Clinical Practice Statement

Do Steroids Improve Clinically Relevant Outcomes in Patients with Septic Shock?

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Recommendations

- When corticosteroids are administered to patients with septic shock, there is a consistent and meaningful improvement in the time to reversal of circulatory shock, faster improvement in organ dysfunction (most notably respiratory failure requiring mechanical ventilation), and decreased ICU length of stay.
- Although the literature remains mixed, a subset of the most severely ill patients with septic shock may have improved mortality with a seven-day course of steroids.

Introduction

Sepsis is a dysregulated host response to infection that may progress to septic shock, a state of global hypoperfusion that often requires fluid resuscitation and vasopressors to support adequate oxygen delivery. Septic shock results in both macro- and microcirculatory failure, which ultimately progresses to multi-organ dysfunction and potentially death.[1,2] Depending on the patient population, mortality for septic shock can exceed 50%. Relative adrenal insufficiency can be seen in up to 60% of patients with septic shock.

Steroids with glucocorticoid and mineralocorticoid effects (e.g., hydrocortisone) have been given to patients with sepsis since the 1950s.[3-8] In the 1980s, studies that evaluated the administration of supraphysiologic doses of steroids (i.e., 30 mg/kg methylprednisolone) to patients with severe sepsis failed to demonstrate clinical benefit.[9] As a result of these studies, the administration of high-dose steroids to patients with septic shock is currently not recommended. More recent studies have evaluated the administration of physiologic doses of steroids to patients with septic shock.

The current initial management of sepsis and septic shock consists of isotonic crystalloid fluid administration, appropriate broad-spectrum antibiotics, source control (debridement of infected tissue, drainage of contained purulence, or removal of contaminated medical devices), and potentially vasopressors when required to reach a MAP of > 65 mmHg. Physiologic doses of hydrocortisone (200-300 mg/day) are also recommended for patients with septic shock.[10,11] Its main therapeutic effects on improving blood pressure, tissue perfusion, and organ function are believed to be due to improved vascular tone, renal sodium and water retention, and myocardial function. Hydrocortisone may improve hemodynamics by restoring sensitivity of peripheral vascular and myocardial tissue receptors to catecholamines and attenuating nitric oxide mediated vasodilation.[12-14]

Executive Summary

In 2010, the Clinical Practice Committee (CPC) of the American Academy of Emergency Medicine (AAEM) published a Clinical Practice Guideline (CPG) titled "Do Steroids Administered in the Emergency Room Improve Mortality or Shock Reversal in Patients with Septic Shock?". In the years since the 2010 CPC CPG, numerous studies have been published evaluating the use of corticosteroids in patients with septic shock. This CPC Statement Update is a review of literature that has been published on the use of corticosteroids for septic shock since the initial CPC Statement in 2010. Publications in which corticosteroids were administered as a component of combination therapy or publications focused on patients infected with COVID-19 were not included in this review. Twelve peer-reviewed studies relevant to the clinical question were identified and evaluated by the authors following the established CPC format. These articles included randomized clinical trials of physiologic-dose steroids in septic shock[15-18], a large registry[19], a retrospective cohort study[20], a randomized trial of patients with severe sepsis treated with steroids[21], meta-analyses of previous clinical trials of steroids for septic shock[22-24], and studies (a prospective cohort and a randomized trial) that compared bolus dose administration to continuous infusions of steroids.[25,26]

Four randomized clinical trials have been published since 2010 that, either directly or indirectly, assessed the impact of hydrocortisone in the treatment of patients with septic shock.[15-18] Two of these four trials demonstrated faster resolution of shock and improvement in organ failure.[15,18] Only one of these four randomized trials demonstrated lower 90-day mortality in patients with septic shock who received a 7-day combination of hydrocortisone and fludrocortisone.[15] Similarly, three meta-analyses also found a significant improvement in shock reversal, but no change in 28-day mortality for patients with septic shock who received corticosteroids.[22-24] In contrast, a large registry-based study of almost 18,000 patients demonstrated an association of higher mortality among patients with septic shock who received physiologic doses of hydrocortisone.[19] Only two, small, single-center studies

published since 2010 evaluated bolus dose administration of steroids compared to a continuous infusion and found conflicting results.[25,26]

Conclusions:

This 2022 CPC Update identified twelve studies published since the initial CPC Statement in 2010 relevant to the use of corticosteroids in septic shock. Evidence from several of these studies demonstrates that the administration of physiologic doses of corticosteroids to patients with septic shock results in a meaningful improvement in the time to reversal of circulatory shock and faster improvement in organ dysfunction. The impact of corticosteroids in septic shock on patient mortality remains uncertain.

Literature Search Strategy

As per the AAEM CPC expedited search strategy, we searched for original research and systematic reviews relevant to steroid administration for septic shock published since 2010, the year of the previous CPC statement on this topic. We did not include case reports or small case series. We also excluded a 2017 study by Marik et al., since it bundled steroids, thiamine, and vitamin C in the intervention group.

Key Words: “steroids” AND “septic shock”

This strategy yielded a total of twelve relevant studies that were included in our review. (See Table of Reviewed Articles)

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