Adjunctive Effects of Vitamin C and Thiamine on Inflammation, Oxidative Stress, and Clinical Outcomes in Sepsis

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Abstract

Sepsis is a leading cause of morbidity, mortality, and healthcare burden worldwide, with limited targeted therapies beyond standard supportive care. Current management strategies focus primarily on controlling infection and achieving hemodynamic stabilization but often fail to address the pathophysiological processes of inflammation, oxidative stress, and microvascular injury. Vitamin C (ascorbic acid) is a potential antioxidant and immunomodulator that has gained attention as an adjunctive therapy due to its role in reducing oxidative damage, regulating inflammatory responses, and supporting catecholamine synthesis. In addition, the synergistic combination of vitamin C and thiamine has been proposed to enhance cellular metabolism and provide organ protection in critically ill patients. In this study, we investigated the effects of vitamin C, both alone and in combination with thiamine, on clinical outcomes and biochemical markers in patients with sepsis. Our findings provide new insights into the potential role of vitamin supplementation in modulating disease progression and improving prognosis, highlighting its possible integration into sepsis management strategies.

Keywords: Sepsis; Vitamin C; Thiamine; Oxidative Stress; Adjunctive Therapy

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Introduction

Sepsis is a major global health challenge and is responsible for approximately 25%–30% of hospital mortality. In the United States alone, the burden of sepsis not only translates into high morbidity and mortality but also generates enormous healthcare costs, with annual expenditures exceeding twenty million dollars. Despite its prevalence and severity, effective targeted therapies remain limited, and management largely depends on supportive strategies [1, 2].

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection. It is a condition in which the body's defense mechanisms spiral into a damaging cascade that can lead to multi-organ failure and death [3, 4]. Current treatment protocols do not directly address the underlying pathophysiology of sepsis. Instead, clinical management emphasizes early recognition and rapid initiation of broad-spectrum antibiotics, intravenous fluids, and vasopressors when indicated. The therapeutic framework is thus centered on stabilizing hemodynamics, eradicating the source of infection, and preventing progression to septic shock. However, even when these measures succeed in restoring perfusion and maintaining adequate cardiac output, patients with severe sepsis often die from ongoing organ dysfunction [5, 6]. Emerging evidence suggests that mortality in septic shock is frequently linked to microvascular injury and dysregulation driven by overwhelming inflammation [7]. Current standard treatments, however, fail to target the inflammatory and oxidative stress pathways central to the disease process. In fact, some therapies may inadvertently exacerbate tissue damage. For instance, the bactericidal effects of antibiotics can intensify inflammatory responses by releasing bacterial

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toxins. This reality underscores an urgent need for novel adjunctive therapies aimed at modulating inflammation and oxidative stress, in addition to standard care.

Among the candidates for adjunctive therapy, ascorbic acid (vitamin C) has attracted growing attention. Vitamin C plays multiple physiological roles, as it is a potent antioxidant, an anti-inflammatory agent, and an immune-modulating compound [8]. Beyond these properties, it functions as a cofactor in the synthesis of endogenous catecholamines and vasopressin, and enhances adrenergic receptor activity, all of which are critical in the management of septic shock. Importantly, studies have shown that nearly 90% of patients with septic shock suffer from hypovitaminosis C, while approximately 40% exhibit outright deficiency—rates significantly higher than those observed in patients with non-septic critical illness [9]. These findings have led to the hypothesis that vitamin C supplementation may serve as a safe, inexpensive, and effective adjunctive treatment for sepsis by mitigating oxidative stress and dampening the overwhelming inflammatory response [10, 11]. In addition, there is growing interest in combining vitamin C with other supportive agents, such as thiamine (vitamin B1), given its synergistic effects on cellular metabolism and oxidative stress pathways.

The present study builds upon this hypothesis by investigating the impact of vitamin C, alone or in combination with thiamine, on inflammation, oxidative stress, and cellular function in patients with sepsis. By evaluating clinical outcomes alongside biochemical markers, this research seeks to clarify whether these vitamins can improve prognosis in critically ill septic patients. The results may provide valuable insights for refining therapeutic protocols and advancing supportive care in intensive care settings, potentially reshaping the future management of sepsis.

