Commentary

The key advance in the treatment of sepsis in the last 10 years … doing less

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Published: 16 February 2006
This article is online at http://ccforum.com/content/10/1/122
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Critical Care 2006, **10:**122 (doi:10.1186/cc4849)

Abstract

Although many pharmaceutical and technological advances are heavily touted, they have had relatively little impact on overall outcome improvements in the critically ill. Acting on the increasing recognition that 'less may be best' has, in my opinion, been the greatest single advance in patient management in the intensive care unit in the past 10 years. Although certainly not qualifying as a 'brave new world' in terms of daring and exciting innovation, the importance of (often covert) iatrogenic complications should not be underestimated.

About 20% of patients admitted to intensive care fail to leave the intensive care unit (ICU) alive, and a further 8 to 10% die in hospital. Alas, no new product – pharmaceutical or technological – has had an obvious major impact on overall ICU outcomes. Activated protein C, for example, is currently used in about 2 to 4% of patients admitted to UK ICUs. Assuming the 19% relative reduction in mortality reported in the PROWESS study [1], this translates to an outcome improvement in less than 1% of all patients admitted to the ICU. Yet more than a quarter of patients admitted to UK ICUs have sepsis diagnosed within 24 hours of admission [2], and probably as many again develop sepsis during their stay. I prescribe corticosteroids in septic shock with concurrent adrenal deficiency [3] and use terlipressin in catecholamine-unresponsive septic shock [4] but any benefit gained also applies to a minority of my septic patients. I can provide anecdotal examples where I am convinced that the above interventions have provided benefit to individual patients but cannot persuade myself of their broad impact. The emphasis must surely be placed on early recognition of sepsis and appropriate interventions to prevent deterioration in organ function, such as Rivers's goal-directed strategy [5]. However, such stratagems should ideally be implemented long before the patient requires intensive care; otherwise, diminishing returns are likely. Institution of such an approach once the patient has been admitted to the ICU has not shown benefit in major studies [6,7], suggesting an evolution in pathophysiological mechanisms [8] that are no longer amenable to pre-emptive or early therapeutic approaches.

So what has been done within my ICU that has made a difference? The answer is, probably, less. Less aggressive ventilation with increasing tolerance of still-acceptable levels of hypercapnia and hypoxaemia. Less reliance on endotracheal intubation in preference to noninvasive modes of ventilation. Less paralysis. Less sedation. Less use of etomidate. Lower blood pressure targets requiring less use of catecholamines. Less fluid loading (to avoid the 'Michelin man' syndrome). Fewer blood transfusions. Shorter-duration antibiotic courses with an increasing emphasis on monotherapy. Less nutritional neglect but also less persistence with enteral feeding in the presence of gastrointestinal intolerance. Less acceptance of high blood glucose levels. Less attention to monitoring superfluous variables and derived parameters, but a greater emphasis on attention to basics including maintaining or restoring the adequacy of organ perfusion, although with the relatively insensitive tools that we currently have available.

Has 'less' had a clearly demonstrable effect on outcome? To give a few notable examples, mortality in studies of acute respiratory distress syndrome has fallen impressively from 48–59% between 1983 and 1991 to 25–26% since 2000 [9], and is probably related to less harmful ventilatory techniques, notably lower tidal volumes. Randomised studies of non-invasive versus invasive ventilation in both respiratory and cardiac conditions show improved outcomes for non-invasive ventilation [10], possibly related to the avoidance of endotracheal intubation and the requirement for sedation. A lower haemoglobin threshold for blood transfusion is also beneficial [11], emphasising the likely immune-modifying effects of allogenic blood that are not immediately manifested as a transfusion reaction. Similarly, a tight target range of

ICU = intensive care unit.

blood glucose as part of a prolonged enhanced insulin-calorie regimen significantly improved mortality and morbidity [12].

Surely there is a lesson from the above that we must continue to apply but must also develop still further. The above advances have arisen from a realisation that overuse or misuse of drugs or devices, and/or excessively striving for physiological or biochemical normality, may provide short-term gains but at the expense of longer-term detriment [13]. A greater understanding of both disease pathophysiology and iatrogenic harm will, I believe, lead to even better management, and thus further enhance outcomes.

Competing interests

The author declares that they have no competing interests.

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