CRITICAL CARE

COMMENTARY

Arterial pressure optimization in the treatment of septic shock: a complex puzzle

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See related research by Dunser *et al.*, http://ccforum.com/content/13/6/R181

Abstract

Arterial pressure optimization in septic shock is a critical, yet poorly understood component of resuscitation. New data suggest that, during the routine management of patients with severe sepsis, there is no association between mean arterial pressure achieved and outcome as long as the mean arterial pressure is maintained at or above 70 mmHg. Although these data add important new evidence to our understanding of arterial pressure management, there are still many unanswered questions upon which future investigations should focus.

In the previous issue of *Critical Care* Dunser and colleagues presented the results of post-hoc analysis that add another piece to the puzzle of understanding optimal arterial pressure goals in the treatment of sepsis [1]. The authors examine data from a control group of severe sepsis patients enrolled in an interventional trial that mandated hemodynamic management to specific therapeutic targets, one of which was achievement of a mean arterial pressure (MAP) of 70 mmHg or higher through the use of vasopressors. Dunser and colleagues analyzed the association between the average MAP, both as a continuous variable and grouped into quartiles, and mortality. What they found was no association between average MAP, or MAP quartiles above 70 mmHg, and 28-day mortality. They did, however, report an association between vasopressor load and mortality.

In his classic text *Physiology of Shock* published in 1950, Dr Carl J Wiggers wrote 'In short, there are no pathognomonic signs of shock ... The instability of a patient's condition, along with progressive deterioration, constitutes the best evidence of shock. In the assessment of such determination, the trend of arterial pressures remains one of our best criteria' [2]. For over a century, arterial hypotension has been intensely studied as a central cause of organ hypoperfusion and subsequent organ injury in critically ill patients. This includes patients with hemorrhage [2], heterogeneous populations of pre-hospital patients [3] and emergency department patients [4], and specific disease states such as pulmonary embolism [5], acute myocardial infarction [6], post-cardiac arrest syndrome [7], and sepsis [8]. Because of both the universal availability of its measurement and its association with severity of illness, medical care providers frequently use blood pressure to communicate with each other about the hemodynamic stability of patients.

We agree with the authors' contention that consensus recommendation of a goal for MAP as a therapeutic target in septic shock management is more or less an arbitrary number that represents a minimal threshold that experts would consider clinically acceptable [9]. One randomized controlled trial for the resuscitation of patients with sepsis used a MAP of 65 mmHg or higher as a goal for hemodynamic support; however, the MAP goal was part of the interventional algorithm for both arms of the trial (that is, treatment and control) and therefore MAP was effectively removed from the experiment [10]. The data presented in Dunser and colleagues' study are important and allow the conclusion that, during routine management of patients with severe sepsis, there is no association between MAP achieved and outcome as long as the MAP is maintained at or above 70 mmHg.

It is important to note in this study, however, that a MAP of 70 mmHg was not tested as a threshold or target for hemodynamic support. This would have required an investigation in which patients were assigned to different MAP thresholds as therapeutic targets (for example, 60 mmHg, 65 mmHg, 70 mmHg, and so forth) and outcomes were compared between these groups. No such large-scale definitive study has been performed to date.

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We are therefore left to manage patients with consensus recommendations and our best clinical judgment.

Another important point of discussion of Dunser and colleagues' report centers on a secondary finding. They conclude that their data indicate an association between vasopressor load and both mortality and disease-related events. Intuitively this makes sense: the more vasopressor support a patient requires, the more severely ill the patient is and thus the more likely the patient is to suffer either drug or disease-related morbidity and mortality. These data do not, however, allow the conclusion stated in their paper – that elevating MAP >70 mmHg by augmenting vasopressor dosages may increase mortality. This conclusion would require an experimental design that allowed testing of cause and effect rather than an analysis of association. In our opinion, a more likely reason for the association between higher vasopressor doses and poor outcome would be some combination of more refractory sepsis-induced vasodilation and lower cardiac output, both assumed to be linked to poorer prognosis. An important consideration as it relates to vasopressor therapy is being constantly vigilant in minimizing vasopressor dosage by targeting the lowest pressure that can be assured to be providing adequate tissue perfusion while assuring that additional volume infusion – or, in some patients, inotropic therapy – will allow reduction of vasopressor therapy.

There are many factors about the cardiovascular support of sepsis that remain relatively unknown. Although arterial blood pressure is important and is clearly associated with outcome, the overarching goal of cardiovascular support is to optimize blood flow to tissues. The relationship between arterial pressure and flow is complex and incompletely understood [11]. There is possibly also no single optimal MAP that can be applied to all sepsis patients, as patient-specific factors are probably extremely important in determining patient response. Pre-existing disease, intact autoregulation and distribution of flow, among other factors, all play a role in the optimal MAP level an individual patient needs in order to achieve optimal outcomes.

Let us suppose for a moment that an optimal MAP for sepsis cardiovascular support was clearly identified, associated with improved outcomes, and widely accepted and utilized in clinical care. While a critical piece of the sepsis puzzle would be filled, many others would still be missing – such as the optimal time frame in which the goal should be reached, the optimal therapeutic methods to achieve the goal (for example, fluids, vasopressors), and how long the goal must be maintained. So it appears that the more we learn about cardiovascular support in sepsis, the less we actually know.

Abbreviations

MAP = mean arterial pressure.

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Competing interests

The authors declare that they have no competing interests.

Published: 19 January 2010

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doi:10.1186/cc8194
Cite this article as: Jones AE, *et al.*: Arterial pressure optimization in the treatment of septic shock: a complex puzzle. *Critical Care* 2010, **14:**102.