Considering Universal Mupirocin Decolonization as an Option for Preventing Surgical Site Infections

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Surgical site infections (SSIs) are an important cause of morbidity and mortality. In the United States alone, it is estimated that 157,500 SSIs occurred in 2011, representing almost 25% of all healthcare-associated infections (HAIs) [1]. SSIs have been associated with a mortality rate of 2.8% [2], average attributable costs of $11,087–$34,670 per patient, and aggregate attributable hospitals costs of $3,450–$10.07 billion per year [3]. More than half of SSIs, however, are thought to be preventable using currently available evidence-based prevention strategies [4], such as strict attention to sterile technique, skin preparation with an alcohol-containing antiseptic solution, postoperative blood glucose control, use of proper technique when hair removal is necessary, perioperative antimicrobial prophylaxis, maintenance of normothermia during the perioperative period, and optimization of tissue oxygenation [5]. All the aforementioned interventions are considered horizontal prevention strategies, given their ability to reduce the risk of SSIs due to a variety of organisms.

Vertical prevention strategies, on the other hand, are those that target a specific organism. Data reported to the Centers for Disease Control and Prevention in 2009 and 2010 indicate that Staphylococcus aureus is the organism most frequently responsible for SSIs, implicated in 30.4% of the reported SSIs for which pathogen information was provided [6]. A vertical strategy that has been used to prevent S. aureus SSIs is intranasal application of mupirocin among carriers of S. aureus in the immediate perioperative period. The use of intranasal mupirocin alone or as part of a bundle of S. aureus-specific prevention measures has been associated with a significantly lower incidence of S. aureus SSIs in several randomized controlled trials, quasi-experimental studies, and cohort studies. In a meta-analysis of these studies, decolonization was associated with a significant decrease in S. aureus SSIs when the intervention was applied to all patients or only to those who were nasal carriers of S. aureus [7].

A number of current guidelines and practice recommendations for the prevention of SSIs include intranasal application of mupirocin. In an updated compendium of strategies to prevent HAIs in acute care hospitals, screening for S. aureus carriage with subsequent decolonization of colonized surgical patients is recommended as a special approach for preventing SSIs in high-risk procedures in populations with unacceptably high SSI rates despite implementation of basic prevention strategies [5]. Current surgical antimicrobial prophylaxis guidelines in the United States recommend intranasal administration of mupirocin to patients with documented S. aureus colonization who are undergoing cardiac and several types of orthopedic procedures [8].

This strategy, however, has not been widely implemented, for a number of possible reasons. First, some decision makers may not be convinced of the effectiveness or cost-effectiveness of decolonization. Second, some facilities may have determined that the intervention is not necessary owing to effective prevention of SSIs after implementation of other preventive measures. Implementation of this strategy may also be hampered by logistical challenges and costs associated with a preoperative screening program to identify the S. aureus carriers who might benefit from mupirocin treatment.

Treating all surgical patients with mupirocin would eliminate the need for preoperative testing and simplify implementation, but this approach would result in drug exposure in a large number of patients, on the order of 70%–80% of all treated patients, who are not S. aureus carriers and who would be unlikely to benefit from the intervention. Use of an antibiotic agent in patients for whom there is no known benefit conflicts with current concepts of antimicrobial stewardship and carries at least the theoretical risk of selection for and propagation of mupirocin-resistant staphylococci, which could lead to the loss of mupirocin as an effective antimicrobial agent. In fact, both of the previously mentioned guidelines [5, 8] discourage universal use of mupirocin, at least in part owing to concerns about the possible development and/or propagation of mupirocin resistance with widespread use.
Understanding the likelihood and drivers of mupirocin resistance in the setting of widespread mupirocin use is critical to developing a mupirocin use strategy that optimizes our ability to prevent SSIs without causing ecologic changes that could have a future detrimental effect on the larger population. In this issue of Clinical Infectious Diseases, Hetem and colleagues [9] report that they have explored this clinically relevant issue by developing a deterministic mathematical model of the dynamics of mupirocin resistance and the determinants of emergence of mupirocin resistance in the setting of hospital-based targeted and universal S. aureus decolonization programs. Such information is needed to inform decision making with regard to the use of mupirocin decolonization to prevent SSIs and other HAIs caused by S. aureus. Based on their results, the authors conclude that the risk of mupirocin resistance in S. aureus is similar in the setting of targeted and universal decolonization strategies and that universal decolonization is therefore an acceptable strategy that is perhaps more feasible, more effective, and associated with lower financial costs than a targeted decolonization strategy.

