Commentary The challenge of sepsis

Mitchell M Levy

Professor of Medicine, Brown University, Director, Medical Intensive Care Unit, Rhode Island Hospital, Providence, RI, USA

Corresponding author: Mitchell M Levy, Mitchell_Levy@brown.edu

Published online: 15 November 2004 This article is online at http://ccforum.com/content/8/6/435 © 2004 BioMed Central Ltd Critical Care 2004, 8:435-436 (DOI 10.1186/cc3009)

Related to Research by Poeze et al., see page 513

In this issue of *Critical Care*, Poeze and coworkers [1] report the results of an international survey of physicians' attitudes about sepsis. There are several important messages for clinicians that emerge when reviewing the results of this survey. First, most physicians believed there was no single consensus definition of sepsis, despite the original consensus definitions published in 1992 [2]. Second, the large majority of intensivists believed that better monitoring is needed to diagnosis sepsis earlier. Third, the large majority of respondents believed that patients are treated too late to reverse the onset of sepsis. Finally, patients and their families have a poor understanding of the condition, which makes communication with care givers difficult.

Taken together, these findings identify the challenges most clinicians face when dealing with sepsis in the intensive care unit, namely how best to identify these patients, when to initiate treatment, how to monitor the progress (both resolution and deterioration) of the disease, and how to communicate with patients and families about the nature of one of the most common diseases in critically ill patients.

In the past the need for clinicians to identify and stage critically ill patients with sepsis at the bedside was less important than it is today. Until recently few interventions were available to clinicians that may improve survival in patients critically ill with severe sepsis or septic shock. For many years, the only interventions of proven value in the treatment of patients with sepsis were early institution of appropriate antibiotics, adequate resuscitation, and, finally, good source control [3,4]. These interventions were and continue to be fundamental components of management for critically ill patients with sepsis. However, these interventions, although of obvious importance, were applicable to all patients with infection. They were not specific to patients with sepsis, severe sepsis, or septic shock. Therefore, the need to identify and stage patients with sepsis was of little clinical importance, and there was no impetus for the bedside clinician to value a staging system for sepsis. This almost certainly has fostered confusion, expressed by the survey respondents, regarding clear definitions of sepsis.

It is important to note that each of the issues raised by respondents in the survey has been addressed in the literature over the past several years. These have led to significant changes in the way in which diagnosis and treatment of sepsis in critically ill patients should be approached.

In response to this survey, conducted in 2001, an international sepsis definitions conference, sponsored by several international critical care societies, was convened in 2001 and tasked with revisiting the sepsis definitions originally published in 1992. The findings of the conference were published in 2002 and reaffirmed the original three stages of the host response to infection [5]: sepsis, severe sepsis, and septic shock. For the practicing clinician, there are now clearly defined consensus definitions of sepsis. Unfortunately, we still lack precise markers that permit early identification of these critically ill patients. However, a staging system, which remains hypothesis generating, was identified by the international definitions conference. This system, named PIRO (predisposition, infection, response, and organ dysfunction), is a model designed to stage as well as monitor the host response to infection on the basis of factors believed to be pertinent to outcomes. Whether the PIRO system will evolve into a useful tool for bedside clinicians will depend on the results of future investigations and epidemiologic studies.

Recently published studies have demonstrated decreased mortality and morbidity as a result of interventions and therapeutics applied to patients with sepsis [6–9]. These

new data, resulting from rigorously performed, randomized controlled trials, combined with previous data for beneficial interventions not specific to sepsis management [9–13], lend significant weight to the belief that critical care clinicians can now significantly reduce mortality in patients with severe sepsis and septic shock. These studies have changed the way in which management of sepsis is now viewed by clinicians. Results from these studies are so robust that they have formed the basis for consensus guidelines that were recently published [14,15] and that, taken together, are the foundation for a new, global standard of care in the management of sepsis.

The publication of Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock earlier this year [14,15] was the culmination of phase II of the Surviving Sepsis Campaign. Initiated by the combined efforts of the International Sepsis Forum, the European Society of Intensive Care Medicine, and the Society of Critical Care Medicine in 2002, the Campaign is an international effort to facilitate improvements in sepsis treatment and management through the implementation of guidelines to create a global standard of care for sepsis, thereby reducing mortality from sepsis by 25% over 5 years. An unprecedented 11 organizations sponsored the evidence-based and expert opinion guidelines. Another of the stated goals of the Campaign, and one that directly addresses an issue identified by the survey, is to raise public awareness of sepsis as a common and deadly disease in critically ill patients.