Methods

This study was designed as a randomized, single-blind, placebo-controlled clinical trial at Shariati Hospital, Tehran, Iran. It was conducted during the period 2023–2024. The trial protocol was approved by the Ethics Committee of Tehran University of Medical Sciences under the ethics code IR.TUMS.SHARIATI.REC.1402.272.

Study Objectives

This study aims to investigate whether high-dose adjunctive administration of vitamin C and vitamin B-complex can influence clinical outcomes, specifically changes in SOFA score and mortality, in critically ill patients admitted to the ICU with a diagnosis of sepsis or septic shock..

Inclusion and Exclusion Criteria

Patients enrolled in this study were adults (≥18 years of age) with an initial diagnosis of sepsis or septic shock, based on the Sepsis-3 definition outlined in the 2016 Surviving Sepsis Campaign guidelines [12].

Inclusion Criteria

The inclusion criteria for this study were the diagnosis of sepsis or septic shock within the first 12 hours of ICU admission. Also, the study was according to 3-hour sepsis bundle recommendations.

Exclusion Criteria

Patients were excluded from the study if they were under 18 years of age, pregnant, suffering from end-stage diseases such as stage IV cancer or advanced heart failure, in need of emergency surgery, HIV-positive with a CD4 count below 50, or known to have glucose-6-phosphate dehydrogenase (G6PD) deficiency. Table 1 presents a comparison of established definitions, the Sepsis-3 definition, and the Surviving Sepsis Campaign (SSC) guidelines for sepsis and septic shock [12].

Sample size calculation

According to a study by Iglesias et al., the mean duration of vasopressor use in the intervention and control groups was 27 ± 22 hours and 53 ± 38 hours, respectively. Using G*Power software version 3.1.9.4, and considering a significance level of 5%, a power of 90%, and an anticipated dropout rate of 31%, the required sample size was calculated to be 90 patients (45 in each group) [13].

Intervention

A total of 90 patients were enrolled in the study and allocated equally into two groups. One patient in the intervention group was excluded following a diagnosis of advanced cancer during treatment. Therefore, 44 patients remained in the intervention group and 45 patients in the control group.

Patients were randomly assigned to either the intervention or control group using block randomization with a block size of six. The intervention group received vitamin C at a dose of 2000 mg every 8 hours, along with two ampoules of vitamin B-complex every 8 hours. The control

Table 1: Comparison of established definition, sepsis-3 definition, and SSC guidelines [12].

	Established Definition (used by CMS)	**Sepsis-3 definitions**	**SSC guidelines**
Sepsis	Presumed/known infection+≥2 systemic inflammatory response syndrome criteria	Includes: hypotension + normal lactate (shock)	Sepsis = severe sepsis
Sever Sepsis	Sepsis + end organ dysfunction, lactate >4 mmol/L	Not a category	established severe sepsis definition
Septic Shock	Sepsis + refractory hypotension (± lactate)	Vasopressors and lactate >2 mmol/L	Sepsis + refractory hypotension (± lactate)
Mortality Ratio: $\frac{Observed\ Mortalit}{Expected\ Mortality}$	Sepsis= low acuity $\frac{Observed\ Mortality\ low}{Expected\ Mortality\ low}$	Sepsis= higher acuity $\frac{Observed\ Mortality\ higher}{Expected\ Mortality\ low}$	-

Table 2: Sequential Organ Failure Assessment Score

Variables	**SOFA score**				
	0	1	2	3	4
Respiratory	PaO_2/FiO_2: > 400 SpO_2/FiO_2: > 302	PaO_2/FiO_2: < 400 SpO_2/FiO_2: < 302	PaO_2/FiO_2: < 300 SpO_2/FiO_2: < 221	PaO_2/FiO_2: < 300 SpO_2/FiO_2: < 142	PaO_2/FiO_2: < 100 SpO_2/FiO_2: < 67
Cardiovascular (doses in mcg/kg/min)	MAP ≥ 70 mm Hg	MAP ≥ 70 mm Hg	Dopamine ≤ 5 or ANY dobutamine	Dopamine > 5 Norepinephrine ≤ 0.1 Phenylephrine ≤ 0.8	Dopamine > 15 or Norepinephrine > 0.1 Phenylephrine > 0.8
Liver (bilirubin, mg/dL)	< 1.2	1.2-1.9	2.5-5.9	6.0-11.9	> 12
Renal (creatinine, me/dL)	< 1.2	1.2-1.9	2.0-3.4	3.5-4.9	>5.0
Coagulation (platelets × 10^3 /mm^3)	≥ 150	< 150	< 100	< 50	< 20
Neurological (GCS score)	15	13-14	10-12	6-9	<6

