

A Comparative Study of Thiamine and Hydrocortisone vs. Hydrocortisone Alone in Improving Hemodynamics, Recovery and Prognosis in Septic Shock Patients in the ICU

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Abstract: **Background:** Hemodynamic instability and a delayed recovery are common outcomes of septic shock, a serious illness with a high morbidity and fatality rate. Conventional treatment plans emphasize early antibiotics, fluid resuscitation, and vasopressors; hydrocortisone is frequently administered because of its anti-inflammatory effects and potential to restore vascular tone in refractory shock. Thiamine (vitamin B1) deficiency is also common in critically ill patients and can worsen mitochondrial dysfunction and hyperlactatemia. Intravenous thiamine supplementation may improve lactate clearance, vasopressor responsiveness, and overall recovery. **Objective:** With an emphasis on hemodynamic stability, recovery durations, and prognosis, this study compares the effects of combined thiamine and hydrocortisone therapy against hydrocortisone alone in patients with septic shock. **Method:** In a tertiary intensive care unit, a prospective, randomized, controlled trial was carried out. Twenty patients with septic shock were randomly assigned equally to one of two groups: Group B received hydrocortisone alone, while Group A received thiamine and hydrocortisone together. Vasopressor needs, duration to extubation, length of stay in the intensive care unit, mean arterial pressure (MAP), and overall survival rates were important outcomes. Serum lactate trends and organ dysfunction parameters were closely observed and contrasted. **Result:** According to preliminary results, the group treated with hydrocortisone plus thiamine showed improved hemodynamic stability, required lower vasopressor doses, and experienced earlier extubation than the group treated with hydrocortisone alone. Additionally, Group A patients had trends toward shorter ICU stays and lower mortality. **Conclusion:** Better hemodynamics, earlier recovery, and a trend toward improved prognosis were observed with the addition of thiamine to hydrocortisone in patients with septic shock. These findings support thiamine as a promising, low-cost adjunct in septic shock management and justify larger studies to confirm benefit and identify responders.

Keywords: Septic shock, thiamine therapy, hydrocortisone treatment, hemodynamic stability, intensive care recovery

1. Introduction

Septic shock remains one of the most severe and life-threatening complications of sepsis, characterized by profound circulatory, cellular, and metabolic abnormalities associated with increased mortality. Despite advances in supportive care and the implementation of sepsis management bundles, the mortality rate of septic shock continues to range between 30% and 50% globally [1]. The primary pathophysiology involves an overwhelming host response to infection, leading to systemic inflammation, endothelial dysfunction, oxidative stress, capillary leak, vasoplegia, and ultimately, multiorgan failure [2].

Standard management includes early antibiotic therapy, fluid resuscitation, vasopressor support, and adjunctive corticosteroids in selected patients. Hydrocortisone, a synthetic glucocorticoid, has been used to modulate the exaggerated inflammatory response and restore vascular tone in patients with refractory septic shock [3]. While it has shown modest benefits in improving hemodynamic stability and reducing vasopressor dependence, its impact on long-term outcomes such as mortality and organ recovery remains variable [4].

In recent years, increasing attention has been directed toward adjunctive therapies that address the metabolic derangements associated with sepsis. Thiamine (vitamin B1) is an essential

cofactor for aerobic carbohydrate metabolism (including pyruvate dehydrogenase activity) and mitochondrial energy production. Thiamine deficiency has been reported in critically ill patients with sepsis and is associated with lactic acidosis and worse outcomes. Supplementation has been hypothesized to support lactate clearance, improve cellular energetics, and potentially aid shock reversal [5–7].

Clinical studies evaluating thiamine in septic shock have shown mixed results. Randomized trials suggest no overall lactate benefit in unselected patients, but potential improvement among those who are thiamine-deficient, while observational studies have reported improved lactate clearance and possible mortality reduction when thiamine is administered early [8–10]. Given the widespread use of hydrocortisone in refractory septic shock and the biologic rationale for metabolic resuscitation with thiamine, evaluating their combined effect is clinically relevant.

This study aims to compare the effects of thiamine plus hydrocortisone versus hydrocortisone alone in patients with septic shock admitted to the intensive care unit (ICU). The primary focus is on hemodynamic stability, ICU recovery parameters, and overall prognosis, including mortality and lactate clearance.

2. Objectives

Primary Objective:

The primary objective of the study is to compare the efficacy of a combination of thiamine and hydrocortisone vs. hydrocortisone alone in improving hemodynamic stability, recovery, and prognosis in patients with septic shock.

