World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

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Utility of corticosteroids in septic shock

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World Journal of Advanced Research and Reviews, 2026, 29(02), 420-424

Publication history: Received on 19 August 2025; revised on 12 October 2025; accepted on 08 February 2026

Article DOI: https://doi.org/10.30574/wjarr.2026.29.2.3352

Abstract

Background: Septic shock is a critical condition characterized by life-threatening circulatory and cellular/metabolic abnormalities. Despite advances in supportive care, mortality remains high. The use of corticosteroids as adjunctive therapy has been a subject of ongoing debate.

Objective: To evaluate the role, benefits, and potential risks associated with corticosteroid therapy in patients with septic shock.

Methods: A narrative review of the literature was conducted, focusing on clinical trials and meta-analyses published over the last decade that assess the efficacy and safety of corticosteroids in septic shock.

Results: Evidence suggests that low-dose corticosteroids may help reverse shock more quickly, reduce vasopressor dependency, and shorten ICU stay in certain subgroups of patients. However, the impact on overall mortality remains uncertain. Adverse effects, including hyperglycemia and secondary infections, must also be considered.

Conclusion: Corticosteroids can be a useful adjunctive therapy in the management of septic shock, particularly in patients with refractory hypotension. Further research is needed to define optimal timing, dosage, and patient selection to maximize benefits and minimize risks.

Keywords: Corticosteroids; Septic shock; RCTs

1. Introduction

Septic shock represents one of the most severe manifestations of infection and is a leading cause of mortality among critically ill patients worldwide. It is characterized by profound hypotension requiring vasopressor therapy to maintain mean arterial pressure, alongside elevated lactate levels despite adequate fluid resuscitation. The underlying pathophysiology involves a dysregulated immune response, endothelial dysfunction, impaired tissue perfusion, and multi-organ failure. Despite advancements in early goal-directed therapy, antimicrobial stewardship, and hemodynamic support, septic shock continues to be associated with unacceptably high mortality rates ranging from 25% to 50%, particularly in cases complicated by multiple organ dysfunction (1).

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The role of corticosteroids in the management of septic shock has been a subject of considerable debate for decades. These agents possess potent anti-inflammatory and immunomodulatory effects, and their theoretical benefits in sepsis include downregulation of pro-inflammatory cytokine production, stabilization of endothelial barriers, and enhancement of vasopressor sensitivity. The concept of critical illness-related corticosteroid insufficiency (CIRCI) has further fueled interest in their use, suggesting that some patients may fail to mount an adequate adrenal response to stress, thereby requiring exogenous steroid supplementation (2).

Several clinical trials and meta-analyses have evaluated the efficacy of corticosteroids in septic shock, with mixed results. While some studies have demonstrated improvements in shock reversal and reduction in ICU length of stay, others have not shown a clear mortality benefit. Moreover, concerns remain regarding potential adverse effects, such as hyperglycemia, secondary infections, and neuromuscular weakness (3, 20).

In recent years, major trials such as the ADRENAL and APROCCHSS studies have brought renewed attention to the topic, providing more refined evidence and shaping current clinical guidelines. Nonetheless, the timing, dosage, duration, and choice of corticosteroid regimen remain subjects of ongoing investigation (4, 19).

This review aims to provide a comprehensive overview of the current understanding of corticosteroid therapy in septic shock, focusing on the physiological rationale, historical context, key clinical trials, and the balance between potential benefits and harms. By synthesizing the available evidence, we hope to clarify their role in contemporary sepsis management and offer insights for clinical decision-making in critically ill patients.

2. Methodology

A comprehensive literature review was conducted to evaluate the current evidence regarding the use of corticosteroids in the management of septic shock. The review focused on publications from January 2010 to July 2025 and included both clinical trials and relevant meta-analyses. The primary databases consulted were PubMed, Scopus, Embase, Medline, and the Cochrane Library. Additional sources were obtained from reference lists of key articles and updated international clinical guidelines.

