

Intravenous antibiotic prophylaxis against infective endocarditis in penicillin-allergic dental patients

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Sir,

I read with great interest the article by Farshidfar *et al.*¹ recently published in this journal, and agree with the authors' notice on the nooks and crannies of the 2021 American Heart Association (AHA)'s guideline on antibiotic prophylaxis against infective endocarditis (IE) in penicillin-allergic dental patients who cannot take oral medication. Two additional points worth mentioning are:

1. A meta-analysis by *Pichichero* and *Casey*² included nine clinical trials published until 2005, and revealed that the first-generation cephalosporins and cefamandole (a parenteral second-generation cephalosporin), which share a chemical side chain similar to penicillin or amoxicillin, exerted immunologic cross-reactivity in penicillin-allergic patients (odd ratio [OR] = 4.79; 95% confidence interval [CI], 3.71 to 6.17; $P < .00001$)² with current estimates of prevalence of 2% to 5% (data in year 2021).³ In contrast, second- and third-generation cephalosporins generally have different side chains from penicillin and amoxicillin, and were not associated with any increase in the risk of cross-reactivity with penicillin (second-generation: OR = 1.1; 95% CI, 0.6 to 2.1; third-generation: OR = 0.5; 95% CI = 0.2 to 1.1) with current estimated of prevalence of 1% to 2% (data in year 2021).⁴ Clinical challenges, skin testing, and monoclonal antibody studies can detect similarities in the side chain structure, and subsequently, help predict cross-allergy between cephalosporins and penicillins. The findings of this meta-analysis support the recommendations of the American Academy of Pediatrics and Sinus and Allergy Health Partnership to use selected second- and third-generation cephalosporins (cefuroxime, cefpodoxime, ceftriaxone, and cefdinir) in penicillin-allergic children as treatment for acute otitis media and acute sinusitis.²
2. There have been evidenced that avoiding β -lactams (penicillins and cephalosporins) when they are the drug of choice is associated with worse outcomes, such as increased risk of surgical site infections, nephrotoxicity, and *Clostridioides difficile* infection. In addition, use of second-line antibiotic classes in patients with penicillin allergies may result in other adverse effects, decreased safety, and antimicrobial resistance.⁵ A recent US large cohort study ($n = 4,206,480$) by *Macy et al.*⁵ retracted the warning against cephalosporin use in penicillin-allergic patients. In this cohort, there were no

significant differences in the rates of anaphylaxis, allergies to new antibiotic classes, antibiotic treatment failure, all-cause mortality, hospital days, and new (secondary) infections with *Clostridioides difficile*, methicillin-resistant *Staphylococcus aureus*, and vancomycin-resistant *Enterococcus*, when cephalosporins were prescribed in patients with penicillin allergy.⁵

3. Intravenous macrolides are also available, for example, clarithromycin 500 mg powder (Bowmed Ibisqus Ltd., Wrexham, UK; Ethypharm GmbH, Schönefeld, Germany) and azithromycin 500 mg powder (Zedbac®, Aspire Pharma Ltd., Petersfield, UK; Dr. Friedrich Eberth Arzneimittel GmbH, Ursensollen, Germany) for solution for preparation of an infusion vial. However, it is noteworthy that intravenous macrolides should be slowly infused with the rate of *ca.* one hour per infusion, to prevent thrombophlebitis (data from: <https://www.medicines.org.uk/emc>; Arznei aktuell 2021, ifap Service-Institut für Ärzte und Apotheker GmbH, Planegg, Germany).

Taken all together, some modifications can escape from the gap of the 2021 AHA's guideline on antibiotic prophylaxis against IE. Intravenous ceftriaxone (as a third-generation cephalosporin), clarithromycin, and azithromycin are alternative antibiotic choices for penicillin-allergic dental patients who are unable to take oral medication.

CONFLICTS OF INTEREST

The author indicates full freedom of manuscript preparation. There was no potential conflict of interest as regards this study.

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