group received normal saline as a placebo at equivalent dosing intervals. The therapeutic regimen was administered for a maximum duration of four days.

No modifications were made to corticosteroid therapy as part of the study protocol. Patients who were already receiving corticosteroids as part of their standard treatment continued their regimen without alteration.

Study Procedure

Patients were evaluated at four predetermined time points. Baseline demographic and clinical information were recorded, and all required laboratory tests were performed prior to initiation of the intervention. Following the start of treatment, patient data and laboratory results were collected at 24, 48, 72, and 96 hours after initiation.

All interventions conducted in this study adhered to the principles of the Declaration of Helsinki (1964). Patient confidentiality was strictly maintained; no personal identifiers were recorded in the study database, and data collection was performed using coded identifiers only.

Outcome Assessment

The primary outcomes of the study were the resolution of septic shock and changes in the SOFA score. Resolution of shock was defined as the time from initiation of treatment until the discontinuation of all vasopressor support. Changes in SOFA score were defined as the difference between the baseline SOFA score and the score recorded on day 4, which was considered the maximum duration of therapy according to the study protocol.

SOFA scores were calculated daily, starting from the first day of ICU admission, using the same methodology for all patients. In cases where patients were discharged or died before day 4, the last available SOFA score was carried forward and used for the subsequent days. For patients in whom the PaO_2/FiO_2 ratio was not available for SOFA calculation, the SpO_2/FiO_2 ratio was used as a surrogate measure.

Table 1 outlines the SOFA score, which assesses the extent of organ dysfunction in critically ill patients across respiratory, cardiovascular, hepatic, renal, coagulation, and neurologic systems. Higher SOFA scores are associated with increased mortality risk, and an increase above baseline in the presence of infection indicates sepsis (Table 2).

Table 3: Frequency of patients in each study group

Study Group	Number of Patients
Intervention Group	44
Control (Placebo) Group	45

Table 4: Comparison of Demographic Factors of Patients in the Intervention and Control Groups

Demographic Factors	Intervention Group	Placebo Group	P-value
Age	65.1 ± 13.64	63.7 ± 13.18	0.6
Weight	74.2 ± 13.27	72.1 ± 14.10	0.9
Sexuality	Male 21 (47.7%)	Male 19 (42.2%)	0.3

Table 5: Comparison of comorbidities between patients in the intervention and control groups

Comorbidities	Intervention Group	Control Group	P-value	Comorbidities	Intervention Group	Control Group	P-value
Cirrhosis	0	1 (2.2%)	1.0	CAD or IHD	17 (38.6%)	14 (31.1%)	0.5
ESRD	4 (9.1%)	1 (2.2%)	0.1	HF	12 (27.3%)	9 (20.0%)	0.2
CKD	7 (15.9 %)	4 (8.9%)	0.2	DM	16 (36.4 %)	2 (44.4%)	0.2
Morbid Obesity	5 (11.4 %)	8 (17.8%)	0.5	Dementia or Alzheimer	4 (9.1%)	3 (6.7 %)	0.7
Immunocompromised	2. (9.1%)	3 (6.7%)	0.4	COPD	15 (34.1 %)	12 (26.7 %)	0.4
Malignancy	17 (38.6%)	14 (31.1%)	0.3	-	-	-	-

Secondary Outcomes

Secondary outcomes of this study were ICU mortality, vasopressor use, and acute kidney injury (AKI). ICU mortality was determined based on whether patients survived until discharge from the ICU and hospital. Vasopressor use was evaluated by recording whether patients were receiving vasopressors at study entry, whether additional vasopressors were required during the study, and the total duration of vasopressor therapy. AKI was defined according to established guidelines as an increase in serum creatinine greater than 0.3 mg/dl, an increase of more than 1.5 times the baseline level, or the need for renal replacement therapy (RRT). Based on these criteria, both changes in serum creatinine and the requirement for RRT were assessed for all patients.

