



Corticosteroids in Septic Shock: Hype, Hope or Help?

An Emergency Medicine Blog

A 65-year-old man with a history of IV drug use presents with a fever and confusion. His only medical history includes chronic obstructive pulmonary disease managed with inhalers and steroids. His T is 103°F (39.4°C), BP is 65/20 mm Hg, HR is 142 bpm, RR is 28/min, and SpO₂ is 95% on room air. The patient is given 3,000 mL of fluids with an unchanged blood pressure. He is started on maximal doses of norepinephrine and epinephrine with a blood pressure of 72/33 mm Hg. What is the most appropriate next treatment to administer?

What is Septic Shock?

Septic shock is the most severe form of sepsis, a life-threatening response to infection that can lead to tissue damage, organ failure, and death. It is characterized by:

- **Hypotension:** Persistent low blood pressure despite adequate fluid resuscitation.
- **Organ Dysfunction:** Failure of one or more organs, often including the kidneys, lungs, or liver.
- **High Mortality Rate:** Without timely intervention, septic shock has a high mortality rate, making rapid treatment essential.

The Role of Steroids

Steroids, specifically corticosteroids, are anti-inflammatory medications that can modulate the immune response. Their use in septic shock is grounded in the idea that they may help counteract the overwhelming inflammatory response that characterizes the condition.

Mechanisms of Action

Corticosteroids work by:

- **Reducing Inflammation:** They inhibit the production of pro-inflammatory cytokines, which can help control the inflammatory cascade associated with sepsis.
- **Enhancing Vascular Responsiveness:** Steroids may improve the responsiveness of blood vessels to catecholamines (like epinephrine), potentially stabilizing blood pressure.
- **Modulating Immune Response:** They help restore balance in the immune system, which can be dysregulated in septic patients.

Current Guidelines and Recommendations

The Surviving Sepsis Campaign guidelines have evolved, and the current consensus recommends the use of corticosteroids in patients with septic shock. Here are key points:

- **Dosing:** The recommended dose is typically hydrocortisone 200 mg per day, administered in continuous or divided doses.
- **Timing:** Early initiation of steroid therapy (within the first few hours of septic shock diagnosis) is preferred.
- **Duration:** Treatment is generally continued until hemodynamic stability is achieved, often around 7-10 days

Benefits and Risks

Benefits

1. **Improved Outcomes:** Studies have shown that early corticosteroid therapy can reduce mortality rates in patients with septic shock.
2. **Faster Recovery:** Steroids may help improve hemodynamic stability more quickly, potentially leading to faster recovery times.
3. **Reduced Duration of Shock:** Patients may experience shorter episodes of shock, decreasing the need for prolonged vasopressor therapy.

Risks

1. **Infection Risk:** Corticosteroids can suppress the immune response, raising concerns about secondary infections.
2. **Glycemic Control:** Steroids can lead to elevated blood sugar levels, necessitating careful monitoring, especially in diabetic patients.
3. **Psychiatric Effects:** Some patients may experience mood swings or cognitive changes during treatment.

Recent Research Findings

Recent studies have reinforced the role of corticosteroids in septic shock management. A landmark meta-analysis concluded that steroid therapy is associated with reduced mortality, particularly in patients with

YEAR	RCT	MORTALITY IMPROVED?
2002	ANNANE	YES
2008	CORTICUS	NO
2016	HYPRESS	NO
2018	ADRENAL	NO
2018	APROCCHSS	YES

ANNANE

- **Key finding:** Low-dose hydrocortisone with fludrocortisone improved 28-day survival in septic shock patients with relative adrenal insufficiency.
- **Limitations:** Small sample size, potential selection bias.

CORTICUS

- **Key finding:** Hydrocortisone alone did not improve mortality in septic shock patients, regardless of adrenal insufficiency status.
- **Strengths:** Larger sample size, well-designed study.

HYPRESS

- **Key finding:** Hydrocortisone did not prevent progression to septic shock in patients with severe sepsis.
- **Strengths:** Well-designed study, large sample size.

ADRENAL

- **Key finding:** Hydrocortisone did not improve mortality in septic shock patients, but it did show some beneficial effects on secondary outcomes like time to shock reversal and ICU length of stay.
- **Strengths:** Very large sample size, multicenter study.

APROCCHSS

- **Key finding:** Hydrocortisone plus fludrocortisone improved survival in septic shock patients.
- **Strengths:** Well-designed study, clear inclusion criteria.

Conclusion

Steroid use in septic shock has emerged as a critical component of management strategies, offering significant benefits in terms of mortality and recovery. However, like any treatment, it is not without risks. As the medical community continues to research and refine approaches to septic shock, the use of corticosteroids will likely remain a focal point in improving patient care.

As always, decisions regarding steroid therapy should be made collaboratively between healthcare providers and patients, considering the unique circumstances of each case. With continued research and evolving guidelines, we can hope to enhance outcomes for those battling this life-threatening condition.

References

- Dellinger, R. P., Levy, M. M., Rhodes, A., Annane, D., Gerlach, H., Opal, S. M., Sevransky, J. E., Sprung, C. L., Douglas, I. S., Jaeschke, R., Osborn, T. M., Nunnally, M. E., Townsend, S. R., Reinhart, K., Kleinpell, R. M., Angus, D. C., Deutschman, C. S., Machado, F. R., Rubenfeld, G. D., Webb, S. A., ... Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup (2013). Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Critical care medicine*, 41(2), 580–637. <https://doi.org/10.1097/CCM.0b013e31827e83af>
- Lamontagne, F., Rochweg, B., Lytvyn, L., Guyatt, G. H., Møller, M. H., Annane, D., Kho, M. E., Adhikari, N. K. J., Machado, F., Vandvik, P. O., Dodek, P., Leboeuf, R., Briel, M., Hashmi, M., Camsooksai, J., Shankar-Hari, M., Baraki, M. K., Fugate, K., Chua, S., & Marti, C. (2018). Corticosteroid therapy for sepsis: a clinical practice guideline. *BMJ*, 362, k3284. <https://doi.org/10.1136/bmj.k3284>
- Pitre, T., Drover, K., Chaudhuri, D., Zeraaktkar, D., Menon, K., Gershengorn, H. B., Jayaprakash, N., Spencer-Segal, J. L., Pastores, S. M., Nei, A. M., Annane, D., & Rochweg, B. (2024). Corticosteroids in Sepsis and Septic Shock: A Systematic Review, Pairwise, and Dose-Response Meta-Analysis. *Critical Care Explorations*, 6(1), e1000. <https://doi.org/10.1097/ccc.0000000000001000>
- Rochweg B, Oczkowski SJ, Siemieniuk RAC, Agoritsas T, Belley-Cote E, D'Aragnon F, Duan E, English S, Gossack-Keenan K, Alghuroba M, Szczeklik W, Menon K, Alhazzani W, Sevransky J, Vandvik PO, Annane D, Guyatt G. Corticosteroids in Sepsis: An Updated Systematic Review and Meta-Analysis. *Crit Care Med*. 2018 Sep;46(9):1411-1420. doi: 10.1097/CCM.0000000000003262. PMID: 29979221.
- Sprung, C. L., Annane, D., Keh, D., Moreno, R., Singer, M., Freivorst, H., Laterre, P.-F., Reinhart, K., Cuthbertson, B. H., Payen, D., & Briegel, J. (2008). Hydrocortisone Therapy for Patients with Septic Shock. *New England Journal of Medicine*, 358(2), 111–124. <https://doi.org/10.1056/nejmoa071366>gel, K., Weiss, Y. G., Benbenishty, J., Kalenka, A., Fo