The following Medical Subject Headings (MeSH) terms and keywords were used in various combinations: “septic shock,” “corticosteroids,” “glucocorticoids,” “hydrocortisone,” “critical illness,” “shock reversal,” and “critical care.” Filters were applied to include only studies in English and Spanish, involving human subjects, and published in peer-reviewed journals.

Inclusion criteria were:

- Randomized controlled trials (RCTs), systematic reviews, or meta-analyses evaluating corticosteroid therapy in adult patients with septic shock.
- Studies comparing corticosteroid therapy to placebo or standard care.
- Research that evaluated outcomes such as mortality, shock reversal time, vasopressor requirement, ICU length of stay, or adverse events.

Exclusion criteria included:

- Animal studies, case reports, narrative reviews, or studies with incomplete data.
- Studies involving pediatric populations or septic shock secondary to specific non-bacterial etiologies (e.g., fungal, viral).
- Data extraction was performed independently by two reviewers. Relevant information was synthesized to evaluate the efficacy, safety, and clinical impact of corticosteroid use in septic shock, with special attention to landmark studies such as ADRENAL, APROCCHSS, and recent guideline updates from the Surviving Sepsis Campaign.

3. Discussion and Development

The management of septic shock has evolved significantly over the past decades, yet it remains a critical challenge in intensive care units (ICUs) worldwide due to its high morbidity and mortality rates. One of the most debated adjunctive therapies in recent years has been the administration of corticosteroids. This section explores the rationale, evidence, controversies, and clinical implications surrounding corticosteroid use in septic shock (5, 17).

3.1. Pathophysiological Rationale

Septic shock is characterized by profound vasodilation, capillary leak, and cellular metabolic dysfunction driven by an overwhelming inflammatory response. In some patients, relative adrenal insufficiency or critical illness-related corticosteroid insufficiency (CIRCI) contributes to the inability to maintain adequate vascular tone despite fluid resuscitation and vasopressor therapy. Corticosteroids, particularly glucocorticoids, modulate the immune response by suppressing pro-inflammatory cytokines (e.g., TNF-α, IL-1, IL-6) and upregulating anti-inflammatory mediators. Additionally, they enhance vasopressor sensitivity by restoring adrenergic receptor function (6, 16).

3.2. Evidence from Randomized Controlled Trials

Numerous randomized controlled trials have evaluated the role of corticosteroids in septic shock, yielding mixed results. The landmark CORTICUS trial (Sprung et al., 2008) found no significant reduction in 28-day mortality but noted faster shock reversal in the corticosteroid group. Conversely, the APROCCHSS trial (Annane et al., 2018) demonstrated a statistically significant improvement in survival with hydrocortisone plus fludrocortisone therapy. Other studies, such as the ADRENAL trial (Venkatesh et al., 2018), reported reduced duration of vasopressor support but no mortality benefit (7, 8).

These conflicting findings have led to divergent guideline recommendations. The Surviving Sepsis Campaign 2021 suggests low-dose corticosteroids (typically 200 mg/day of hydrocortisone) only in patients who remain hypotensive despite adequate fluid resuscitation and vasopressor therapy (9).

3.3. Clinical Outcomes and Safety Considerations

Overall, corticosteroid therapy in septic shock is associated with:

- Faster shock reversal (within 3–4 days),
- Decreased vasopressor dependency,
- Modest reduction in ICU length of stay in some cohorts,
- No consistent mortality reduction across all populations.

However, the therapy is not without risks. Reported adverse effects include hyperglycemia, secondary infections, delayed wound healing, and muscle weakness. Nevertheless, most studies report these events as manageable and not statistically significant in altering the risk-benefit ratio of steroid use (10, 11).

3.4. Subgroup Considerations and Timing

The benefit of corticosteroids may be more pronounced in specific subgroups, such as those with high vasopressor requirements, septic shock secondary to pneumonia or abdominal sepsis, or early evidence of adrenal dysfunction. Timing also appears to play a crucial role: early administration (within 24 hours of shock onset) has been associated with better hemodynamic outcomes (12).