Statistical Analysis

All statistical analyses and graphical representations were performed using SPSS software, version 27. Continuous variables were compared between the two groups at each time point using the independent Student's *t*-test. Repeated-measures ANOVA was applied to evaluate changes over time between the groups. Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate. A *p*-value of less than 0.05 was considered statistically significant in all analyses.

Results

In this study, patients were divided into two groups, with 45 patients initially assigned to each group based on the sample size calculation. In the intervention group, one patient was excluded following a later diagnosis of advanced cancer, resulting in 44 patients in the intervention group and 45 patients in the control group. The distribution of patients in each group is presented in Table 3.

The demographic characteristics of patients in both the intervention and control groups are presented in Table 4. According to Table 4, there were no statistically significant differences in demographic characteristics between the treatment and placebo groups ($p > 0.05$). This finding indicates successful randomization in the allocation of participants between the two groups.

The distribution of comorbidities—including cirrhosis, ESRD, CKD, morbid obesity, immunocompromised status, CAD/IHD, heart failure, diabetes mellitus, dementia or Alzheimer's disease, COPD, and malignancy—was compared between the intervention and control groups (Table 5).

At baseline, there were no significant differences in major clinical conditions between the two groups. The proportions of patients requiring mechanical ventilation, receiving vasopressor therapy, or presenting with AKI were comparable between the intervention and control groups (Table 6).

In (Table 7), the comparison of serum creatinine levels between the intervention and placebo groups at baseline and during the first four days of treatment is presented.

Table 8 summarizes the comparison of AKI status at baseline and the subsequent need for renal replacement therapy (RRT) between the intervention

Table 6: Comparison of baseline clinical conditions between patients in the intervention and control groups.

Clinical Condition	Intervention Group	Control Group	P-value
Mechanical Ventilation	19 (43.2%)	23 (51.1%)	0.2
On Vasopressor Therapy	32 (72.7 %)	30 (66.7%)	0.3
AKI	28 (63.6%)	26 (57.8 %)	0.3

Table 7: Comparison of serum creatinine levels between the intervention and placebo groups

Time Point	Intervention Group (Mean ± SD)	Placebo Group (Mean ± SD)	P-value
Creatinine at baseline	0.95 ± 2.07	1.23 ± 1.97	0.3
Creatinine day 1	1.12 ± 1.68	1.07 ± 1.83	0.2
Creatinine day 2	1.09 ± 1.56	0.89 ± 1.70	0.4
Creatinine day 3	1.18 ± 1.71	0.92 ± 1.78	0.4
Creatinine day4	1.02 ± 1.65	0.96 ± 1.79	0.6

Table 8: Comparison of AKI status and need for RRT between the intervention and placebo groups

Parameter	Intervention group	Placebo group	P-value
AKI at baseline	28 (63.6%)	26 (57.8%)	0.3
Need for RRT after enrollment	5 (11.4%)	6 (13.4%)	0.2

Table 9: Comparison of lactate levels between the intervention and placebo groups at baseline and during follow-up

Parameter	Intervention group (Mean ± SD)	Placebo group (Mean ± SD)	P-value
Lactate at baseline	1.39 ± 3.38	1.20 ± 3.12	0.4
Lactate day 1	1.17 ± 2.61	1.08 ± 2.96	00.1
Lactate day 2	1.14 ± 2.45	1.21 ± 2.78	0.1
Lactate day 3	1.43 ± 2.48	1.03 ± 2.84	0.2
Lactate day 4	1.26 ± 2.71	0.95 ± 3.07	0.1

Table 10: Comparison of vasopressor therapy between intervention and placebo groups

	Intervention Group	Placebo Group	P-value
Vasopressor therapy at baseline	32 (72.7%)	30 (66.7%)	0.3
Vasopressor therapy after study enrollment	3 (6.8 %)	7 (15.6 %)	0.03
Vasopressor therapy duration (hours)	19.09 ± 35.6	22.7 ± 48.5	0.007

