Changing antibiotic resistance patterns for *Staphylococcus aureus* surgical site infections

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Beta-lactam antibiotics such as cefazolin are first-line agents for preoperative prophylaxis, whereas clindamycin is often administered to patients with a reported penicillin allergy.[1] Recent studies have reported increased resistance to clindamycin in *Staphylococcus aureus* (SA) isolates from both pediatric and adult populations, and these changes may have implications for surgical site infection (SSI) prophylaxis and empirical management.[2,3] Antibiotic resistance trends of SA isolates recovered from SSIs in adults in the United States have not been recently described.

Methods

We conducted a retrospective observational study of SA isolates recovered from SSIs in patients ≥18 years of age at the Johns Hopkins Hospital between January 1, 2012, and December 1, 2017, for the following procedures: craniotomy, coronary artery bypass grafting (CABG), hysterectomy, cesarean section, colorectal surgery, spinal fusion, laminectomy, and hip and knee arthroplasty (HKA). A list of cultures that grew SA was obtained from Johns Hopkins Pathology Data Services and was cross-referenced with the SSI database maintained by the Department of Hospital Epidemiology and Infection Control. Charts were reviewed to assess for documented penicillin allergy and antibiotic surgical prophylaxis. Due to changes in electronic medical records, antibiotic prophylaxis data were available only for 2015–2017 cases. Trends in the proportion of resistant isolates over time were analyzed using the Cochran-Armitage test for trend. The association between the proportions of resistant isolates and choice of SSI prophylaxis was analyzed using the Fisher exact test. $P < .05$ was considered statistically significant for all tests. Data were analyzed using Stata version 13 software (StataCorp, College Station, TX). The Johns Hopkins University Institutional Review Board approved this study.

Results

In total, 109 cultures from unique patients were included in the study. Clindamycin resistance increased from 20% in 2012 to 38% in 2017 ($P < .01$), while resistance to tetracycline decreased significantly from 20% to 0% during the same period ($P < .01$) (Fig. 1). Trimethoprim-sulfamethoxazole (TMP-SMX) resistance remained relatively unchanged from 10% in 2012 to 13% in 2017 ($P = .63$). Erythromycin resistance decreased from 40% in 2012 to 29% in 2017 ($P = .18$). Between 2012 and 2017, there was a 9% decrease in methicillin-resistant *S. aureus* (MRSA) SSIs ($P = .84$). The distribution of SA SSI by surgery type was as follows: spinal fusion and laminectomy (27%), craniotomy (23%), CABG (17%), cesarean section (12%), colorectal (11%), hysterectomy (8%), and hip and knee arthroplasty (HKA, 2%).

Overall, of 68 cases with available SSI prophylaxis and allergy data, 13 patients (20%) had a reported penicillin allergy. Also, 5 of these patients received clindamycin even though a high severity reaction was recorded in only 1 patient. Of the 5 patients who received clindamycin, 2 developed a clindamycin-resistant SA SSI.

Discussion

Our results show a significant increase in clindamycin resistance among SA isolated from SSIs over the last 6 years at our institution. This finding is in agreement with previous reports of non-SSI SA isolates in children and adults observed in different areas in the United States in recent years.[2,3] Unlike previous reports, SA SSIs at our hospital demonstrated a significant decline in tetracycline resistance. Susceptibility to TMP/SMX remained high throughout the study period, whereas resistance to methicillin declined over the last 3 years.

As reported by others,[4] most patients in our cohort had incomplete allergy histories. Clindamycin is used with high frequency as an alternative to β–lactams in patients with penicillin allergy labels (whether the allergy is true or not).[1] Efforts to optimize antibiotic selection in the operating room may include education on accurate determination and documentation of penicillin allergy histories and decision-support tools to ensure that patients receive β-lactams whenever possible. Also, unnecessary deviations from recommended β-lactam–containing regimens should be reduced as much as possible.

