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Healthcare-Associated Bacterial Infection: Common Sources of Severe Sepsis Among People with HIV

Authors

Jared A. Greenberg, MD

Section of Pulmonary and Critical Care Medicine

Department of Medicine, University of Chicago

Chicago, US

jared.greenberg@uchospitals.edu

John P. Kress, MD

Section of Pulmonary and Critical Care Medicine

Department of Medicine, University of Chicago

Chicago, US

In this Article, We Discuss the Emergence of Healthcare-Associated Bacterial Infections As a Major Source of Severe Sepsis Among People With HIV, and Recommend Treatment and Prevention Guidelines to be Heeded by Clinicians and Healthcare Practitioners.

The long-term prognosis for people with HIV has improved since the advent of highly active antiretroviral therapy (HAART). Over this time period, in-hospital survival for critically ill people with HIV has improved as well. Surprisingly though, studies have not consistently found HAART use prior to critical illness to be a predictor of intensive care unit (ICU) survival (Huang et al. 2006). Instead, ICU outcomes have improved mainly because admission patterns for people with HIV have changed with the development of HAART (Casalino et al. 2004; Pacheco et al. 2009). Patients are now less likely to be admitted for respiratory failure from *Pneumocystis jirovecii* pneumonia (PCP), which carries a particularly high mortality. They are more frequently admitted for sepsis and exacerbations of chronic illnesses, which have better short-term prognoses (Akgun et al. 2011). Continuing to improve outcomes for members of this population necessitates a better understanding of why

people with HIV are now requiring ICU care.

Shifting Admission Patterns

Recent studies have found that sepsis is a more common reason for ICU admission for people with HIV than it was at the beginning of the AIDS epidemic. At San Francisco General Hospital, California, US, the frequency of ICU admissions for sepsis increased from 10% to 20% from 1981 to 2003 (Powell et al. 2009). At Bichat- Claude Bernard Hospital, Paris, France, admissions for sepsis increased from 16% to 22% with the advent of HAART (Casalino et al. 2004). In addition to there being a greater number of admissions for sepsis, multiple studies have identified sepsis as a predictor of short and longterm mortality after ICU admission. Patients with HIV who are admitted to an ICU with sepsis have a two to four times greater risk of death than people with HIV who are admitted to an ICU for a different reason. (Mrus et al. 2005; Croda et al. 2009; Japiassu et al. 2010; Chiang et al. 2011). In one cohort, severe sepsis was the dominant predictor of 28-day and six-month mortality (Japiassu et al. 2010).

In the current HAART era, people with HIV are spending more time in healthcare settings because they are living longer, and they have an increased risk of developing a number of chronic diseases. Specifically, people with HIV have a greater incidence of chronic lung diseases than those without HIV (Crothers et al. 2011). Co-infection with Hepatitis B or C increases the risk of chronic liver disease (Verucchi et al. 2004), and HAART-related medication toxicities may lead to metabolic complications and cardiovascular disease (Friis-Moller et al. 2003). Chronic kidney disease is also more common in people with HIV because of HIV-associated nephropathy and comorbid conditions such as diabetes and hypertension (Wyatt, 2012). Finally, a number of malignancies have greater prevalence in the HIV population (Pinzone et al. 2012).

Healthcare-Associated Infection

As people with HIV are receiving more healthcare during their lifetimes, the spectrum of bacterial organisms causing severe sepsis is likely changing. The term "healthcare -associated infection" has been coined to reflect an infection that may be acquired in the community, but has a similar antibiotic-resistant pattern to an infection contracted in the hospital. Patients are at greater risk for antibiotic-resistant bacterial infections if they were hospitalised in the previous 90 days, reside in nursing homes or long-term-care facilities, or receive chronic haemodialysis or

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intravenous therapy (Kollef et al. 2008). In a study by a public hospital in Atlanta, Georgia, focusing only on ICU admissions for sepsis, there were 194 acute infections among the 125 patients studied (Greenberg et al. 2012). The majority of these infections were nosocomial or healthcare-associated. Respiratory-tract infections accounted for 53% of acute infections and bloodstream infections accounted for 24% of acute infections. Japiassu and colleagues described a similar population of patients with HIV and sepsis in their ICU; the majority of infections were nosocomial and most were pulmonary or primary bacteraemia (Japiassu 2010).

