Imminent Challenges: Carbapenem-Resistant Enterobacteriaceae in Transplant Recipients and Patients With Hematologic Malignancy

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(See the Immunocompromised Hosts Invited Article by Satlin et al on pages 1274–83.)

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In this issue of *Clinical Infectious Diseases*, Satlin and colleagues review the timely and important topic of carbapenem-resistant Enterobacteriaceae (CRE) in solid organ transplant (SOT) recipients and patients with hematologic malignancies. They review epidemiology of CRE infections, resistance mechanisms, potential treatments, and their limitations as well as avenues to reduce the impact of CRE in these patient populations [1]. New York was the initial epicenter of CRE in the United States, but this review demonstrates that the problem is now truly global with 3%–10% of SOT recipients infected in endemic areas. This is concerning as CRE species are sources of outbreaks and highly lethal, with mortality rates of 40% in SOT recipients and 65% in patients with hematologic malignancy. This report emphasizes the importance of infection prevention, antimicrobial stewardship, and development of new antibiotic therapy but leaves a few important questions.

CRE infection is common in transplant recipients and, in fact, SOT independently predicts risk for CRE infection. In some centers, nearly the entire burden of CRE infections resides in SOT recipients [2]. Perhaps just as concerning, CRE infections in transplant recipients have served as index cases of hospital-wide carbapenem-resistant *Klebsiella pneumoniae* outbreaks. It is worth noting that available data are based on retrospective small case series, some with missing duration of illness and mortality data; the impact of these infections may well extend beyond what we glean from these reports.

What can be done to reduce the threat of CRE infections in transplant recipients? Currently, surveillance for CRE is limited, even in hospitals. The authors logically suggest active surveillance in immunocompromised hosts with identification of colonized patients and point out that active surveillance programs and contact precautions have been successful in decreasing nosocomial transmission and preventing further CRE outbreaks. Currently, the Centers for Disease Control and Prevention recommends actively screening patients only in facilities with known CRE transmission or an epidemiologic link to unrecognized CRE [3]. Consideration of active surveillance for CRE colonization in all patients prior to transplant or chemotherapy in institutions with a high prevalence of CRE is also advocated; identification of CRE colonization in these patients may prevent further spread and provide the opportunity for intervention with chlorhexidine bathing to prevent infection. However, the exact contribution of surveillance cultures in decreasing CRE is not known, and to date there is no evidence that surveillance per se will actually reduce transmission. Such strategies may also decrease time to appropriate antibiotic therapy should serious infection occur in these patients. However, these interventions carry significant cost in both human resources and financial investment. For gastrointestinal colonization surveillance, staff cohorting, additional donor screening for CRE, and increased time and effort in the hospital microbiology laboratory may be required (eg, to perform cultures with selective media), as well as increased time and effort from the infection prevention team. Universal chlorhexidine bathing in high-risk areas to prevent or reduce colonization may be more feasible.

Antimicrobial stewardship has also been shown to be critical to preventing...
and managing these infections. The authors point out that usage of carbapenems, other β-lactams, and fluoroquinolones are independent risk factors for CRE infection. Marchaim and colleagues found that in comparing CRE and extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae, CRE and non-ESBL-containing Enterobacteriaceae, and CRE among all 3 comparison groups combined, antimicrobial exposure was an independent predictor of CRE isolation [4]. The most common antibiotics received by those with CRE were carbapenems and fluoroquinolones; many patients (85%) also had cephalosporin exposure. Demand exists for data on antimicrobial stewardship in the SOT population as there currently is nearly none [5]. Data on antimicrobial stewardship in hematology/malignancy are also lacking; strategies such as prospective audit of antibiotic prescribing in cancer patients with febrile neutropenia or chemotherapy are needed. A recent review provides several tools for clinicians in managing cases of CRE and reveals important research gaps. Priority interventions include aggressive infection control practices such as active surveillance and decolonization in both recipient and donor, antimicrobial stewardship (especially for carbapenems and fluoroquinolones), and considering use of combination therapy. To boost development of antibiotics to treat infections caused by these organisms, the Infectious Diseases Society of America has proposed initiatives including new regulatory pathways, public–private partnerships, and tax credits. Recently introduced legislation for a Limited Population Antibacterial Drug pathway would allow the US Food and Drug Administration to approve drugs for narrow use based on smaller clinical trials for treatment of patients with infections who have few or no treatment options. As more life-threatening superbugs emerge, we must rise to the challenge so we can continue to provide our transplant recipients the best chance of infection-free survival.

Notes

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