Section: Emergency Medicine

Original Research Article

METABOLIC RESUSCITATION WITH THIAMINE IN SEPSIS: CLINICAL OUTCOMES FROM A MATCHED COHORT STUDY

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ABSTRACT

Background: Sepsis and septic shock continue to be leading causes of death in intensive care units worldwide, often involving metabolic disturbances due to mitochondrial dysfunction. Thiamine (vitamin B1), a critical cofactor in oxidative energy production, is commonly deficient among critically ill individuals. The objective of this research was to evaluate the therapeutic effects of prompt thiamine administration via intravenous route in individuals presenting with sepsis and septic shock.

Materials and Methods: This retrospective cohort analysis encompassed adult intensive care unit patients hospitalized for sepsis or septic shock during the period from March 2024 to February 2025. Participants were grouped based on whether they received intravenous thiamine (200 mg every 12 hours) within the first 24 hours of presentation. Propensity score matching was used (1:1) to balance key baseline factors including age, SOFA score, lactate level, comorbidities, and ventilator support. The main endpoint measured was 28-day mortality, with supplementary end-points including elimination of lactate, change in SOFA score over 72 hours, vasopressor-free days, and ICU length of stay.

Results: A total of 172 patients were analyzed, with 86 patients in each matched group. Thiamine recipients showed higher lactate clearance at 24 hours (38.0% vs. 21.0%; p=0.014), greater reductions in SOFA score (3.2 vs. 2.4; p=0.027), and more vasopressor-free days (4 vs. 2 days; p=0.034). The thiamine group had significantly less mortality at 28 days. (32.6% vs. 45.3%; p=0.048).

Conclusion: Administration of thiamine in the early phase of sepsis or septic shock was associated with better clinical outcomes and reduced mortality. These findings support the need for future randomized trials to establish its definitive role in sepsis therapy.

Keywords: Thiamine, septic shock, lactate metabolism, ICU mortality, vasopressors, SOFA score, critical care, resuscitation.

INTRODUCTION

Sepsis and septic shock remain critical challenges in modern intensive care medicine, contributing substantially to global ICU admissions and deaths. According to the Sepsis-3 definitions, sepsis is now understood as a severe, life-threatening syndrome resulting from a dysregulated response to infection that leads to acute organ dysfunction. Septic shock, a more severe variant, involves persistent hypotension and metabolic abnormalities despite adequate fluid resuscitation and carries a particularly high risk of death.[1] Although there have been advancements in supportive care, including timely antibiotics and vasopressors, mortality in sepsis continues to range between 25% and 50%, depending on severity and patient comorbidities.[2]

A growing body of research highlights mitochondrial failure and energy metabolism disruption as key components in the pathogenesis of sepsis. One notable manifestation of this dysfunction is lactic acidosis, often observed in critically ill patients due

to impaired oxidative metabolism. Thiamine (vitamin B1) plays a pivotal role in mitochondrial enzymatic pathways, serving as a coenzyme for pyruvate dehydrogenase and α-ketoglutarate dehydrogenase—enzymes essential for ATP production via aerobic respiration.[3,4] In the setting of thiamine deficiency, pyruvate cannot be efficiently metabolized, leading to lactate accumulation and worsening cellular hypoxia.

Thiamine deficiency is frequently encountered among ICU patients due to factors such as prolonged illness, poor nutritional intake, renal loss, and increased metabolic demands. Earlier studies estimate that approximately one-third of critically ill patients may present with thiamine insufficiency, a figure that may be even higher among those with septic shock.[5] These observations have led to the hypothesis that thiamine supplementation could help restore mitochondrial function and reduce organ dysfunction in sepsis.

Clinical interest in this intervention has been supported by several studies. In a randomized trial, Donnino et al. found that intravenous thiamine improved lactate clearance in septic shock patients who were thiamine-deficient, suggesting a potential metabolic benefit.[6] Additionally, Woolum et al. reported that early thiamine administration in septic patients was linked with improved lactate normalization and lower in-hospital mortality.[7] Given thiamine's safety, low cost, and mechanistic plausibility, it is considered a promising adjunctive agent in the management of sepsis.

Despite these findings, existing evidence remains limited and somewhat inconsistent. Most prior studies have small sample sizes, lack uniform dosing protocols, or are limited by design flaws. Moreover, it is still unclear whether thiamine provides a survival advantage in an unselected sepsis population, or whether its benefits are restricted to individuals with confirmed deficiency. Therefore, further investigation in broader ICU populations is warranted.

This study was undertaken to explore the effects of intravenous thiamine on clinical outcomes in patients admitted with sepsis or septic shock to a tertiary care center. By applying a propensity score-matched design, the study aims to reduce selection bias and provide more reliable insights into the therapeutic potential of thiamine in this high-risk cohort.

