic reactions that were clinically indolent. Cefazolin can safely be administered independent of penicillin allergy status.