Penicillin Allergy Linked to MRSA, *C difficile* Infections

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Patients with a documented penicillin allergy have a higher risk of developing new methicillin-resistant *Staphylococcus aureus* (MRSA) and *Clostridium difficile* infections, a study has shown.

The population-based matched cohort study was published online June 27 in the *British Medical Journal*.

"[M]ore than half of the increased MRSA risk and more than one third of the increased *C difficile* risk among patients with penicillin allergy was attributable to administered β lactam alternative antibiotics," write Kimberly G. Blumenthal, MD, from Harvard Medical School and Massachusetts General Hospital, Boston, and colleagues.

Most patients with a reported penicillin allergy are not truly allergic to penicillin. In one study of individuals with a penicillin allergy label, 95% of were found to be penicillin tolerant after undergoing allergy testing.

Nevertheless, the penicillin allergy label affects how clinicians prescribe antibiotics to these patients and often leads to use of antimicrobial agents that have a wider spectrum of activity than penicillin and increased toxicity.

Indeed, misuse of broad-spectrum antibiotics is a risk factor for developing MRSA and *C difficile* infection.

To examine the public health effect of penicillin allergy labels, Blumenthal and colleagues evaluated the link between a newly recorded penicillin allergy and the risk of developing MRSA and *C difficile* infections.

Using a general practice electronic medical record database in the United Kingdom, the researchers examined a matched cohort of adults who were enrolled in the system from 1995 through 2015 and who had no previous diagnosis of MRSA or *C difficile* infections.

Blumenthal and colleagues also identified patients with a first recorded penicillin allergy in their medical records and matched them with up with five penicillin users without allergy, according to age, sex, and study entry date.

The study included a total of 301,399 adults without previous MRSA or *C difficile* infection, 64,141 of whom had a penicillin allergy and 237,258 of whom were matched comparators.

The primary outcome was incident MRSA and *C difficile* infections; secondary outcomes included use of β lactam antibiotics and β lactam alternative antibiotics.

During a mean follow-up of 6 years, 1365 of the 301,399 adults in the study developed MRSA (442 patients with penicillin allergy; 923 comparators) and 1688 developed *C difficile* infection (442 patients with penicillin allergy; 1246 comparators).

According to the researchers, the adjusted hazard ratios among patients with penicillin allergy were 1.69 (95% confidence interval [CI], 1.51 - 1.90) for MRSA and 1.26 (95% CI, 1.12 - 1.40) for *C difficile* infection.

The adjusted incidence rate ratios for antibiotic use among penicillin allergy patients were 4.15 (95% CI, 4.12 - 4.17) for macrolides, 3.89 (95% CI, 3.66 - 4.12) for clindamycin, and 2.10 (95% CI, 2.08 - 2.13) for fluoroquinolones.

The investigators also found that 55% of the increased risk of developing MRSA infection and 35% of the increased risk of developing *C difficile* infection were attributable to greater use of β lactam alternative antibiotics.

The increased risk of developing MRSA and *C difficile* infections was also mediated by greater use of fluoroquinolones, clindamycin, and macrolides (55% and 26%, respectively); fluoroquinolones and macrolides (54% and 24%, respectively); fluoroquinolones and clindamycin (26% and 20%, respectively); and fluoroquinolones alone (24% and 16%, respectively).

The results of this study corroborate those of previous studies showing that patients with a documented penicillin allergy have a greater risk of developing MRSA infection and *C difficile* infection.

The findings also highlight the strong association between antibiotic prescribing in outpatient settings and risk of developing MRSA, the authors say.

"As infections with resistant organisms increase, systematic efforts to confirm or rule out the presence of true penicillin allergy may be an important public health strategy to reduce the incidence of MRSA and *C difficile*," Blumenthal and colleagues conclude.

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