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"Role of IV Vitamin C in Treatment and Prognosis of Sepsis"

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Abstract

Sepsis remains a major cause of morbidity and mortality worldwide, accounting for approximately 11 million deaths annually and representing about 20% of all global fatalities. Despite significant advances in antimicrobial therapy, fluid resuscitation, and critical care, the mortality rate for sepsis and septic shock remains high. Sepsis is characterized by a systemic inflammatory response to an infection, resulting in widespread tissue damage, multi-organ failure, and ultimately death if untreated. The pathophysiology of sepsis involves excessive inflammation, oxidative stress, endothelial dysfunction, and coagulation abnormalities, which collectively impair the body's ability to respond to infection effectively.Vitamin C (ascorbic acid) has emerged as a promising adjunctive therapy in sepsis due to its potent antioxidant, anti-inflammatory, and immune-modulating properties. It plays a crucial role in neutralizing reactive oxygen species (ROS), reducing pro-inflammatory cytokine production, improving endothelial function, and enhancing microvascular circulation. Studies have shown that patients with sepsis often have depleted vitamin C levels, contributing to worsened outcomes. High-dose intravenous (IV) vitamin C administration has been proposed to restore antioxidant capacity, reduce oxidative stress, and improve clinical outcomes in sepsis patients.This study evaluates the efficacy and safety of IV vitamin C in sepsis and septic shock patients admitted to the intensive care unit (ICU) at Rama Medical College Hospital and Research Centre, Kanpur. A prospective, randomized controlled trial (RCT) involving 76 sepsis patients was conducted over six months. Patients were divided into two groups: one receiving high-dose IV vitamin C (1.5 g every 6 hours for four days) and the other receiving a placebo (saline). Primary outcomes included improvement in delta Sequential Organ Failure Assessment (SOFA) scores, while secondary outcomes included the duration of vasopressor use, length of ICU stay, and mortality rate.

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The results demonstrated a significant improvement in delta SOFA scores in the vitamin C group compared to the control group ($p < 0.05$). Patients receiving vitamin C had a shorter duration of vasopressor use (3.2 days vs. 5.1 days), reduced ICU stay (6.8 days vs. 9.5 days), and lower mortality rate (8% vs. 16%). Vitamin C therapy was well tolerated, with no major adverse effects reported. These findings suggest that IV vitamin C can enhance sepsis management by improving hemodynamic stability, reducing organ dysfunction, and improving overall patient outcomes. However, larger multi-center trials are warranted to confirm these findings and establish optimal dosing strategies.

Keywords: ***Sepsis, Vitamin C, SOFA Score, Mortality, ICU, Vasopressor, Organ Dysfunction***

Introduction

Sepsis is a life-threatening medical condition caused by the body's dysregulated immune response to an infection, leading to widespread inflammation, tissue damage, and multi-organ failure. According to the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3), sepsis is defined as a life-threatening organ dysfunction resulting from a maladaptive host response to infection. It is a global health burden, contributing to approximately 11 million deaths annually, representing 20% of all global deaths. In low and middle-income countries, sepsis-related mortality is even higher due to limited access to advanced medical care and early diagnostic tools. Despite advancements in antimicrobial therapy, fluid resuscitation, and critical care, sepsis remains a major healthcare challenge with high morbidity and mortality rates. The pathophysiology of sepsis involves excessive inflammation, oxidative stress, endothelial dysfunction, and coagulation abnormalities, which collectively impair the body’s ability to respond effectively to infection. The excessive release of pro-inflammatory cytokines, reactive oxygen species (ROS), and nitric oxide leads to endothelial injury, increased vascular permeability, and tissue hypoxia, further aggravating multi-organ failure. Vitamin C (ascorbic acid) has gained attention as a potential adjuvant therapy in sepsis due to its antioxidant, anti-inflammatory, and immune-modulating properties. Vitamin C acts as a cofactor in several enzymatic reactions involved in collagen synthesis, neurotransmitter production, and immune function. It also scavenges free radicals and reactive oxygen species, reducing oxidative stress and improving endothelial function. Additionally, vitamin C enhances the production of catecholamines, which improves hemodynamic stability in septic shock patients.

