Vitamin C (ascorbic acid) levels are low in all septic patients. With the global incidence of sepsis being estimated at 15 to 19 million cases each year and continuing to increase, it is key to develop treatments that reduce morbidity and mortality amongst the patients affected. 1,8 There remains a need for further investigation of the benefits of steroids, thiamine, and ascorbic acid.

INTRODUCTION

❖ Septic shock, a form of distributive shock, is one potential complication of the host immune response to an underlying infection and creates devastating health burdens worldwide.6

❖ Recent literature suggests a synergistic benefit in using steroids, thiamine and ascorbic acid supplementation in septic shock (STASIS).3

❖ Vitamin C (ascorbic acid) levels are low in all septic patients.6 Experimentally ascorbic acid provides benefits to many of the consequences of the host immune response seen in septic shock patients, including endothelial cell damage and dampening the pro-inflammatory response.2

❖ Hydrocortisone and ascorbic acid function in a complementary fashion, by increasing the other’s efficacy.1 Ascorbic acid reverses the oxidation of glucocorticoid receptors making the receptor more accessible, and hydrocortisone increases the expression of the transporter needed to move ascorbic acid into the cell.7

❖ Thiamine deficiency is also common in septic patients.4 Replenishing thiamine is thought to prevent hyperoxalosis and thus protect renal function.5

❖ We hypothesize that septic shock patients, as defined by the Sepsis-3 criteria, who are treated with steroids, thiamine and ascorbic acid supplementation will demonstrate a lower 28-day mortality rate than those who received the current standard of care.

RESULTS

1. Patients who presented to Vidant Medical Center with or who developed septic shock, and met inclusion/exclusion criteria were included in this retrospective cohort study, utilizing medical chart review.

2. Patients were separated into two groups based on the treatment modality they received, 1) standard of care including resuscitation fluids, antihypotensive vasopressors, and/or hydrocortisone or 2) standard of care supplemented with steroids, thiamine and ascorbic acid.

3. Following the administration of medications, patients were analyzed based on etiology of septic shock, intravenous (IV) fluids given in the initial 24 hours of septic shock, net fluid balance at end of intensive care unit (ICU) stay, ICU length of stay, days on a mechanical ventilator, number of vasopressors administered, highest dosage of vasopressors given, presence of delirium using the Confusion Assessment Method for the ICU (CAM-ID), blood transfusion during septic shock, renal replacement therapy (RRT), modified Rankin scale, discharge disposition, and mortality at 28 days.

4. Changes in the treatment quality comparing standard of care to STASIS were analyzed using a paired t-test and chi-square analysis.

Figure 1. Mortality rate. The mean modified Rankin score for patients treated with the standard of care was 7.7 (95% CI: 6.4-9.0) and the STASIS group had a mean modified score of 7.3 (95% CI: 5.7-8.9). There was a significant difference in the modified Rankin score at the end of the ICU stay between the STASIS and standard of care patients (p=0.001).

Figure 2. IV fluid intake (L) given in the initial 24 hours of septic shock. For standard of care patients, mean IV fluids given in initial 24 hours was 4.9 L (95% CI: 4.0-4.6 L). In STASIS patients, mean IV fluids given in initial 24 hours was 5.8 L (95% CI: 5.5-6.1 L). There was no significant difference in the amount of IV fluids given within the initial 24 hours between the two groups (p=0.099). Additionally there was a significant difference in the need for RRT (p<0.01). There was a significant association between the STASIS patients and blood transfusions (p<0.01).

Figure 3. Not fluids (L) at the end of the ICU stay. The standard of care patients mean fluid intake was 7.7 L (95% CI: 6.4-9.0) and the STASIS group had a mean fluid intake of 28.1 L (95% CI: 14.5-45.1 L). There was no significant difference in the net fluid balance at the end of the ICU stay between the STASIS and standard of care patients (p=0.08).

Figure 4. ICU length of stay (LOS) (days). The mean ICU LOS in the standard of care group was 7.9 days (95% CI: 6.7-9.5) and the mean for the STASIS group was 13 days (95% CI: 10.6-16.9). There was a significant increase in the ICU LOS in the STASIS patients (p=0.004).

Figure 5. Total mechanical ventilator (MV) days. Patients treated with the standard of care required a mean of 6.4 MV days (95% CI: 5.7-7.0) while STASIS patients required a mean of 13.8 days (95% CI: 10.1-17.5) on the mechanical ventilator. STASIS patients required a significantly higher number of days on the mechanical ventilator (p<0.001).

Figure 6. Number of vasopressors following treatment for septic shock. Patients who received the standard of care required a mean of 1.8 vasopressors (95% CI: 1.5-2.1) while STASIS patients required a mean of 2.7 vasopressors (95% CI: 2.3-3.2). There was a significant difference in the number of vasopressors required between the groups. When the dosages of norepinephrine and epinephrine were compared, STASIS patients also required a higher dosage of norepinephrine (p=0.003) with no significant difference in the amount of epinephrine (p=0.084).

REFERENCES


DISCUSSION

1. Septic shock patients who received steroids, thiamine and ascorbic acid did not experience a reduction in the 28-day mortality rate.

2. 23.9% of the standard of care patients experienced delirium compared to the 6.9% of STASIS patients.

3. Neurologic dysfunction is linked to poor outcomes in sepsis patients.1 If STASIS patients have fewer incidence of delirium, it is likely this supplementation could result in better treatment outcomes.

4. STASIS patients did require a longer ICU stay, higher number of vasopressors and more days on the mechanical ventilator.

5. STASIS patients tended to begin the supplementation trial with a poorer prognosis. Despite the limitations of a retrospective study, there was no significant difference in amount of resuscitation fluids or net fluid balance at the end of the ICU stay. However, there was an association between STASIS patients and receiving a blood transfusion.

6. Some literature proposes that thiamine helps to preserve renal function.5 We did find there was no significant difference in the need for RRT between the two groups.

7. With the global incidence of sepsis being estimated at 15 to 19 million cases each year and continuing to increase, it is key to develop treatments that reduce morbidity and mortality amongst the patients affected.1,8 There remains a need for further investigation of the benefits of steroids, thiamine, and ascorbic acid.

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