

Letters

COMMENT & RESPONSE

In Reply Mraovic et al disagree with the recommendation to administer cefazolin for prophylaxis of surgical site infections to patients with a history of penicillin allergy, asserting that the risk of severe anaphylaxis is too great. This recommendation is based on the difference in frequency of dual cefazolin-penicillin allergy between patients with confirmed penicillin allergy (3.0%) and patients with unconfirmed penicillin allergy (0.6%).¹ We acknowledge the risk of hypersensitivity to cefazolin is indeed greater for patients with confirmed penicillin allergies, but we suggest this greater risk may not be entirely specific to cefazolin but to the patient population with drug allergies.

Beltran et al² reported reactions to perioperative antibiotics among patients labeled as having an allergy to penicillin. Hypersensitivity reactions to cefazolin (0.7%) were lower than to clindamycin (2.0%) and ciprofloxacin (16%).² Fosnot et al³ assessed immediate hypersensitivity to perioperative antibiotics in patients labeled as having an allergy to penicillin. Among 690 patients, the 15 immediate hypersensitivity reactions were similar for patients receiving clindamycin (2.4%), vancomycin (2.2%), and cefazolin (1.7%).³ Multiple drug allergy syndrome is the most likely explanation for these findings. Landry et al⁴ reviewed a large database to assess the frequency of multiple drug allergy syndrome. The authors identified a total of 1819 patients who tested positive for at least 1 medication and 45 (2.5%) who tested positive for at least 2 medications. Twenty-six of 45 patients (54.2%) with multiple drug allergy syndrome were allergic to a natural penicillin (penicillin, amoxicillin, ampicillin). The second allergy was of another antibiotic for 13 patients (50%), none of which was cefazolin. These data indicate that the risk of hypersensitivity to another (unrelated) antibiotic is higher for patients with an index penicillin allergy.

Even when considering the most conservative estimates provided by Mraovic et al, giving cefazolin may be associated with a 2-fold decreased mortality among patients with reported penicillin allergy whom we are not able to formally test. Assuming (1) the occurrence of no anaphylactic reactions from second-line antibiotics, (2) a perioperative anaphylaxis-associated case fatality rate of 3.8%,⁵ and (3) a 30-day surgical site infection case fatality rate of 3.6%,⁶ we would project a mortality of 0.07% to 0.14% in patients receiving cefazolin vs 0.14% to 0.29% in patients receiving second-line antibiotics. This implies saving 1 additional life for each 667 to 1429 additional surgeries performed. This back-of-the-envelope calculation is based on single point estimates considering mortality from only 2 causes (antibiotic anaphylactic reactions

and/or surgical site infections) and should therefore be interpreted with caution.

For patients with anaphylactic penicillin allergy histories or a history of allergy to multiple β -lactam antibiotics, preoperative allergy assessments can be implemented to optimize perioperative antibiotic choice and guide future β -lactam antibiotic use. We agree that more data about cefazolin hypersensitivity are needed but disagree with cefazolin avoidance in perioperative patients with penicillin allergy histories.

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