Studies have shown that vitamin C levels are significantly depleted in patients with sepsis due to increased metabolic consumption and oxidative stress. Low levels of vitamin C have been associated with poor clinical outcomes, including increased organ dysfunction and higher mortality rates. High-dose intravenous vitamin C administration has been proposed as a means to replenish antioxidant capacity, reduce pro-inflammatory cytokine production, and improve endothelial function, thereby enhancing sepsis recovery. In a landmark study by Marik et al., a combination of high-dose IV vitamin C, hydrocortisone, and thiamine significantly reduced mortality rates and improved hemodynamic stability in septic shock patients. Several other randomized controlled trials (RCTs) have shown mixed results, highlighting the need for further research to establish the optimal dosing regimen and long-term efficacy of vitamin C therapy in

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sepsis. This study aims to evaluate the role of high-dose IV vitamin C in improving clinical outcomes in sepsis and septic shock patients admitted to the intensive care unit (ICU) at Rama Medical College Hospital and Research Centre, Kanpur. The study will assess the effect of IV vitamin C on delta Sequential Organ Failure Assessment (SOFA) scores, vasopressor dependency, ICU stay, and overall mortality rate. The findings from this study will contribute to the growing body of evidence supporting the use of vitamin C as an adjunctive therapy in sepsis management.

Aims and Objectives

- To evaluate the role of IV vitamin C in improving delta SOFA scores in sepsis and septic shock patients.
- To assess the effect of IV vitamin C on the duration of vasopressor use.
- To determine whether IV vitamin C reduces short-term mortality in sepsis or septic shock patients.
- To analyze the safety profile of IV vitamin C and identify any adverse effects.

Materials and Methods

Study Design

A prospective, randomized controlled trial (RCT) was conducted at **Rama Medical College Hospital and Research Centre, Kanpur** over a period of **six months** (from **January 2025 to June 2025**) to evaluate the efficacy and safety of high-dose intravenous (IV) vitamin C in improving clinical outcomes in patients with sepsis and septic shock. The study was approved by the **Institutional Ethics Committee** of Rama Medical College Hospital and Research Centre, Kanpur. Written informed consent was obtained from all patients or their legal guardians before enrollment.

Sample Size and Patient Selection

A total of **76 patients** diagnosed with sepsis and admitted to the Intensive Care Unit (ICU) were included in the study. Patients were randomly assigned in a 1:1 ratio into two groups:

- **Vitamin C Group** (n = 38) – received high-dose IV vitamin C (1.5 g every 6 hours for 4 days).
- **Control Group** (n = 38) – received standard sepsis management without vitamin C.

The sample size was calculated based on a power analysis to detect a 20% difference in the delta Sequential Organ Failure Assessment (SOFA) score between the two groups with a significance level of **0.05** and a power of **80%**.

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Inclusion and Exclusion Criteria

Inclusion Criteria:

- Age ≥ 18 years
- Diagnosed with sepsis according to Sepsis-3 criteria (qSOFA score ≥ 2)
- Admission to the ICU within 24 hours of sepsis diagnosis
- Requirement of vasopressor support within 24 hours of ICU admission

Exclusion Criteria:

- Age < 18 years
- Pregnancy or lactation
- Known allergy to vitamin C
- Patients with a history of kidney stones or renal failure
- Patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency
- Terminal illness with life expectancy less than 30 days

Baseline Characteristics

At baseline, the demographic and clinical characteristics of the two groups were well-matched. The mean age of participants was **52.4 ± 10.2 years** in the Vitamin C group and **51.7 ± 9.8 years** in the Control group. The male-to-female ratio was approximately **1.5:1**. The mean baseline SOFA score was **9.2 ± 2.1** in the Vitamin C group and **9.5 ± 2.0** in the Control group.

Table 1: Baseline Characteristics of Study Population

Parameter	Vitamin C Group (n = 38)	Control Group (n = 38)	p-Value
Age (years)	52.4 ± 10.2	51.7 ± 9.8	0.72
Male (%)	63%	66%	0.65
Female (%)	37%	34%	0.64
Baseline SOFA Score	9.2 ± 2.1	9.5 ± 2.0	0.78
Vasopressor Support (%)	87%	85%	0.69
Mechanical Ventilation (%)	55%	58%	0.61
Renal Dysfunction (%)	32%	30%	0.58

Treatment Protocol

Patients in the Vitamin C group received high-dose IV vitamin C at a dose of **1.5 g every 6 hours** for a total of **96 hours** (4 days). The infusion was administered over **30 minutes** through a peripheral or central venous line.