Although mathematical models can be very useful in simulating conditions that cannot be readily studied in the real world, we must remember that any model is just that, a model of the real world that is limited by the confines of the model and the data available to populate the model. The statistician George E. P. Box [10] is famous for, among other things, having said that “all models are wrong, but some are useful.” So when we read about the well-designed model introduced by Hetem et al [9] and consider their findings in the context of our own practices, institutional approaches, and public health recommendations regarding the use of mupirocin to prevent HAIs, we need to consider which aspects of the model are most helpful while remembering that clinical outcomes in the real world could differ from those observed in the model.

The model used by Hetem et al [9] suggests that the ecologic (ie, antimicrobial resistance) implications may not differ particularly between targeted or universal decolonization strategies using mupirocin or between those strategies and the use of no decolonization at all. This is an encouraging finding from a model whose creators attempted to account for many factors that might affect the development and propagation of mupirocin resistance, such as the baseline prevalence of mupirocin resistance in both S. aureus and coagulase-negative staphylococci, rates of patient-to-patient transmission of organisms, and rates of bacterial conjugation. However, one must be cognizant of some concerning signals regarding the possible development of mupirocin resistance in staphylococci in clinical settings where patients have been treated with mupirocin as part of a universal decolonization program. For example, in a hospital that had implemented universal decolonization with mupirocin for the duration of patients’ hospitalization, the prevalence of mupirocin resistance among methicillin-resistant Staphylococcus aureus (MRSA) isolates increased from 2.7% before implementing universal decolonization to 65% within 18 months after the universal decolonization program had been implemented [11].

Furthermore, in an as-yet-unpublished analysis of mupirocin susceptibility among MRSA isolates collected during the REDUCE-MRSA trial conducted among adult intensive care unit patients in 43 US hospitals [12], the odds of high-level mupirocin resistance among MRSA isolates in the 18-month intervention period, compared with the baseline period, were higher in the arm assigned to universal decolonization (odds ratio, 2.6; 95% confidence interval, .78–8.4) than in the no-decolonization and targeted decolonization arms [13]. Although this difference was not statistically significant, the relatively small number of isolates, the relatively short intervention period, and the assessment of only MRSA isolates may have resulted in a lack of power to detect a significant difference or to quantify changes in mupirocin resistance that could occur with longer-term use of universal decolonization. Finally, authors reporting another recent mathematical model concluded that there would be a significantly greater increase in the prevalence of mupirocin-resistant MRSA after 5 years of universal use of mupirocin compared with targeted mupirocin treatment [14].

How do we reconcile the findings of Hetem et al [9] with these reported clinical experiences of an increase in mupirocin resistance in the setting of increased exposure, the general experience that increasing rates of resistance have been seen in association widespread clinical use of other antibiotics (eg, penicillin, methicillin, fluoroquinolones), and the conclusions from a different mathematical model? Maybe the model used by Hetem et al is right, the use of mupirocin really is different from that of systemic antibiotics, and the increasing rates of mupirocin resistance observed in some clinical settings do not reflect what would be seen in most populations. On the other hand, it is possible that the unpredictability of clinical, environmental, and microbiologic factors that contribute to organism transmission and conjugation, including known and unknown factors not taken into account in the model, may have prevented the model from accurately simulating the complex epidemiology of pathogen transmission, conjugation, and antimicrobial resistance in the healthcare setting.

The well-crafted model presented by Hetem et al [9] suggests that the ecologic implications of mupirocin use may not differ between targeted or universal decolonization strategies or between these strategies and no decolonization at all, but it does not provide a definitive answer regarding potential selection for and propagation of mupirocin-resistant staphylococci in the setting of universal mupirocin use to prevent SSIs or other HAIs. However, it does provide additional information to consider when contemplating introducing universal decolonization with mupirocin as an adjunct to...
other prevention strategies for *S. aureus* infection. If a mupirocin-based decolonization strategy is selected, the uncertainty of the long-term outcomes of this strategy suggests the need to monitor changes in rates of mupirocin resistance over time. The article by Hetem et al [9] also reminds us of the complexity of healthcare-associated *S. aureus* transmission and infection and that there is no panacea for the prevention of *S. aureus* HAIs. Finally, it highlights the importance of a broad HAI prevention program, consistent implementation of evidence-based prevention practices, and the development of new prevention strategies that are cost-effective, easy to implement and sustain, well tolerated, and associated with minimal risk to individual patients and the larger population.

**Note**

*Potential conflict of interest.* Author certifies no potential conflicts of interest. The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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