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Hydrocortisone, Vitamin C, and Thiamine for the Treatment of Severe Sepsis and Septic Shock: A Prospective Randomized Controlled Study

Dr Sunil Patil[1], Dr Shruti Tandon[1]
Corresponding Authors: J. D. Sunvala[1], Indraneel Raut[1], Susheel Bindroo[1]
[1] Jaslok Hospital and Research Centre, Mumbai, Maharashtra, India

Abstract
Background
Sepsis and septic shock remain major causes of morbidity and mortality worldwide. Recent evidence suggests that a combination of intravenous vitamin C, hydrocortisone, and thiamine may improve outcomes in critically ill septic patients.
Methods
A prospective randomized controlled study was conducted in 50 adult patients diagnosed with severe sepsis or septic shock. Twenty-five patients received standard therapy plus intravenous vitamin C, hydrocortisone, and thiamine, whereas twenty-five patients received standard treatment alone. The primary outcomes were reversal of shock and 28-day mortality. Secondary outcomes included intensive care unit (ICU) length of stay, vasopressor duration, procalcitonin (PCT) clearance, Sequential Organ Failure Assessment (SOFA) score improvement, and requirement for renal replacement therapy (RRT).
Results
Twenty-five patients were included in each group. Twenty-eight-day mortality was lower in the treatment group compared with the control group (48% vs 56%). Mean vasopressor duration was reduced in the treatment group (120.24 vs 126 hours). PCT clearance was higher in the treatment arm (0.43 vs 0.37), and improvement in SOFA scores was greater (ΔSOFA 4.71 vs 3.43). Renal replacement therapy was required in 48% of treated patients and 24% of controls. Mean ICU length of stay was comparable between groups (8.44 vs 8.04 days).
Conclusion
The combination of vitamin C, hydrocortisone, and thiamine demonstrated favourable trends in mortality reduction, organ dysfunction improvement, and biomarker clearance. Larger adequately powered studies are required to confirm these findings.

Keywords
Sepsis; Septic Shock; Vitamin C; Thiamine; Hydrocortisone; Critical Care Medicine

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I. Introduction

Sepsis and septic shock are life-threatening conditions associated with substantial mortality despite advances in critical care management. Contemporary treatment strategies primarily focus on source control, antimicrobial therapy, haemodynamic optimisation, and organ support.

Vitamin C possesses antioxidant properties and plays an important role in endothelial function and immune regulation. Thiamine is a critical cofactor in mitochondrial energy metabolism and is frequently deficient in critically ill patients. Hydrocortisone has been used in septic shock because of its anti-inflammatory and vasopressor-sensitising characteristics.

The combined use of vitamin C, hydrocortisone, and thiamine has been proposed as a metabolic resuscitation strategy aimed at attenuating organ dysfunction and improving survival in septic shock. This study evaluated the efficacy of this therapeutic combination in patients with severe sepsis and septic shock.

II. Materials and Methods

Study Design
Prospective randomized controlled clinical study conducted in critically ill patients diagnosed with severe sepsis or septic shock.
Patient Population
Fifty adult patients meeting diagnostic criteria for severe sepsis or septic shock and having serum procalcitonin levels greater than 2 ng/mL were enrolled.

Inclusion Criteria

- Age ≥18 years
- Severe sepsis or septic shock
- Evidence of infection
- Procalcitonin >2 ng/mL

Exclusion Criteria

- Pregnancy
- Death within 24 hours of admission
- Terminal illness

Intervention

Treatment Group (n=25)

- Vitamin C 1.5 g IV every 6 hours for 4 days
- Hydrocortisone 50 mg IV every 6 hours for 5 days
- Thiamine 200 mg IV every 12 hours for 4 days

Control Group (n=25)

- Standard ICU management alone

Endpoints

Primary Outcomes

- Reversal of shock
- 28-day mortality

Secondary Outcomes

- ICU length of stay
- Vasopressor duration
- Procalcitonin clearance
- SOFA score improvement
- Requirement for renal replacement therapy

III. Results

Clinical Outcomes

Outcome	Treatment (n=25)	Control (n=25)
28-day mortality	12 (48%)	14 (56%)
ICU stay (days)	8.44	8.04
Vasopressor duration (hours)	120.24	126
PCT clearance	0.43	0.37
Δ SOFA	4.71	3.43
Renal replacement therapy	12 (48%)	6 (24%)

The treatment group demonstrated lower mortality, shorter vasopressor duration, greater PCT clearance, and improved SOFA score reduction when compared with controls.

IV. Discussion

This prospective randomized study evaluated the therapeutic effects of adjunctive vitamin C, hydrocortisone, and thiamine among patients with severe sepsis and septic shock.

The treatment group demonstrated numerically lower mortality and improved biological markers of recovery. Increased PCT clearance and greater SOFA score reduction suggest improved resolution of systemic inflammation and organ dysfunction. Although differences were clinically encouraging, definitive statistical significance could not be established using the available aggregate dataset.

These findings are broadly consistent with earlier investigations that suggested possible benefits of metabolic resuscitation therapy in septic shock. However, subsequent trials have yielded mixed results, highlighting the ongoing uncertainty regarding the efficacy of this treatment strategy.

Limitations

- Single-centre study
- Small sample size
- Aggregate outcome data available for analysis
- Baseline demographic characteristics unavailable
- Limited power to detect mortality differences

V. Conclusion

Adjunctive therapy with vitamin C, hydrocortisone, and thiamine demonstrated promising trends toward reduced mortality and improved organ dysfunction in patients with severe sepsis and septic shock. Further large-scale multicentre randomized trials are necessary to establish the definitive role of this therapeutic strategy.

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