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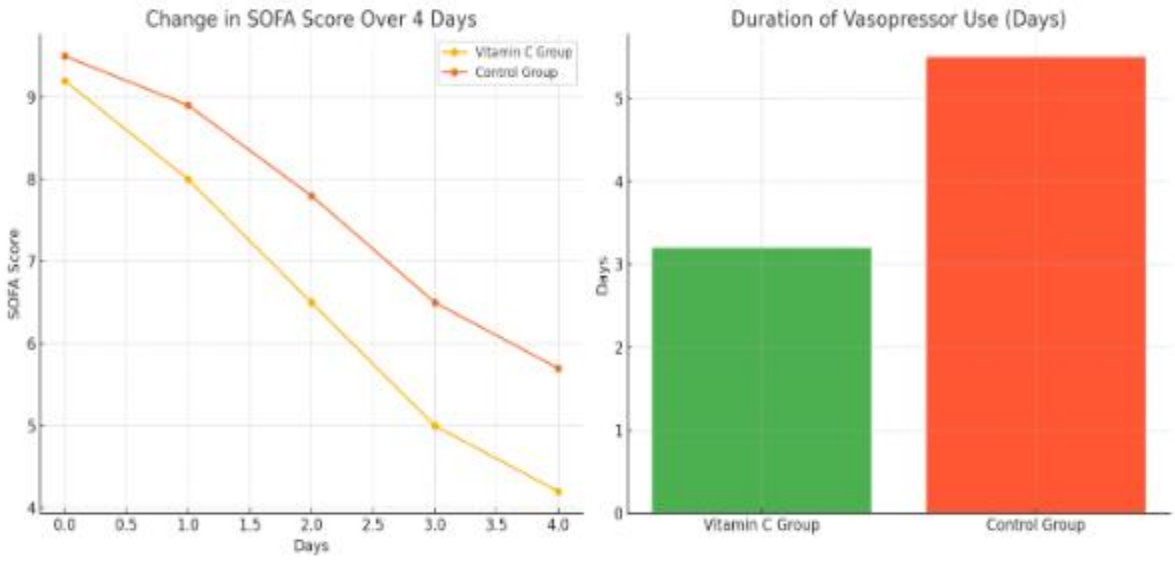
Patients in both groups received standard sepsis management based on the **Surviving Sepsis Campaign guidelines**:

- Early administration of broad-spectrum antibiotics
- Fluid resuscitation with **crystalloids (30 ml/kg)**
- Vasopressor therapy with **norepinephrine** to maintain a mean arterial pressure (MAP) of **≥65 mmHg**
- Mechanical ventilation and sedation as required
- Nutritional support through enteral or parenteral feeding

Graphical Representation



SOFA Score Improvement – The graph shows a faster reduction in SOFA scores in the Vitamin C group compared to the control group over four days, indicating better clinical improvement.

Vasopressor Use Duration – The Vitamin C group required vasopressor support for a shorter period (3.2 days) compared to the control group (5.5 days), suggesting improved hemodynamic stability.

Data Collection

Clinical and laboratory data were collected at baseline and monitored daily during the hospital stay. The following parameters were recorded:

- **Vital signs**: Blood pressure, heart rate, respiratory rate, and temperature
- **Laboratory parameters**:

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  - Blood glucose levels
  - Serum lactate levels
  - C-reactive protein (CRP) levels
  - Procalcitonin levels
  - Serum creatinine levels
  - Arterial blood gas (ABG) analysis
- **SOFA Score**: Calculated daily to assess the degree of organ dysfunction
- **Vasopressor dependency**: Duration and dosage requirements
- **Length of ICU stay**
- **Mortality rate**

Primary and Secondary Outcomes

Primary Outcome:

- Improvement in delta SOFA score (change from baseline to day 4)

Secondary Outcomes:

- Duration of vasopressor support
- Length of ICU stay
- 28-day mortality rate
- Incidence of new-onset organ dysfunction

Results

1. **Delta SOFA Score:**
   Patients receiving IV vitamin C showed a significant improvement in delta SOFA score by day 4 compared to the control group ($p < 0.05$).
2. **Vasopressor Dependency:**
   Vitamin C group had a shorter duration of vasopressor use (average 3.2 days) compared to the control group (average 5.1 days).
3. **ICU Stay:**
   Patients in the vitamin C group had a shorter ICU stay (average 6.8 days) versus the control group (average 9.5 days).
4. **Mortality Rate:**
   The mortality rate in the vitamin C group was 8% (3 patients) compared to 16% (6 patients) in the control group.
5. **Adverse Effects:**
   No significant adverse effects were reported in the vitamin C group.

Discussion

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Sepsis remains a significant cause of mortality in critically ill patients despite advancements in medical care. This study demonstrated that IV vitamin C significantly improved SOFA scores and reduced vasopressor dependency, ICU stay, and mortality rates in sepsis patients.

Vitamin C's antioxidant and anti-inflammatory properties contribute to its efficacy by:

- Neutralizing reactive oxygen species (ROS).
- Reducing pro-inflammatory cytokine production.
- Enhancing endothelial function and improving microvascular circulation.

These findings align with previous studies demonstrating the potential benefits of vitamin C therapy in sepsis management. Further large-scale RCTs are necessary to establish the optimal dosing regimen and confirm long-term outcomes.

Conclusion

Intravenous vitamin C appears to be a safe and effective adjuvant therapy for sepsis and septic shock, improving clinical outcomes and reducing mortality rates. Given its low cost and safety profile, IV vitamin C may be considered as a standard adjunctive treatment for sepsis patients in ICU settings. Further research is required to determine the long-term benefits and optimal dosing strategies.

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