Table 11: comparison of SOFA scores between the intervention and placebo groups from baseline through day 4

	Intervention group (Mean ± SD)	Placebo group (Mean ± SD)	P-value
SOFA score at baseline	2.39 ± 8.21	2.48 ± 7.93	0.3
SOFA score day 1	2.23 ± 7.05	2.25 ± 7.17	0.6
SOFA score day 2	2.24 ± 638	2.32 ± 6.46	0.7
SOFA score day 3	2.21 ± 4.91	1.92 ± 5.73	0.08
SOFA score day 4	2.28 ± 4.61	2.71 ± 5.84	0.01

and placebo groups. No statistically significant differences were observed between the two groups.

Table 9 presents the comparison of serum lactate levels between the intervention and placebo groups at baseline and during the first four days of follow-up. Although lactate levels demonstrated a decreasing trend in both groups, no statistically significant differences were observed.

Table 10 presents the comparison of vasopressor therapy between the intervention and placebo groups. The table outlines the proportion of patients receiving vasopressors at baseline, the need for vasopressors after study enrollment, and the overall duration of vasopressor therapy.

Table 11 presents the comparison of SOFA scores between the intervention and placebo groups from baseline through day 4. The table reports the mean values and standard deviations for each time point, along with the corresponding *p*-values.

Figure 1 illustrates the trend of SOFA scores in the intervention and control groups over a 96-hour period. Both groups demonstrated a gradual decline

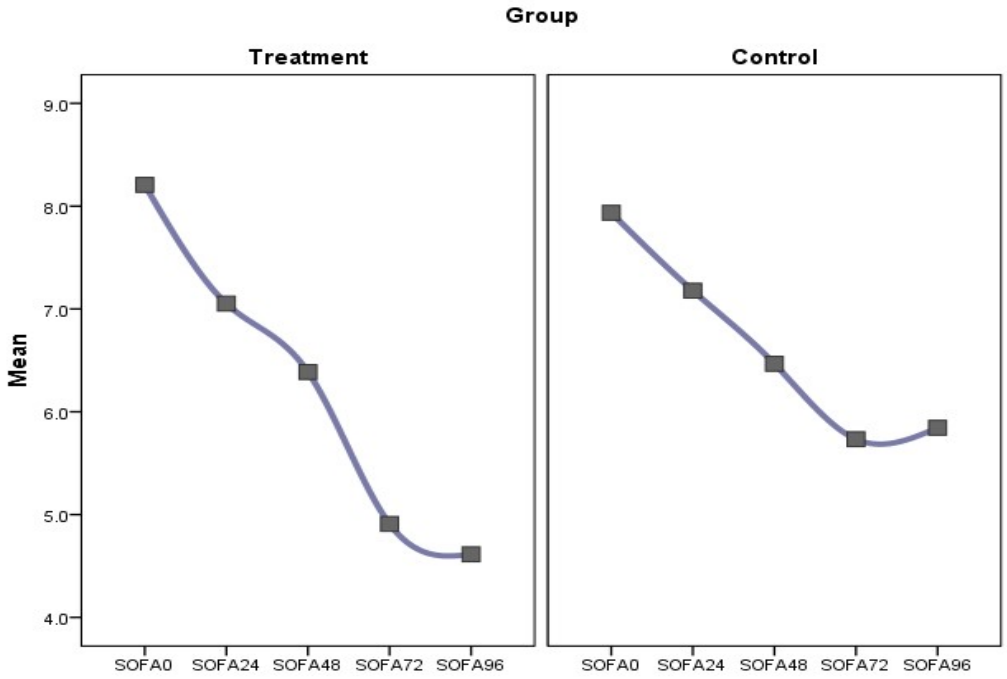

Figure 1: SOFA score trends in control and comparison groups.

Table 12: comparison between alive discharge rates from ICU and hospital

	Intervention group	Placebo group	P-value
Alive discharge from ICU	18 (40.9%)	12 (26.6%)	0.09
Alive discharge from hospital	13 (29.5%)	8 (17.8%)	0.12

in SOFA scores; however, the reduction was more pronounced in the intervention group by day 4.