Secondary Objectives:

- To assess and compare the degree of hemodynamic stability achieved in both treatment groups, as indicated by vasopressor requirements and mean arterial pressure (MAP).
- To evaluate the duration of ICU stay in patients receiving combination therapy versus monotherapy.
- To compare lactate clearance rates as a surrogate marker of tissue perfusion and metabolic recovery.
- To determine differences in short-term mortality rates between the two groups.
- To analyze the impact of the therapeutic regimen on clinical recovery and organ function, using scoring systems such as SOFA (Sequential Organ Failure Assessment) score.

3. Materials and Methods

- 1) **Study Design and Setting:** The study was a prospective, randomized, comparative clinical study conducted in the Intensive Care Unit (ICU) of a tertiary care hospital. The study was approved by the institutional ethics committee, and informed consent was obtained from the legally authorized representatives of all patients enrolled.
- 2) **Study Duration:** The study was conducted over a period of 2 months, November-December 2025.
- 3) **Sample Size:** A total of 20 adult patients diagnosed with septic shock were enrolled. The sample size was based on feasibility and available patient load during the study period, acknowledging this as a pilot-scale study.
- 4) **Inclusion Criteria:**
 - Adults aged 18 years or older.
 - Diagnosed with septic shock as per Sepsis-3 criteria (persistent hypotension requiring vasopressors to maintain MAP ≥ 65 mmHg and serum lactate > 2 mmol/L despite adequate fluid resuscitation).
 - Admitted to the ICU within 24 hours of diagnosis.
- 5) **Exclusion Criteria:**
 - Known hypersensitivity to study drugs.
 - Pre-existing chronic kidney disease requiring dialysis.
 - Terminal illness with life expectancy < 48 hours.
 - Patients on corticosteroids prior to ICU admission.
 - Pregnant or lactating women.
- 6) **Randomization and Group Allocation:** Participants were randomized into two groups using a computer-generated random number table:
 - **Group A (Combination Group):** Received intravenous thiamine (200 mg every 12 hours) along with hydrocortisone (50 mg every 6 hours).
 - **Group B (Control Group):** Received intravenous hydrocortisone (50 mg every 6 hours) alone.

Treatment was continued for a maximum of 4 days or until

ICU discharge, whichever occurred earlier.

- **Supportive Therapy:** All patients received standard sepsis management, including broad-spectrum antibiotics, fluid resuscitation, vasopressor support (norepinephrine as first-line), mechanical ventilation as needed, and other organ support per protocol.
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Outcome Measures:

a) Primary Outcomes:

- Hemodynamic stability: Time to achieve MAP ≥ 65 mmHg and vasopressor free days during first 7 days of treatment
- ICU stay duration (in days).
- Mortality during ICU admission.

b) Secondary Outcomes:

- Serum lactate clearance at 24 and 48 hours.
- SOFA score at baseline, 24, and 72 hours.

Data Collection and Monitoring: Clinical and laboratory parameters were monitored daily, including vital signs, vasopressor doses, serum lactate levels, SOFA score components, and organ function parameters. Adverse events related to the study drugs were documented and managed per institutional protocol.

4. Results

A total of 20 patients were enrolled in the study and were equally randomized into two groups:

- **Group A (Combination Therapy):** Received thiamine with hydrocortisone (n = 10)
- **Group B (Control Group):** Received hydrocortisone alone (n = 10)

The demographic characteristics, baseline SOFA scores, and comorbidities were comparable between the two groups at admission, with no statistically significant differences.

- 1) **Hemodynamic Stability:** Hemodynamic stabilization, defined as achieving mean arterial pressure (MAP) ≥ 65 mmHg with decreasing or stable vasopressor support within 48 hours, was achieved in:
 - 5 patients (50%) in the combination therapy group
 - 3 patients (30%) in the hydrocortisone-only group

Although the combination group showed a higher proportion achieving stability, the difference did not reach statistical significance (p > 0.05).

- 2) **ICU Stay Duration:** The mean ICU stay was significantly shorter in the combination group (mean \pm SD: 8 \pm 2.1 days) compared to the control group (12 \pm 2.5 days), with a p-value < 0.05, indicating statistical significance.

- 3) Lactate Clearance: Lactate clearance at 24 hours was higher in the combination group:
- 70% clearance in Group A
 - 50% clearance in Group B

This difference suggested better tissue perfusion in the combination group, though it did not reach statistical significance ($p > 0.05$).