MATERIALS AND METHODS

This retrospective cohort study was carried out in the intensive care unit (ICU) of a tertiary care academic hospital over 18-month duration, spanning from March 2024 to February 2025. The primary objective was to analyze the effectiveness of thiamine administration in patients with septic shock. Data was collected from hospital records of patients

Adults patients fulfilling the criteria for sepsis or septic shock were screened for inclusion. Sepsis was defined as a documented or suspected infection leading to a rise in Sequential Organ Failure Assessment (SOFA) score of two points or more. Septic shock was characterized by persistent hypotension that necessitated vasopressor support to maintain a mean arterial pressure (MAP) of 65 mmHg or higher, along with an elevated lactate level exceeding 2 mmol/L, despite adequate fluid administration. Patients were excluded if they were discharged or died within 24 hours of ICU admission, had a known history of chronic alcohol dependence or were receiving long-term thiamine therapy, or had incomplete laboratory or clinical data. Individuals who had been treated with experimental therapies such as high-dose vitamin C or corticosteroid bundles outside standard protocols were also excluded.

Eligible patients were grouped based on whether they had received intravenous thiamine supplementation within 24 hours of ICU admission. The intervention group consisted of patients who were administered intravenous thiamine at a dose of 200 mg twice daily. The decision to administer thiamine was made independently by the treating physician and was not influenced by the research team. Patients who did not receive thiamine served as the comparison group.

For all included patients, baseline demographic data such as age, gender, and pre-existing comorbid conditions were collected. Clinical variables, including initial SOFA scores, lactate levels at admission, need for vasopressor or ventilatory support and site of infection, and were also recorded. All-cause mortality at 28 days served as the principal outcome measure. Supplementary outcomes comprised lactate elimination within 24 hours, vasopressor-free duration, SOFA score improvement across 72 hours, and ICU stay length.

To reduce confounding and selection bias inherent in observational studies, propensity score matching (PSM) was applied. Propensity scores were calculated using logistic regression based on variables such as age, baseline SOFA score, serum lactate, infection source, comorbid conditions, and requirement for mechanical ventilation. A 1:1 nearest-neighbor matching method was used, applying a caliper width of 0.2 standard deviations of the logit of the propensity score. This created well-balanced cohorts suitable for outcome comparison.

Data analysis was conducted using IBM SPSS Statistics version 26.0. Continuous variables were summarized using means with standard deviations or medians with interquartile ranges, depending on distribution. Group comparisons utilized independent t-tests or Mann-Whitney U tests for continuous variables, whereas categorical data were analyzed using chi-square tests or Fisher's exact tests. Statistical significance was defined as a two-sided p-value below 0.05. The Institutional Ethics Committee provided approval for this research.

RESULTS

Table 1: Baseline Characteristics After Matching

Variable	Thiamine Group (n=86)	Non-Thiamine Group (n=86)	p-value
Age (years)	62.1 ± 13.4	63.5 ± 14.1	0.54
Male Gender (%)	61.6%	59.3%	0.74
Diabetes Mellitus (%)	39.5%	40.7%	0.86
Chronic Kidney Disease (%)	17.4%	18.6%	0.80
Baseline SOFA Score	9.1 ± 2.8	9.3 ± 2.7	0.58
Admission Lactate (mmol/L)	4.6 ± 1.9	4.7 ± 2.1	0.67
Mechanical Ventilation (%)	70.9%	73.3%	0.72

Table 2: Comparison of Clinical Outcomes Between Thiamine and Non-Thiamine Groups

Outcome Measure	Thiamine Group (n=86)	Non-Thiamine Group (n=86)	p-value
Lactate Clearance at 24 hours	38.0% (IQR: 28–52)	21.0% (IQR: 13–33)	0.014
SOFA Score Reduction (72 hrs)	3.2 ± 1.1	2.4 ± 1.3	0.027
Vasopressor-Free Days (7 days)	4 days (IQR: 2–6)	2 days (IQR: 1–5)	0.034
28-Day Mortality	28 deaths (32.6%)	39 deaths (45.3%)	0.048
ICU Length of Stay	9 days (IQR: 6–14)	10 days (IQR: 7–15)	0.44

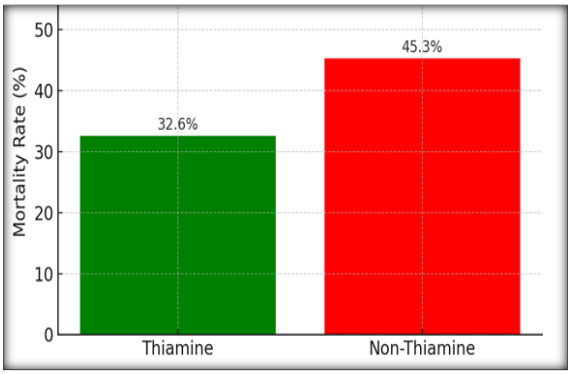

Figure 1: 28- day mortality

Following propensity score matching, both study groups (n=86 each) were well balanced in terms of baseline clinical characteristics. The mean age in the thiamine group was 62.1 ± 13.4 years compared to 63.5 ± 14.1 years in the controls (p = 0.54). 61.6% of thiamine cohort and 59.3% of controls were males (p = 0.74). The prevalence of diabetes mellitus was 39.5% and 40.7%, respectively (p = 0.86), and chronic kidney disease was observed in 17.4% and 18.6% (p = 0.80). Baseline SOFA scores were similar (9.1 ± 2.8 vs. 9.3 ± 2.7, p = 0.58), as were admission lactate levels (4.6 ± 1.9 mmol/L vs. 4.7 ± 2.1 mmol/L, p = 0.67), and the need for mechanical ventilation (70.9% vs. 73.3%, p = 0.72). These non-significant p-values confirm successful matching and comparability between the groups.