The table below (Table 12) presents data on alive discharge rates from the ICU and hospital, comparing two groups with associated p-values of 0.09 and 0.12, respectively. These values suggest no statistically significant difference between the groups in both scenarios. This information highlights the outcomes of patient care across different settings.

Effect of The Intervention on Vasopressor Use

Based on the study findings, after initiation of the treatment, the number of patients requiring vasopressor therapy was significantly lower in the intervention group compared to the control group. In addition, the mean duration of vasopressor administration was also reduced significantly in the intervention group relative to controls.

It should be noted that a number of patients, independent of the study protocol, received corticosteroids during their treatment course. To determine whether the observed results were independent of corticosteroid use, an ANCOVA analysis was performed. In this analysis, corticosteroid administration was considered a covariate, and the outcome variable was defined as the time to discontinuation of vasopressors. The results demonstrated that the study intervention remained a statistically significant factor in reducing vasopressor requirements, even after adjusting for corticosteroid use (P-value = 0.001).

Discussion

Interpretation of Findings on Vasopressor Use

The findings of the present study indicate that high-dose vitamin C and vitamin B-complex, as an adjunctive therapy, can significantly accelerate the resolution and recovery from septic shock. This observation is consistent with results from other comprehensive studies, where ascorbic acid in combination with corticosteroids has also been shown to exert beneficial effects in improving inflammatory and infectious conditions associated with sepsis. Importantly, both the current study and prior investigations suggest that the positive therapeutic

impact of high-dose vitamin supplementation is evident even when considered independently of hydrocortisone administration. This supports the role of vitamins as a meaningful adjunctive treatment strategy to enhance recovery in patients with sepsis [14, 15].

However, not all studies have reported similar outcomes. For instance, Fujii et al. found that treatment with vitamin C and vitamin B-complex combined with hydrocortisone, compared to hydrocortisone alone, did not significantly improve survival, reduce mortality, or decrease vasopressor requirements. Their statistical analyses, both with and without adjustment for hydrocortisone use, consistently demonstrated no clear benefit in accelerating the resolution of septic shock. Consequently, they concluded that this therapeutic approach was ineffective in enhancing shock recovery [16].

Differences in vasopressor outcomes across studies

Several factors may explain the heterogeneity observed in outcomes related to vasopressor use across different studies. One important consideration is the geographic and demographic context. Positive results have been more frequently reported in East Asian and North American populations (predominantly in cohorts with a higher proportion of Caucasian patients), while studies from Western Europe and New Zealand have more commonly reported neutral or negative findings [17, 18].

Another relevant factor is the type and source of sepsis. Studies demonstrating beneficial outcomes were largely conducted in populations with pulmonary-origin sepsis, particularly pneumonia, whereas trials reporting negative or inconclusive results tended to include higher proportions of gastrointestinal or bloodstream infections.

Taken together, when integrating the findings of previous studies with the present results, it can be suggested that high-dose vitamin C and vitamin B-complex therapy may accelerate the trajectory of recovery from sepsis and reduce vasopressor requirements. However, its ultimate impact on sepsis resolution and overall mortality remains uncertain and, in some cases, ineffective. These observations underscore the need for additional supportive interventions beyond corticosteroid use in order to optimize patient outcomes.

SOFA Score outcomes

In our study, patients who received the intervention showed a clear and significant reduction in SOFA scores by the fourth day compared to the placebo group. This means that the treatment appeared to slow the progression of organ failure and supported faster recovery. Our findings are consistent with earlier work by Marik et al. and Fowler et al., who also reported that early use of vitamin C with thiamine helped prevent organ dysfunction, especially kidney failure, and was linked to lower mortality in sepsis and septic shock [19, 20].

On the other hand, the study by Iglesias et al. did not show the same benefit. In their trial, vitamin C and thiamine did not significantly improve SOFA scores, which contrasts with what we and others have observed [13].

