

Vasopressor and corticosteroid therapy in patients with septic shock

Septic shock is a life-threatening condition resulting from an aberrant host response to infection, characterised by severe hypotension and tissue hypoperfusion that requires vasopressors to correct the subsequent end-organ dysfunction. Despite advances in critical care, septic shock remains a significant cause of morbidity and mortality, resulting in high healthcare expenditure and cost. The management of such patients is multifaceted, necessitating a coordinated approach that involves early recognition, aggressive resuscitation, targeted antimicrobial therapy and ongoing monitoring and supportive care. The goal of treatment is to restore haemodynamic stability and improve tissue perfusion, while minimizing the risk of complications. Clinicians are faced with multiple treatment decisions regarding vasopressors, such as choice of the most appropriate first-line agent and its route of delivery, the use of a combination of vasopressors as well as what adjunctive medications to use, with the aim of stabilising haemodynamics. In an edition of “How I Do It” in the journal, *Chest*, Teja *et al.*^[1] provide a comprehensive overview of management strategies to these common clinical decisions in a case-based discussion.

The use of noradrenaline as the first-line vasopressor agent in septic shock is well-established and supported by the authors. However, noradrenaline and other catecholaminergic vasopressors can increase the risk of arrhythmias and myocardial ischaemia, which may adversely affect the outcome of patients. The authors highlight the need for individualised treatment strategies, considering patient-specific factors to tailor the choice of initial and subsequent vasopressors. For example, in patients with septic shock that may be unable to tolerate the adrenergic-related side effects of noradrenaline such as those with poor cardiac reserve who have, or are at risk for, supraventricular arrhythmias, the authors recommend the use of agents without β_1 receptor activity (vasopressin or phenylephrine).

Teja *et al.* discuss the concept of combining a second vasopressor as an adjunctive therapy in patients with refractory septic shock. This addition can offer distinct advantages such as targeted receptor specificity and a complementary mechanism of action. While the authors use vasopressin as the preferred second vasopressor, they suggest the choice of the adjunctive agent be based on the patient's specific hemodynamic profile. For instance, the addition of adrenalin favoured in patients where impaired cardiac output is thought to contribute to shock.

The decision to introduce a second vasopressor should be expedited in patients with inadequate response to the first-line vasopressor. Evidence supporting the optimal timing of adding a second vasopressor is scant. The authors highlight the need to balance the expected benefit of meeting perfusion goals against the side-effect profile of high dose vasopressor therapy. Aggressive vasoconstriction, to achieve haemodynamic goals, may lead to potential complications such as arrhythmias and digital ischaemia. On the other hand, the addition of vasopressin has been shown to decrease noradrenaline requirements and consequently reduce the risk of atrial fibrillation as well as the need for dialysis.^[2]

In patients with escalating vasopressor requirements, the authors advocate adding corticosteroids concurrently with a second vasopressor.

The use of corticosteroids in patients with septic shock has been the topic of debate and this review contributes to the ongoing discussion. There is significant variability of results across trials conducted on the risk v. benefit of corticosteroid use in septic shock which has resulted in heterogeneity in the management. The rationale for corticosteroid therapy lies in their immunomodulatory properties and affect on enhancing vascular tone, resulting in a reduction of vasopressor requirements. The current Surviving Sepsis campaign (SSC) guidelines differ in their recommendation to Teja *et al.*, suggesting the addition of low-dose corticosteroids in patients with persistent vasopressor requirements for more than 4 hours after their initiation.^[3] The recommendation is based on moderate quality evidence from recent randomised control trials indicating a shorter duration to resolution of shock with the use of corticosteroids.

Teja *et al.* recommend starting hydrocortisone plus fludrocortisone for 7 days, a practice not specified in the current SSC guidelines. One of the main reasons for their suggestion of this combination of corticosteroids is based on trials suggesting a mortality benefit with hydrocortisone plus fludrocortisone v. hydrocortisone alone.^[4]

The mean arterial pressure (MAP) is the most widely accepted haemodynamic parameter used for titrating vasopressors. Achieving and maintaining appropriate MAP targets are crucial for ensuring adequate organ perfusion while mitigating the complications associated with hypoperfusion. Previous guidelines have recommended targeting a MAP > 65 mmHg for initial resuscitation.^[2] However, recent clinical trials show that targeting a MAP of 60 – 65 mmHg has a similar 90-day mortality outcome compared with higher MAP targets.^[5] Furthermore, maintaining MAP within this range decreased the exposure to vasopressors and risk for supraventricular arrhythmias possibly conferring a better outcome for patients with septic shock. Teja *et al.* thus recommend a MAP in this target range over higher MAPs, which aligns with the current SSC guidelines.

Timely initiation of vasopressors to achieve MAP targets is crucial to improving outcomes in patients with septic shock. Historically, conventional teaching has been to administer vasopressors via central venous catheters due to the concern of extravasation into surrounding tissue resulting in necrosis. However, recent studies have indicated that when given for a limited duration, the risk of extravasation is marginal with the administration of vasopressors via peripheral lines.^[6] Teja *et al.* recommend the short-term use of low-dose vasopressors via peripheral IV lines and that central venous catheter insertion be reserved for haemodynamically-unstable patients with escalating vasopressor requirements, as well as those who require additional ports for the administration of multiple medications.

Septic shock is a multifaceted condition requiring a comprehensive and individualised approach to its management. Teja *et al.* provide a useful guide for clinicians, summarising evidence on how to escalate vasopressor and corticosteroid therapy in patients with septic shock. The authors' proposed algorithm for the management of hypotension at various stages of septic shock is a practical tool that clinicians can use to guide their decision-making.

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