

Early goal-directed therapy should be used in septic shock

George A Skowronski

The inflammatory response to sepsis generally progresses from early evidence of SIRS (systemic inflammatory response syndrome) to severe sepsis and septic shock. Few would deny the importance of early intervention in this process, and this is supported both by everyday clinical experience and by scientific evidence.

The cardiovascular abnormalities associated with this progression are well known to all intensivists. Intravascular volume depletion, vasodilatation and myocardial depression lead to a whole-body oxygen debt, characterised by progressive lactic acidosis and progressive organ failure.

As with trauma, the existence of a "golden" interval has been proposed, although its duration is uncertain and probably variable. A number of studies^{1,2} support the proposition that delay in instituting appropriate antibiotic therapy adversely affects outcome. Similarly, there is evidence in a number of specific conditions to support the idea that early source control improves outcome.³

Although all resuscitation implies the use of some type of goal, the modern pioneer of goal-based resuscitation was Shoemaker,⁴ who first demonstrated that "supranormal" values for cardiac index, whole-body oxygen delivery and oxygen consumption were statistically associated with improved survival from major surgery and critical illness. However, subsequent prospective studies by Shoemaker and numerous others, targeting a variety of end-points achieved by various means, have yielded contradictory results. These studies were confounded by heterogeneous patient populations, relatively late enrolment and varying illness severity.

The study by Rivers et al,⁵ which forms the basis of the Surviving Sepsis Campaign guidelines,⁶ suffers similarly from a number of difficulties. It was unblinded, done in a single centre and used a "package" of end-points and treatments, making interpretation difficult. Nevertheless, the basic clinical goals of central venous pressure, mean arterial pressure and urine output would be accepted by all clinicians as suitable targets of resuscitation.

The use of an additional central venous saturation target in the treatment group resulted in the more liberal

use of intravenous fluids, dobutamine and blood transfusion, and a reduction in mortality. Whether it was the use of one or more of these treatment modalities that improved outcome in the treatment group, or the fact that the additional guiding measurement provided a better measure of the adequacy of resuscitation, cannot be reliably answered from the study.

Despite these criticisms, the results of the Rivers et al study must be viewed in the broader context of our understanding of the progressive nature of the underlying pathophysiology of the septic process. From this perspective, it would be hard not to conclude that adherence to an early, aggressive resuscitation protocol with rational, objective measurements of the adequacy of cardiovascular resuscitation is likely to improve outcomes. However, the precise roles of venous oxygen saturation, dobutamine and blood transfusion may require more study.

Author details

George A Skowronski, Senior Specialist
Intensive Care Unit, St George Hospital, Sydney, NSW.
Correspondence: g.skowronski@unsw.edu.au

References

- 1 Ibrahim EH, Sherman G, Ward S, et al. The influence of inadequate antimicrobial treatment of bloodstream infections on patient outcomes in the intensive care unit setting. *Chest* 2000; 118: 146-55.
- 2 Leibovici L, Shraga I, Drucker M, et al. The benefit of appropriate empirical antibiotic treatment in patients with bloodstream infection. *J Intern Med* 1998; 244: 379-86.
- 3 Moss RL, Musemeche CA, Koloske AM. Necrotizing fasciitis in children: prompt recognition and aggressive therapy improve survival. *J Pediatr Surg* 1996; 31: 1142-6.
- 4 Shoemaker WC, Appel PL, Kram HB, et al. Prospective trial of supranormal values of survivors as therapeutic goals in high-risk surgical patients. *Chest* 1988; 94: 1176-86.
- 5 Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001; 345: 1368-77.
- 6 Dellinger RP, Carlet JM, Masur H, et al. Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. *Crit Care Med* 2004; 32: 858-73. □