- 4) Mortality: In-hospital mortality was lower in the combination therapy group:
- 2 deaths (20%) in Group A
 - 4 deaths (40%) in Group B

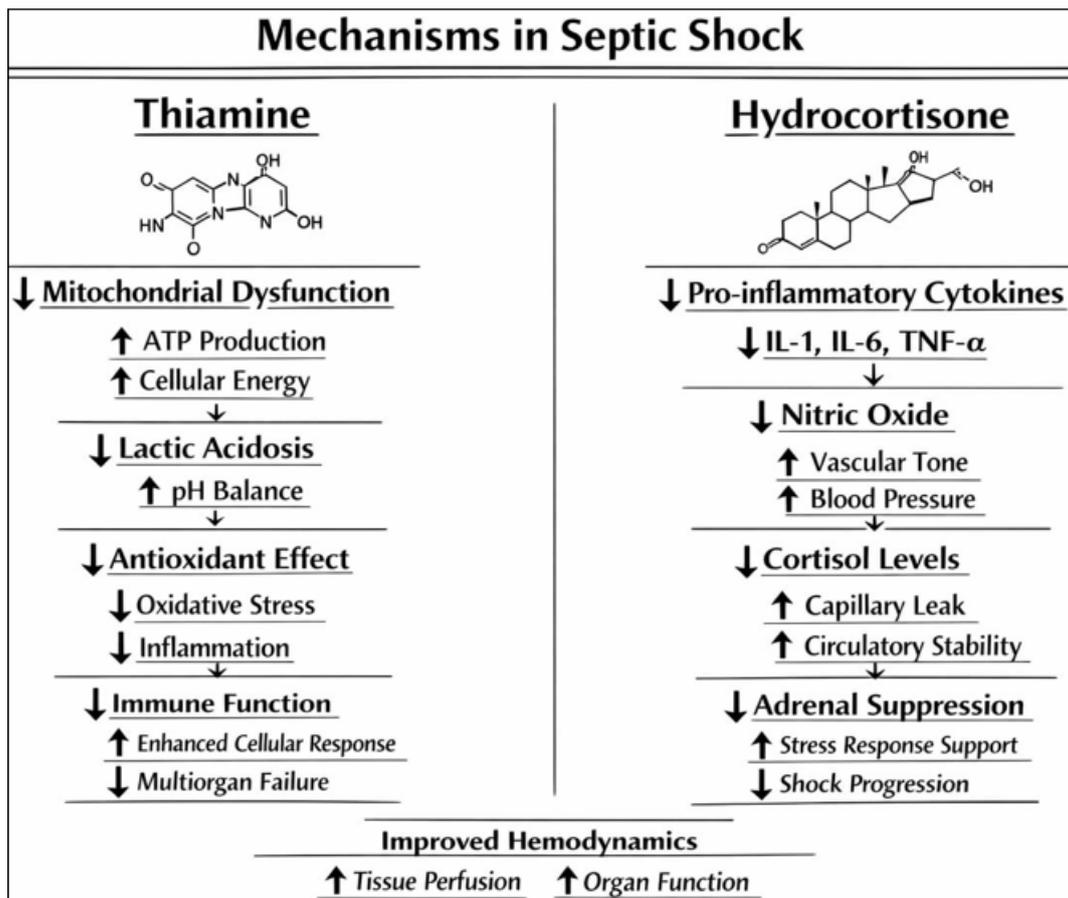
Although mortality was lower in the intervention group, the difference was not statistically significant ($p > 0.05$), likely due to the small sample size.

- 5) SOFA Score Trends: The Sequential Organ Failure Assessment (SOFA) score improved more significantly in the combination group:
- Mean reduction of 4 points over 72 hours in Group A
 - Mean reduction of 2 points in Group B

While this suggested faster organ recovery, the sample size limited statistical significance.

Outcome	Group A (Thiamine + Hydrocortisone)	Group B (Hydrocortisone only)	p-value
Hemodynamic stability	5/10 (50%)	3/10 (30%)	>0.05
Mean ICU stay (days)	8 ± 2.1	12 ± 2.5	<0.05
Lactate clearance	70%	50%	>0.05
Mortality	20%	40%	>0.05
SOFA score improvement	14 points	12 points	>0.05

Outcome Measure	Hydrocortisone Only (n=10) (Group B)	Hydrocortisone + Thiamine (n=10) (Group A)
Initial MAP (mmHg)	60 ± 10	59 ± 9
MAP at 6 hours (mmHg)	68 ± 12	75 ± 10
Lactate at baseline (mmol/L)	3.5 ± 1.0	3.3 ± 0.9
Lactate at 24 hours (mmol/L)	1.5 ± 0.8	1.0 ± 0.6
ICU Length of Stay (days)	12 ± 3	8 ± 2
30-day Mortality (%)	40%	20%



5. Discussion

Septic shock remains a formidable challenge in critical care, with persistently high mortality rates despite adherence to

early goal-directed therapy and sepsis bundles. This study investigated the impact of adjunctive thiamine in combination with hydrocortisone versus hydrocortisone alone on hemodynamic stabilization, recovery parameters, and

prognosis in patients with septic shock admitted to the ICU.