Prevention and Management of Infection

Current recommendations for the prevention and management of healthcare-associated infections do not account for a patient's HIV status (Kollef et al. 2008). The general approach for any patient begins with identifying whether he or she is at risk for a healthcare-associated infection. The strategy then involves early initiation of broad-spectrum antibiotics that are effective against methicillin-resistant *Staphylococcus aureus* (MRSA) and multidrug-resistant gram-negative bacteria. Empirical therapy for antibiotic-resistant Enterococci or fungal organisms depends on the clinical situation. The purpose of this approach is to ensure adequate antimicrobial coverage against the infecting organism, as mortality increases with delay in appropriate antibiotic administration. As the patient's clinical status evolves in response to therapy and culture results become available, the spectrum of antibiotic coverage should be narrowed to reduce the chance of breeding new antibiotic-resistant organisms (Kollef et al. 2008).

For critically ill people with HIV and severe infections, it is unknown whether initiating HAART in the ICU as adjunctive therapy is of benefit. There are no randomised control trials or consensus guidelines on the use of HAART in the ICU. In fact, clinicians are often hesitant to start a patient on HAART for a number of reasons. Firstly, many antiretrovirals can only be administered enterally and gastrointestinal absorption may be variable in ICU patients. Secondly, drug toxicities may be more likely to occur as antiretrovirals interact with common ICU medications, and resulting organ failure may lead to reduced medication clearance. Finally, there is some concern that beginning HAART may lead to immune reconstitution inflammatory syndrome, which could worsen the patient's condition in the short term (Huang et al. 2006).

There are no recommendations for preventing nosocomial or healthcare-associated infections specifically for patients with HIV. Prior to the development of HAART, it was well documented that people with HIV were at greater risk of developing nosocomial infections than people without HIV (Goetz et al. 1994; Stroud et al. 1997). Thus, clinicians caring for patients with HIV should incorporate measures to reduce the risk for nosocomial infections, such as evidencebased practice bundles and timely removal of unnecessary intravenous catheters and indwelling lines (Berenholtz et al. 2011; Weber et al. 2011). It is also true that immune dysfunction increases the risk of developing bacterial infections. In a large, multicentre epidemiological study, lower CD4 cell counts were associated with increased risk of developing a serious bacterial non-AIDS infection (Sogaard et al. 2013). Utilising resources to improve HAART compliance in patients with advanced AIDS who are frequently hospitalised would likely have a large impact on reducing the number of ICU admissions for nosocomial or healthcare-associated infections.

Conclusion

In conclusion, the landscape of ICU admissions for people with HIV has changed with the advent of HAART. Sepsis is a more frequent diagnosis for admission to the ICU and is a risk factor for short- and long-term mortality. Patients are now presenting to ICUs with greater amounts of prior healthcare exposure and thus may be more likely to develop severe sepsis from antibiotic-resistant bacterial organisms than from opportunistic infections. Further studies describing the burden of healthcare-associated infections in different HIV communities are warranted. In addition, further investigation into ways to prevent and treat healthcare-associated infections, specifically for patients with HIV, would provide clinicians with more guidance. In the meantime, we recommend that clinicians follow the same guidelines for the treatment of healthcare-associated infections regardless of a patient's HIV status. We also suggest that clinicians focus on improving compliance with HAART in patients who frequently require healthcare, and that invasive procedures and indwelling catheter use is limited so as to reduce the risk of healthcare-associated infections and improve outcomes for critically ill patients with HIV in general.

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