One possible reason for these differences could be the baseline levels of vitamin C deficiency in the patients. Iglesias and colleagues reported average levels around 21 μmol/L, while in the Marik and Fowler studies the levels were lower (15 and 17 μmol/L, respectively). We did not measure vitamin C levels in our patients, so it is difficult to determine exactly how much this factor influenced our outcomes. Still, it seems reasonable to assume that patients with more severe deficiency might respond better to supplementation.

Overall, these findings suggest that high-dose vitamin C and thiamine may work best when started early and in patients who have not yet reached advanced stages of organ failure. In such cases, the treatment could make a meaningful difference in improving SOFA scores and supporting recovery.

Mortality outcomes

According to the results of our study, there was no clear or statistically significant difference in mortality rates between the intervention and control groups. This finding is consistent with previous studies, which also did not report a meaningful reduction in mortality with the use of this treatment protocol.

Although the intervention group showed a higher proportion of patients discharged alive, this observation cannot be considered strong evidence on its own, and caution is required when interpreting it. One of the main limitations underlying this outcome is the relatively small and homogeneous study population, which reduces the ability to detect differences in hospital mortality and in the length of stay.

Conclusion of Findings

Based on the findings of the present study and their comparison with previous reports, treatment with high-dose vitamin C and vitamin B-complex appeared to reduce the need for vasopressors and to slow the progression of organ dysfunction, thereby supporting a more favorable trajectory toward reversal

of septic shock.

However, given the lack of significant improvement in mortality outcomes, tissue perfusion parameters, and direct effects on SOFA scores, it can be concluded that this therapeutic approach may require integration with other treatment strategies in order to achieve more consistent and clinically meaningful benefits.

In addition, the absence of a protective effect against AKI or the need for RRT highlights the need for targeted strategies to address renal complications in patients with sepsis. At the same time, caution should be maintained regarding the potential risks of high-dose vitamin C administration, emphasizing the importance of further evaluation of both efficacy and safety in larger, well-designed trials.

Limitations and Future Directions

One of the key limitations of this study was that the exact plasma concentrations of ascorbic acid were not measured. This assessment is not routinely performed in most clinical settings and would typically require a dedicated research protocol separate from standard therapeutic practice. Based on the dosing regimen applied, it is unlikely that toxic levels of vitamin C were reached. However, precise monitoring of plasma levels would provide a more comprehensive understanding of both safety and therapeutic efficacy.

Another limitation was the heterogeneity of treatment strategies in critically ill patients with sepsis. Variations in corticosteroid administration, use of different potencies, and additional invasive interventions for diagnosis and treatment may have influenced inflammatory responses and patient outcomes. Although statistical techniques were used to adjust for these confounding factors, complete elimination of their impact was not possible. Furthermore, additional clinical data were collected during the study, including microbiological cultures, antibiotic use, surgical interventions, ventilator management, and nutritional support with electrolyte monitoring. These parameters were beyond the scope of the present analysis but will be explored in future publications.

Future prospective trials should incorporate baseline assessment of thiamine and ascorbic acid deficiencies, as well as serial plasma measurements following intravenous administration, to better define the therapeutic impact of these vitamins. Larger sample sizes and multicenter designs, particularly those involving both academic and non-academic institutions, would also enhance the generalizability and robustness of findings, ultimately supporting stronger evidence to guide clinical practice.

Conclusion

The presented study reinforces the growing evidence that adjunctive vitamin therapy, particularly with vitamin C and its combination with thiamine, may offer physiological benefits in the management of sepsis. While our results suggest favorable effects on inflammatory modulation, oxidative stress reduction, and hemodynamic support, no definitive mortality benefit was observed. These findings emphasize the need for larger, multicenter randomized controlled trials to validate efficacy and determine optimal therapeutic regimens. Nevertheless, vitamin C-based interventions represent a promising, safe, and cost-effective strategy that could complement existing supportive therapies and contribute to improved outcomes in critically ill septic patients.

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Data Availability

All data produced in this work are included in the current study.

Abbreviations

GSC: Glasgow coma scale
FiO_2: Fraction of inspired oxygen
MAP: Mean arterial pressure
PaO_2: arterial oxygen pressure
SOFA: sequential organ failure (score)
SpO_2: oxygen saturation
AKI: acute kidney injury

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