Antimicrobial Stewardship in Immunocompromised Hosts

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KEYWORDS

• Antimicrobial stewardship • Transplant • Solid organ • Hematologic malignancies • Neutropenia • Fever • Immunocompromised

KEY POINTS

- Immunocompromised hosts are increasingly colonized and infected by multidrug-resistant organisms with limited antimicrobial treatment options.
- Implementation of antimicrobial stewardship strategies in immunocompromised hosts is challenging, but there are multiple opportunities to improve the selection, dosing, and duration of antimicrobial agents.
- Collaboration with local experts, such as oncologists and transplant teams, is fundamental for a successful stewardship program for the immunocompromised population.
- The use of early and appropriate diagnostic testing is essential to guide therapy and minimize nonessential antimicrobial exposure.

INTRODUCTION

For decades, infections have constituted a major threat for patients with febrile neutropenia,[1,2] solid organ transplant (SOT),[3] and hematopoietic stem cell transplantation (HSCT).[4] It is well recognized that the diagnosis and treatment of infections in immunocompromised hosts is more difficult than in persons with normal immune function. The spectrum of potential pathogens is broad, infection often progresses rapidly, and invasive diagnostic procedures are often required for accurate and timely diagnosis.[5] Early and specific microbiologic diagnosis in immunocompromised hosts is essential for guiding treatment and minimizing nonessential antimicrobial therapy with potential serious adverse reactions as well as possible interactions with immunosuppressive agents.[3,4]

Over the past few decades, there has been a dramatic reduction in the development of antimicrobial agents with novel mechanisms of action to combat the rising spread of

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infections caused by antimicrobial multidrug-resistant organisms (MDROs).[6] MDROs are an emerging threat in high-risk immunocompromised hosts, such as SOT and HSCT recipients, and those with hematologic malignancies exposed to cytotoxic chemotherapy and prolonged neutropenia. Although it has long been recognized that these patients are among the highest risk for becoming colonized and developing serious infections, the frequency with which MDROs cause infection in these recipients has increased significantly in the past several years.[7–9]

Numerous studies have been published demonstrating that antimicrobial resistance has an adverse impact on patient safety and quality of care.[10–13] As a result, there is increasing awareness about the importance of judicious use of antimicrobials, or antimicrobial stewardship. To date, there are no antimicrobial stewardship guidelines focusing on high-risk immunocompromised hosts.[14] Appropriate management of antimicrobials in these patients is important but challenging.[15] Furthermore, confirming the presence of infection can be difficult and the diagnostic uncertainty contributes to the use of broad-spectrum antimicrobials for extended periods of time. Other important challenges are the perceptions and behaviors regarding antimicrobial use by multiple physicians caring for these patients. Barriers to the implementation of antimicrobial stewardship strategies in immunocompromised hosts are summarized in **Box 1**. This article focuses on the challenges, opportunities, and areas for further study in the implementation of successful antimicrobial stewardship strategies in high-risk immunocompromised hosts.

GOALS OF ANTIMICROBIAL STEWARDSHIP IN IMMUNOCOMPROMISED HOSTS

Antimicrobial stewardship programs (ASPs) aim to optimize the appropriate selection, dosing, route, and duration of antimicrobial therapy while limiting unintended consequences, such as the emergence of resistance, adverse drug events, and cost.[16] These goals are relevant for immunosuppressed patients because infections have constituted a major threat to the success of transplantation for many decades and

Box 1
Challenges to the implementation of antimicrobial stewardship in immunocompromised hosts

1. Physician perceptions and attitudes—"my patient is sicker than yours"
2. Wide range of possible infectious etiologies with diagnostic uncertainty
3. Impaired inflammatory responses
4. Difficulty in making an early diagnosis
5. Urgency for empiric effective antimicrobial therapy
6. Significant drug toxicities and potent drug interactions
7. Prolonged exposure to prophylactic antibiotics may lead to antimicrobial resistance
8. Increasing antimicrobial resistance with limited therapeutic options to appropriately treat empirically or documented infections
9. Difficulty with distinguishing rejection and graft versus host disease from infections
10. Difficulty in controlling the source of infection due to issues, such as thrombocytopenia, limiting surgical interventions
11. Prolonged duration of immunosuppressed state increases the risk for uncommon presentations of common and uncommon infections
12. Duration of antimicrobial therapy not clearly defined in many infections for these patients