Increasing clindamycin resistance in SSIs SA raises concerns about its use as an alternative surgical prophylaxis agent. Routine use of vancomycin is not recommended given potential risks of emergence of vancomycin-nonsusceptible *Staphylococcus* isolates, its prolonged infusion time, associated toxicity, and evidence that it is inferior to β-lactam agents for surgical prophylaxis.[5] Therefore, infection control and antimicrobial stewardship programs need to discuss alternatives to clindamycin based on each institution's antibiogram and feasibility. At our institution, we recommend vancomycin for patients with severe PCN allergy undergoing clean procedures with implants or cardiac surgery.

We did not specifically collect data on clindamycin use; however, at our hospital, clindamycin is reserved for patients with

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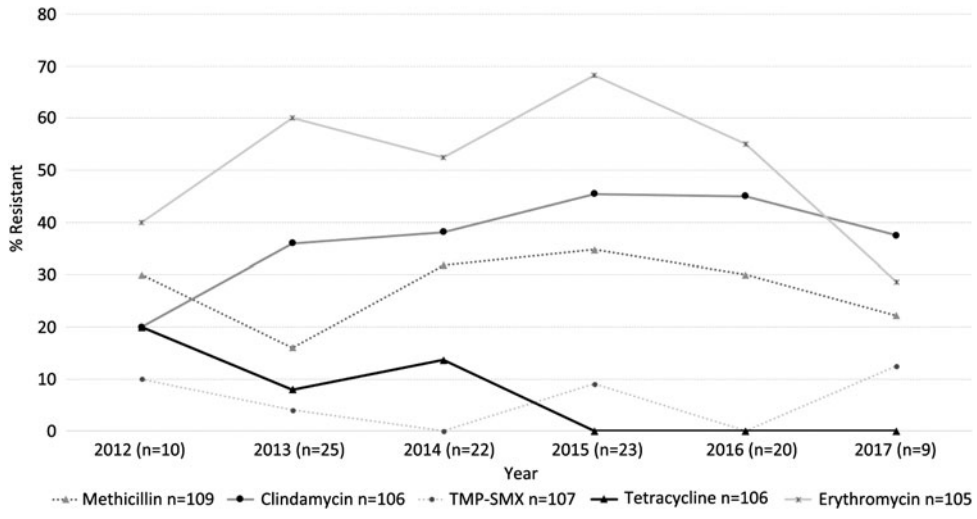


Fig. 1. Temporal trends of antibiotic resistance for *S. aureus* SSIs in patients ≥18 years of age undergoing craniotomy, coronary artery bypass grafting, hysterectomy, C-section, colorectal surgery, spinal fusion, laminectomy, and hip and knee arthroplasty between 2012 and 2017. Trends in methicillin ($P = .84$), erythromycin ($P = .18$) and trimethoprime-sulfametoxazole ($P = .63$) resistance were not statistically significant; all other trends shown were significant ($P < .01$).

severe penicillin allergy, and its use has remained stable over recent years. We hypothesize that clindamycin use for the treatment of skin and soft-tissue infections likely contributes to the observed increase in clindamycin resistance.

Other factors may have contributed to the development of SA SSIs, such as suboptimal decolonization of SA in patients known to be SA carriers and suboptimal preoperative antibiotic dosing. SSI prevention guidelines recommend considering SA screening and decolonization in hospitals and populations with high *S. aureus* rates and high-risk procedures.[5] In our hospital, patients are instructed to shower with a chlorhexidine agent prior to surgery, and preoperative SA screening with a decolonization protocol has been implemented for patients undergoing cardiac and orthopedic surgery.

Although our study was conducted at a single center, many patients undergoing surgery at our hospital come from different states. Furthermore, the observed trends in clindamycin resistance in SA SSIs are consistent with previous observations in SA nonsurgical isolates.[2,3]

In summary, improving penicillin allergy documentation and consideration of alternatives to clindamycin in some circumstances may prevent additional SA SSI cases.

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Inappropriate ceftriaxone use in outpatient acute respiratory infection management

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Ceftriaxone, a parenteral third-generation cephalosporin, is used to treat serious bacterial infections and sexually transmitted diseases.[1] Inappropriate ceftriaxone use contributes to resistance to this important antibiotic and threatens patient safety due to antibiotic-associated adverse events and *Clostridioides difficile*

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