Although there remains a lack of clear markers that might permit precise, early identification and staging of patients with sepsis, clinicians do have important new tools that may assist in the management of these critically ill patients and lead to improved care and survival. The use of consensus definitions for severe sepsis and septic shock will allow identification of those patients who may benefit from the application of the guidelines for management.

Unfortunately, clinicians change very slowly. Historically, transfer of research from the bench to the bedside is a long, tortuous process - one that is not driven by anything very clear and that seems to be based more on fad and coincidence than on a keen, evidence-based evaluation of the literature. Changing clinicians' behaviors in response to published data has long been a glaring failure in medicine. The Surviving Sepsis Campaign represents an important step for international critical care societies. Recognizing the long history of delay in incorporating research into bedside care, these critical care societies have committed to working together to facilitate bench-to-bedside transfer of recent research. In this way, the responses of the participants in the survey published in this issue of Critical Care may serve to improve the care for patients with severe sepsis and septic shock.

Competing interests

The author has received grant support from the Eli Lilly Co. and from Edwards Lifesciences

References

- Poeze M, Ramsay G, Gerlach H, Rubulotta F, Levy M: An international sepsis survey: a study of doctors' knowledge and perception about sepsis. Critical Care 2004, 8:R409-R413.
- Anonymous: American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med 1992, 20:864-874.
- Leibovici L, Shraga I, Drucker M, Konigsberger H, Samra Z, Pitlik SD: The benefit of appropriate empirical antibiotic treatment in patients with bloodstream infection. J Intern Med 1998, 244: 379-386.
- Jimenez MF, Marshall JC: Source control in the management of sepsis. Intensive Care Med 2001, Suppl 1:S49-S62.
- Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, Cohen J, Opal SM, Vincent JL, Ramsay G; SCCM/ESICM/ACCP/ ATS/SIS: 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. Crit Care Med 2003, 31:1250-1256.
- Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, Peterson E, Tomlanovich M; Early Goal-Directed Therapy Collaborative Group: Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001, 345: 1368-1377.
- Annane D, Sebille V, Charpentier C, Bollaert PE, Francois B, Korach JM, Capellier G, Cohen Y, Azoulay E, Troche G, et al.: Effect of treatment with low doses of hydrocortisone and fludrocortisone on mortality in patients with septic shock. JAMA 2002, 288:862-871.
- Bernard GR, Vincent JL, Laterre PF, LaRosa SP, Dhainaut JF, Lopez-Rodriguez A, Steingrub JS, Garber GE, Helterbrand JD, Ely EW, et al.: Efficacy and safety of recombinant human activated protein C for severe sepsis. N Engl J Med 2001, 344:699-709
- Anonymous: Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. N Engl J Med 2000, 342:1301-1308.
- Kress JP, Pohlman AS, O'Connor MF, Hall JB: Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. N Engl J Med 2000, 342:1471-1477.
 van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyn-
- van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F, Schetz M, Vlasselaers D, Ferdinande P, Lauwers P, Bouillon R: Intensive insulin therapy in the critically ill patients. N Engl J Med 2001, 345:1359-1367.
- Samama MM, Cohen AT, Darmon JY, Desjardins L, Eldor A, Janbon C, Leizorovicz A, Nguyen H, Olsson CG, Turpie AG, et al.: A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. Prophylaxis in Medical Patients with Enoxaparin Study Group. N Engl J Med 1999, 341:793-800.
- Cook D, Guyatt G, Marshall J, Leasa D, Fuller H, Hall R, Peters S, Rutledge F, Griffith L, McLellan A, et al.: A comparison of sucralfate and ranitidine for the prevention of upper gastrointestinal bleeding in patients requiring mechanical ventilation. Canadian Critical Care Trials Group. N Engl J Med 1998, 338:791-797.
- Dellinger RP, Carlet JM, Masur H, Gerlach H, Calandra T, Cohen J, Gea-Banacloche J, Keh D, Marshall JC, Parker MM, et al.: Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. Crit Care Med 2004, 32:858-873.
- Dellinger RP, Carlet JM, Masur H, Gerlach H, Calandra T, Cohen J, Gea-Banacloche J, Keh D, Marshall JC, Parker MM, et al.: Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. Intensive Care Med 2004, 30: 536-555.