A significant improvement in lactate clearance was observed in the thiamine group, with a median clearance of 38.0% (IQR: 28–52) versus 21.0% (IQR: 13–33) in the non-thiamine group (p = 0.014). This suggests that thiamine supplementation may support more efficient lactate metabolism and enhanced cellular oxygen utilization. Additionally, patients receiving thiamine experienced greater reductions in SOFA scores over 72 hours (3.2 ± 1.1 vs. 2.4 ± 1.3, p = 0.027), indicating more rapid resolution of organ dysfunction.

Vasopressor dependency was also reduced, with the thiamine group having a higher median number of vasopressor-free days within the first week: 4 days (IQR: 2–6) compared to 2 days (IQR: 1–5) in the control group (p = 0.034). This earlier hemodynamic recovery may reflect better mitochondrial support and cardiovascular stability achieved through thiamine administration.

The thiamine cohort had a significantly lower mortality rate at 28 days (n = 28; 32.6%) compared to 45.3% (39 deaths) in the controls (p = 0.048), highlighting a potentially meaningful survival benefit. While the median ICU length of stay was slightly shorter in the thiamine group—9 days (IQR: 6–14) versus 10 days (IQR: 7–15)—this difference was not statistically significant (p = 0.44), suggesting that while recovery may begin earlier, other factors influence ICU discharge timing.

DISCUSSION

The present study found that thiamine supplementation in patients with sepsis and septic shock was associated with improved metabolic and clinical outcomes, including enhanced lactate clearance, greater organ function recovery, fewer vasopressor days, and reduced 28-day mortality.

Lactate clearance is a widely used surrogate marker for effective resuscitation and tissue perfusion in sepsis. In this study, patients who received thiamine achieved significantly greater lactate clearance at 24 hours (38.0% vs. 21.0%; p = 0.014), reflecting improved oxidative metabolism. This observation is consistent with a randomized trial by Donnino et al., where thiamine administration led to faster lactate normalization in thiamine-deficient patients with septic shock.[6] Although baseline thiamine levels were not measured in our cohort, the observed effect suggests that empiric supplementation may benefit a broader population, including those with undiagnosed subclinical deficiency.

Improved lactate metabolism in the thiamine group was paralleled by a more substantial reduction in SOFA scores over 72 hours (3.2 vs. 2.4; p = 0.027), indicating earlier resolution of organ dysfunction. Woolum et al. similarly reported reductions in SOFA scores among thiamine-treated patients, supporting the role of thiamine in enhancing mitochondrial function and cellular recovery.[7] Moreover, patients receiving thiamine in our study had more vasopressor-free days (median 4 vs. 2; p = 0.034), suggesting earlier hemodynamic stabilization. This benefit has also been observed in previous studies examining vitamin-based resuscitation protocols.[10]

The observed reduction in 28-day mortality (32.6% vs. 45.3%; p = 0.048) is both statistically and clinically significant. While some trials, such as ACTS,[8] and VICTAS,[9] failed to demonstrate a mortality benefit with combination therapy involving thiamine, vitamin C, and corticosteroids, it is possible that the benefits of thiamine may be masked when used in complex regimens or when administered late. In contrast, our study supports early administration of thiamine alone as an independent intervention capable of improving survival. Notably, mortality in the thiamine arm of our study was comparable to that reported by Woolum et al. (32.6% vs. 22%),[7] though differences in baseline severity and inclusion criteria may account for variation.

Interestingly, the length of ICU stay did not differ significantly between groups (9 vs. 10 days; p = 0.44), suggesting that while thiamine may accelerate organ recovery and reduce mortality, it does not necessarily shorten ICU stay. Factors such as rehabilitation needs, ventilator weaning protocols, and non-clinical discharge delays may explain this discrepancy.

CONCLUSION

The findings of this matched cohort study indicate that early intravenous thiamine administration in patients diagnosed with sepsis or septic shock is linked with significant clinical and metabolic improvements. Notably, it enhanced lactate clearance, promoted quicker organ function recovery, increased vasopressor-free days, and reduced 28-day mortality. These advantages were achieved without a statistically significant reduction in ICU stay duration, suggesting that thiamine primarily supports early physiological recovery rather than discharge timing. Given its safety, affordability, and mechanistic rationale, thiamine appears to be a valuable adjunct in sepsis management. Larger-scale prospective trials are recommended to confirm these outcomes and to better define the patient populations that may benefit most.

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Conflicts of Interest: None declared by the authors.

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