ADVANCES IN HEMATOLOGY

Current Developments in the Management of Hematologic Disorders

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Positive Blood Cultures

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H&O What are the morbidity and mortality associated with bloodstream infections?

MW There are approximately 500,000 new cases of bloodstream infections in the United States annually. They are particularly common in people who have vascular access devices, such as those used in chemotherapy or other types of long-term management. Bloodstream infections occur more frequently in people who have compromised immunity, including cancer patients, transplant patients, or patients receiving treatment with immunosuppressive drugs. Other risk factors include corticosteroid therapy, AIDS, physical trauma, multiple sites of trauma that occur in incidents like automobile accidents and gunshot wounds, recent surgery, diabetes mellitus, acute and chronic renal disease, and hepatic cirrhosis.

Mortality from bloodstream infections has decreased over the past 30 years. My colleagues and I performed our first study on bloodstream infections in the mid 1970s. At that time, crude mortality was approximately 40%, and mortality attributed to the bloodstream infection itself was just over 20%. In the early 1990s, we redid the study. We found that the crude mortality had dropped to about 22%, and the mortality attributed to the infection itself was between 17% and 18%. In our current study, based on data from 2004, the crude mortality was still at 20%, but the mortality attributable to the bloodstream infection itself dropped to 12%.

When hospitalized patients develop bloodstream infections—even if they recover from them—their hospitalization likely will be prolonged and their cost of care will be increased.

H&O What is the methodology for your studies on bloodstream infections?

MW Our first study in the 1970s examined 500 patients with bacteremia and fungemia. We redid the study in the early 1990s because there had been significant changes in patient care, more use of vascular access devices, a host of new antibiotics, many more organ transplants, and the advent of HIV and AIDS. We performed the third study in 2004, to see if the findings would reflect the advent of better therapies for HIV and AIDS and the use of new drugs for the adjunctive treatment of sepsis and septic shock. For the latest study, we reviewed the medical records of patients who had positive blood cultures at 3 institutions: Robert Wood Johnson University Hospital, Duke University Medical Center, and the Durham North Carolina VA Hospital. It was a retrospective, observational study, in which we looked at the microbiology, the epidemiology, the demographic characteristics of the patients, and the clinical outcome.

H&O What were the results of your latest study?

MW We found that only about half of all positive blood cultures represented true infections. I think clinicians know this intuitively. We see many coagulase-negative staphylococci, the most common organisms that are grown from blood cultures. Unfortunately, 90% of them are contaminants. When they do represent true infection, it is usually associated either with the presence of an intravenous (IV) catheter or with some other prosthetic material, such as a heart valve, a vascular graft, or a stent. The most common organisms causing true bacteremia have not changed very much over the last several decades. *Staphylococcus aureus* is the most common, *Escherichia coli* is second, enterococci are third, and *Klebsiella*, another gram-negative organism, is fourth.

One of the changes that we have noticed is that *Candida* species have become more common, likely because we now use more broad-spectrum antibacterial therapy. There are more compromised hosts now, and there are

more people who have long-term indwelling catheters, both of which lead to more fungal infections.

Our results confirm those of other studies showing that the most common source of bloodstream infections in the United States is the IV catheter. It is almost impossible to keep IV catheters completely sterile over long periods of time. In the current study, IV catheters were the source of 23% of the episodes of bacteremia and fungemia.

Another important finding is that 81% of the bacteremias and fungemias were associated in some way with a healthcare setting. Approximately 46% were acquired in the hospital, and another 35% were acquired in healthcare settings in the community, such as dialysis centers and IV infusion centers. Included in that additional 35% were people who had been hospitalized within the prior month. Only 19% of bloodstream infections were in people who were not in some way involved with the healthcare system in the month prior to their infection.

H&O What factors were associated with increased rates of death?

MW A multivariate analysis showed that risk of death was associated with increasing age and hypotension, which is a marker for shock. Another risk factor was the absence of fever, that is, the failure of a patient to be able to develop a febrile response to infection. We saw this correlation in all 3 of our studies. Other independent predictors of death included hospital acquisition of infection, AIDS, malignancy, and renal failure.

H&O Did any of the findings from your current study differ from those of your earlier studies?

MW The rate of infections associated with a healthcare setting was much higher in the current study. As I mentioned, 81% of the bloodstream infections were associated with the healthcare setting in some way. In the 2 prior studies, we used conventional definitions of community-acquired infection and hospital-acquired infection, and we found that approximately half of the infections were community-acquired and about half were hospital-acquired. For the current study, we revised our definition of hospital-acquired infection to include patients with current and recent involvement in healthcare settings, such as patients who were receiving home IV therapy, dialysis center patients, and patients who had been hospitalized within the previous month.

One gratifying finding is that outcome has improved with each study. Although crude mortality did not decrease between 1992 and 2004, the number of people dying from infection has been reduced. I think that means we are doing a better job of treating infection.

H&O What are some ways to prevent and treat bloodstream infections?

MW There is now a strong focus on trying to prevent bloodstream infections associated with IV catheters. New Medicare regulations eliminate reimbursement to hospitals for hospital-acquired catheter-associated bacteremia. Hospital administrations are paying more attention to infection control programs and trying to reduce catheter-associated bacteremia.

We learned from our 1997 study that when doctors guess right in their initial choice of antibiotic therapy, then outcome is better. We assessed whether the antibiotic treatment was correct at 3 different points in time. The first point was at the time of the blood culture, before the physician knew the culture result. The second point in time was when the positive culture results were conveyed to the physician. The third point in time was when the test results and antibiotic susceptibility results were available. We found that when physicians guessed right initially, mortality from infection was approximately 10%. When physicians did not guess right initially, but did so after the blood cultures became positive, mortality from infection was 13%. When physicians did not guess right initially and did not change therapy correctly after receiving the report of a positive culture, but changed therapy only after they received the identification and susceptibility result, mortality from infection was 26%. Thus, early treatment with the right antibiotics will improve outcome. We need better methods to assess for early detection of infection and early antibiotic susceptibility. If we can develop technologies and laboratory methods that provide rapid and accurate results, then outcome in these patients will be better.

Suggested Readings

Pien BC, Sundaram P, Raoof N, et al. The clinical and prognostic importance of positive blood cultures in adults. *Am J Med*. 2010;123:819-828.

Weinstein MP, Murphy JR, Reller LB, Lichtenstein KA. The clinical significance of positive blood cultures: a comprehensive analysis of 500 episodes of bacteremia and fungemia in adults. II. Clinical observations, with special reference to factors influencing prognosis. *Rev Infect Dis*. 1983;5:54-70.

Weinstein MP, Towns ML, Quartey SM, et al. The clinical significance of positive blood cultures in the 1990s: a prospective comprehensive evaluation of the microbiology, epidemiology, and outcome of bacteremia and fungemia in adults. *Clin Infect Dis*. 1997;24:584-602.

Weinstein MP, Reller LB, Murphy JR, Lichtenstein KA. The clinical significance of positive blood cultures: a comprehensive analysis of 500 episodes of bacteremia and fungemia in adults. I. Laboratory and epidemiologic observations. *Rev Infect Dis*. 1983;5:35-53.