

Appropriately Designed Studies are Needed before Thiamine and Vitamin C Plus Hydrocortisone are Judged Non-beneficial in Septic Shock

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Dear Editor,

We read with interest the article by Sharma et al. on a randomized controlled trial on the effect of vitamin C plus thiamine in addition to hydrocortisone during the first 96 hours in the intensive care unit in patients with sepsis.¹ Of the 86 patients included in the study, 70% in the control group ($n = 43$) and 58% in the intervention group ($n = 43$) died during their stay in the intensive care unit.¹ None of the primary and secondary endpoints were statistically significant.¹ The study concluded that a combination of vitamin C, hydrocortisone and thiamine had no additional benefit over hydrocortisone alone in patients with septic shock.¹ While excellent, the study also has limitations worth discussing.

The first point relates to the rationale for choosing the specific addition of vitamin C and thiamine to hydrocortisone.¹ A recent review of vitamin C administration in patients with septic shock found that most clinical trials failed to demonstrate a clinical effect of vitamin C administration in patients with sepsis and septic shock.² However, there is evidence that the administration of vitamin C in patients with sepsis due to pneumonia reduces the risk of developing acute respiratory distress syndrome (ARDS).³

The second point is that neither serum vitamin C levels nor serum thiamine levels were measured before patients were randomized to vitamin C and thiamine supplementation. Why would septic patients with normal serum vitamin C and normal thiamine levels benefit from supplementation of these vitamins if they have normal serum levels? Is it conceivable that mortality was higher in the control group than in the intervention cohort because the control group had reduced vitamin C or thiamine levels but was not supplemented?

The third point relates to the discrepancy between the statement in Table 1 that none of the patients in the treatment group or those receiving hydrocortisone alone had neurological disease and the statement that the central nervous system (CNS) was the primary organ from which sepsis originated in nine patients in the verum and control groups. This discrepancy should be resolved.

The fourth point relates to the statement in Table 1 that the heart was not the primary organ from which sepsis originated in either the verum-treated patients or the control subjects.¹ Were patients with endocarditis, myocarditis and pericarditis systematically excluded from participation in the study?

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The fifth point is that the outcome and mortality may strongly depend on the infectious agent responsible for sepsis.⁴ Therefore, we should know the spectrum of pathogens that have been blamed for sepsis and in how many of the included patients no infectious pathogen could be identified. It is also important to know how sensitive the antibiotics used were in eliminating the identified infectious agents.

Overall, the study has limitations that challenge its results and the authors interpretation. Addressing these limitations could further strengthen and reinforce the study. All unanswered questions need to be clarified before readers can uncritically accept the conclusions. Before the conclusion can be drawn that vitamin C and thiamine have no beneficial effect in septic patients, all factors influencing the outcome parameters must be excluded as responsible, the group size must be large enough to obtain reliable results, and the included patients must be homogenized with respect to the causative infectious agent.

DECLARATIONS

Availability of Data and Material

All data are available from the corresponding author.

AUTHORS CONTRIBUTIONS

JF: Responsible for the design and conception, discussed available data with coauthors, wrote the first draft, and gave final approval. FS and CS: Data curation, literature search, discussion, final approval.

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REFERENCES

1. Sharma S, Paneru HR, Shrestha GS, Shrestha PS, Acharya SP. Evaluation of the effects of a combination of vitamin C, thiamine and hydrocortisone vs hydrocortisone alone on ICU outcome in patients with septic shock: A randomized controlled trial. *Indian J Crit Care Med* 2024;28(11):1147–1152. DOI: 10.5005/jp-journals-10071-24852.
2. Alissa A, Alrashed MA, Alshaya AI, Al Sulaiman K, Alharbi S. Reevaluating vitamin C in sepsis and septic shock: A potential benefit in severe cases? *Front Med (Lausanne)* 2024;11:1476242. DOI: 10.3389/fmed.2024.1476242.
3. Fowler AA 3rd. Vitamin C: Rationale for its use in sepsis-induced acute respiratory distress syndrome (ARDS). *Antioxidants (Basel)* 2024;13(1):95. DOI: 10.3390/antiox13010095.
4. van der Poll T, Opal SM. Host-pathogen interactions in sepsis. *Lancet Infect Dis* 2008;8(1):32–43. DOI: 10.1016/S1473-3099(07)70265-7.