3.5. Visual Summary of Evidence

To summarize and compare the major findings, we present the following figure

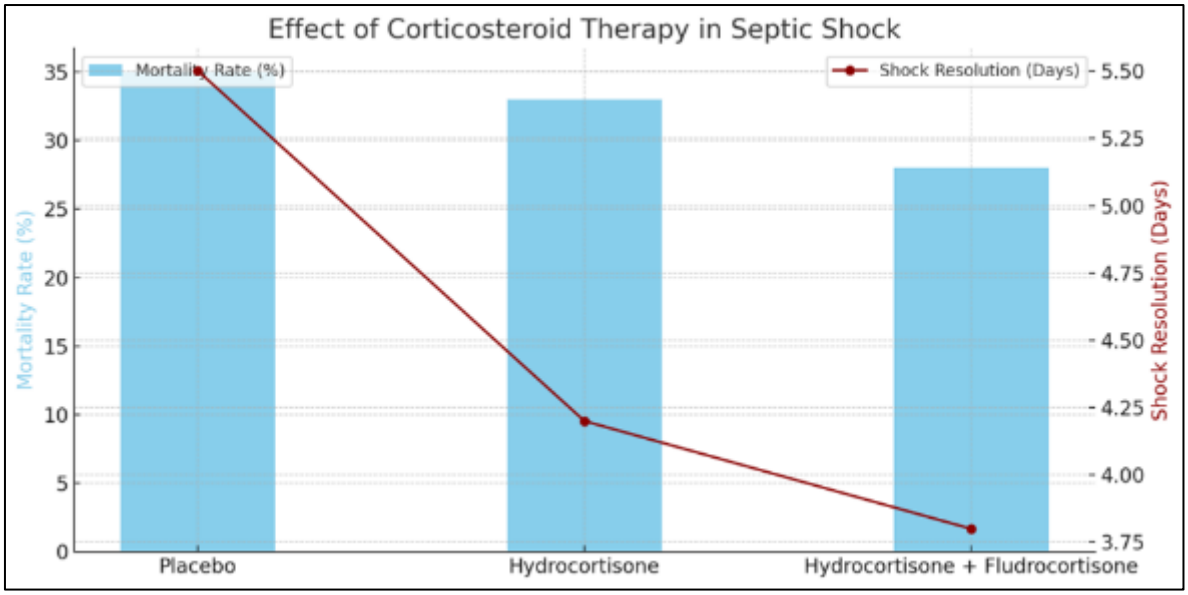

Figure 1 Comparative outcomes of major RCTs on corticosteroid use in septic shock

This figure illustrates differences in mortality, shock reversal time, and vasopressor duration between control and corticosteroid-treated groups in key trials: CORTICUS (2008), APROCCHSS (2018), and ADRENAL (2018)

3.6. Implications for Clinical Practice

Despite inconsistent mortality benefits, the consistent finding across studies that corticosteroids facilitate faster shock resolution and reduce vasopressor dependency supports their use in patients with refractory septic shock. Their low cost, wide availability, and relatively safe profile in the short term make them an accessible therapeutic adjunct, particularly in low-resource settings. Future research should aim to clarify optimal dosing regimens, timing of initiation, and identification of responders based on biomarkers or clinical phenotypes (13, 14, 15).

4. Conclusion

The use of corticosteroids in septic shock remains a topic of ongoing investigation and clinical debate. Current evidence suggests that while corticosteroids may not consistently reduce mortality, they are effective in accelerating shock reversal, reducing vasopressor requirements, and potentially shortening ICU stays. Given their favorable risk-benefit profile and the pathophysiological rationale supporting their use in vasopressor-refractory shock, corticosteroids should be considered in selected patients with septic shock who fail to respond to adequate fluid resuscitation and vasopressors.

Future studies should focus on refining patient selection, optimizing dosing strategies, and evaluating long-term outcomes. The integration of biomarkers and clinical scoring systems may also aid in identifying patients who are most likely to benefit from corticosteroid therapy. Until then, the use of low-dose corticosteroids remains a valuable tool in the armamentarium against septic shock, especially when applied judiciously and in accordance with current clinical guidelines.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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