Vitamins B1 and C Do Not Improve Outcomes in Patients With Sepsis

Brendan Gontarz MD, Levi Craft, MS, Usman Siddiqui MBBS, Carol McGuiness BA, James Dodge, PharmD, Melissa Ulbrick BS, David S Shapiro MD
Department of Surgery

Introduction

Despite continued advances in the care of critically ill patients and clearly defined sepsis guidelines, sepsis, severe sepsis, and septic shock remain a contributor to morbidity and mortality. Vitamin C (ascorbic acid, VC) is an important cofactor for enzymatic function and its use for sepsis has been studied with mixed outcomes. Models used to treat sepsis have included intravenous VC with and without Vitamin B1 and/or corticosteroids and have demonstrated improvement in end organ dysfunction and mortality. Randomized, placebo-controlled trials are limited by questionable reports.

Animal studies have demonstrated benefits to VC in sepsis models, and human studies have shown lower levels of circulating VC during acute illness. We created a model similar to past models, but with two important distinctions: a) we included VC with thiamine without corticosteroids as a requirement, and b) we permitted use of corticosteroids according to the provider preference.

Methods

The trial protocol was approved by the institutional review board of Trinity Health Of New England for Saint Francis Hospital. Enrollment began on 6/6/2018 with recruitment and follow up continued until study end on 2/22/2021. Informed consent was obtained from patient legally authorized representatives (LAR) within 24 hours of sepsis diagnosis. This is a single-center, randomized, double-blinded, placebo-controlled superiority trial comparing the use of vitamin C and thiamine versus treatment with placebo in patients with criteria-based diagnosis of sepsis and septic shock. Corticosteroids were not required.

Primary outcomes were mortality and discharge alive from the index hospitalization. Predicted mortality was calculated with APACHEIV. Secondary outcomes included hospital and ICU lengths of stay, duration of vasopressors, 72-hour change in sequential organ failure assessment (SOFA) score. Multiple statistical analyses were used, including logistic regression to compare patients with and without corticosteroid therapy.

Conclusion

There were no differences in baseline characteristics (Table 1); Predicted mortality based upon APACHEIV scoring demonstrated no difference between control and treatment groups (p=NS, Figure 1); Primary outcomes of mortality and discharge alive from the hospital demonstrated no differences between groups (p=NS, Table 2); Secondary outcomes including hospital and ICU lengths of stay, duration of vasopressors, and 72-hour change in SOFA scores, also demonstrated no differences (p=NS, Table 2).

Discussion

Two important distinctions in this study separate it from previous similar work by Marik, et al. Our results suggested that corticosteroid play a larger role in reducing mortality in sepsis than the addition of Vitamin C and Thiamine, and that previously published effects of Vitamin C, Thiamine, and Corticosteroids together may have reflected this effect. Prior reported synergies were not demonstrated when our groups—selected for corticosteroid use by the provider—were treated with steroids.

Conclusions

• Vitamin C and Thiamine did not render a clinical improvement in mortality, length of stay, or any clinical outcome in our randomized, double-blinded, placebo-controlled trial. The use of Vitamin C and Thiamine should be reconsidered.

Selected References