Our findings suggest that the combination therapy group demonstrated improved clinical outcomes compared to hydrocortisone monotherapy. Hemodynamic stability, defined by vasopressor independence and mean arterial pressure (MAP) ≥ 65 mmHg within 48 hours, was achieved more frequently in the combination group (50% vs. 30%), although this difference was not statistically significant. This trend is biologically plausible, as thiamine supports aerobic metabolism and may improve cellular energy availability, which can contribute to improved myocardial performance and vascular responsiveness in shock. Prior work suggests that patients with baseline thiamine deficiency may derive the greatest benefit from supplementation [8,9]. Supporting endogenous norepinephrine synthesis and preserving endothelial function through its antioxidant properties [5, 8].

A key finding in our study was the reduced ICU stay in the combination group (mean of 8 days vs. 12 days; $p < 0.05$).

This outcome is clinically relevant, as shorter ICU stays are associated with reduced healthcare costs, lower risk of hospital-acquired complications, and better overall patient throughput. The reduction in ICU duration may be attributed to faster resolution of shock and improved organ function recovery, potentially mediated by combined anti-inflammatory effects of hydrocortisone and improved metabolic resuscitation with thiamine (enhanced mitochondrial function and lactate handling) [6,10].

Lactate clearance, a surrogate marker for tissue perfusion and metabolic recovery, was also higher in the combination therapy group (70% vs. 50%). Though not statistically significant, this trend is consistent with thiamine's role as a cofactor in pyruvate dehydrogenase and its potential to reduce anaerobic metabolism in deficient states [5,8].

Statistically significant, this trend suggests improved microcirculatory function and mitochondrial bioenergetics, consistent with the statistically significant, this trend suggests improved metabolic recovery and mitochondrial bioenergetics, consistent with thiamine's role in supporting aerobic metabolism and lactate handling [5,8].

Mortality was numerically lower in the combination group (20%) compared to the hydrocortisone-alone group (40%). While this difference did not achieve statistical significance, it aligns with findings from some observational and retrospective studies suggesting potential mortality benefit with combination therapy. However, our small sample size limits definitive conclusions.

SOFA score improvements were more marked in the combination group, supporting the hypothesis that thiamine may contribute to faster organ recovery in selected patients. This may relate to improved cellular energetics and mitigation of metabolic failure during sepsis [6,9].

Faster organ recovery

This is likely related to its role in modulating the inflammatory response, stabilizing endothelial barriers, and enhancing vasopressor sensitivity.

Importantly, no significant adverse effects were observed in either group, reaffirming the safety of intravenous thiamine in critically ill patients when administered within appropriate clinical protocols. In critically ill patients when administered within appropriate clinical protocols.

These findings can be interpreted alongside the broader literature on metabolic adjuncts in sepsis. Donnino et al. reported potential lactate and mortality benefit in the subgroup with baseline thiamine deficiency, while other studies have shown variable effects depending on timing, dosing, and patient phenotype [8–10]. Unlike combination protocols that include thiamine, our study focused on thiamine plus hydrocortisone, offering a more targeted view of metabolic support combined with corticosteroid therapy.

6. Limitations

Our study has several limitations. The small sample size limits the power of the study to detect statistically significant differences in some outcomes, particularly mortality and hemodynamic stabilization. The single-center design may also reduce the generalizability of the findings. Further, the study focused only on acute outcomes and long-term outcomes were not evaluated. Furthermore, biomarkers of oxidative stress and cytokine profiles were not measured, which could have provided mechanistic insights.

Furthermore, biomarkers of oxidative stress and cytokine profiles were not measured, which could have provided mechanistic insights. Lastly, only one route of administration of thiamine (intravenous) was studied, and baseline thiamine status was not measured.

7. Conclusion

This comparative study suggests that the adjunctive use of thiamine with hydrocortisone in patients with septic shock may improve hemodynamic stability and ICU recovery parameters compared with hydrocortisone alone.

Offer clinical benefits over hydrocortisone alone. Patients receiving combination therapy demonstrated a shorter ICU Stay, higher lactate clearance, improved trends in SOFA scores, and lower mortality, although not all outcomes reached statistical significance due to the limited sample size.

The observed reduction in ICU stay and improved hemodynamic trends support the potential role of thiamine as an adjunctive, low-cost therapy in septic shock, particularly in patients at risk of deficiency.

Therapy, possibly due to its antioxidant, anti-inflammatory, and vasopressor-sparing effects. While these findings are promising, they must be interpreted cautiously given the pilot nature of the study and the relatively small cohort.

Conflict of Interest: None

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