What Current Research Can Teach Medical Personnel About Sepsis Management and Treatment

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The Basic Components of the "Marik Protocol"

(Marik, Khangoora, Rivera, Hooper, & Catravas, 2017)

Vitamin C

Collagen formation, tissue repair, carbohydrate metabolism, lipid and protein synthesis, resistance to infection

Thiamine

Required for carbohydrate metabolism (septic shock increases metabolic demands)

Hydrocortisone

Suppresses inflammation and normal immune response

Who participated in the study?

 Inclusion criteria: primary diagnosis of severe sepsis or septic shock with a procalcitonin level of > 2 ng/mL

 Exclusion criteria: immunocompromised, pregnant, current cytotoxic therapy, diagnosis of immunodeficiency syndrome, 18 years old or younger

Baseline Characteristics

Variable	Treatment Group	Control Group
Age, mean	58.3	62.2
Sex, male	57%	49%
WBC, mean	20.6	17.1
Lactate	2.7	3.1
Procalcitonin	25.8	15.2
Predicted mortality	39.7	41.6

Comorbidities: diabetes, hypertension, heart failure, malignancy, COPD, cirrhosis, stroke, chronic renal failure, morbid obesity, immunocompromised, drug addiction

What was the intervention?

- Treatment Group:
 - 50 mg of hydrocortisone every 6 hours
 - 1.5 g vitamin C every 6 hours
 - 200 mg thiamine every 12 hours
 - Broad spectrum antibiotics

- Control Group (standard protocol):
 - 50 mg of hydrocortisone every 6 hours
 - Broad spectrum antibiotics

Outcome

Variable	Treatment Group	Control Group
Mortality	8.5%	40.4%
Length of Stay in ICU	3-5	4-10
Vasopressor Duration	18.3 hours	54.9 hours
Kidney Replacement Therapy	10%	33%

Vitamin C Study

(Fowler et al., 2014)

- Aim:
 - Determine if the administration of vitamin C had an effect on outcomes of septic patients
 - Determine the safety of Vitamin C

- Low plasma vitamin C concentrations in septic patients are linked to an increased risk for multiple organ failure and decreased risk for survival
- Mean plasma vitamin C levels on admission were subnormal - 17.9 μM
 - \circ 50-70 μ M is normal

Vitamin C Study

- Method: twenty-four patients with severe sepsis in the ICU were randomized 1:1:1 to receive intravenous infusions every six hours for four days
 - High dose Vitamin C (200mg/kg/24hr)
 - Low dose Vitamin C (50mg/kg/24hr)
 - Placebo (Dextrose 5%)

SOFA scores of patients in the beginning of the study (Mortality estimation tool for ICU patients)

Treatment	Mean SOFA Score	
Low dose Vitamin C	10.1 ± 2.0	
High dose Vitamin C	10.8 ± 4.4	
Placebo	13.3 ± 2.9	

Vitamin C Study

- Results:
 - Vitamin C was well-tolerated and safe
 - IV Vitamin C therapy may positively impact multiple organ failure in septic patients
- SOFA scores of patients throughout the study

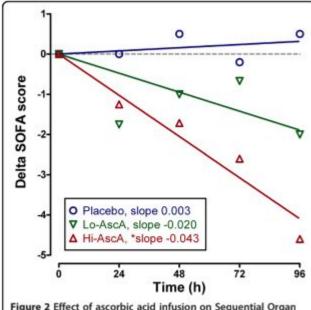


Figure 2 Effect of ascorbic acid infusion on Sequential Organ Failure Assessment (SOFA) score (days 0–4). Daily mean SOFA scores decreased over time with both doses of ascorbic acid infusion (p < 0.05 significantly non-zero) with the higher dose significantly less than placebo (Hi-AscA vs. placebo p < 0.01). Placebo (O), Lo-AscA (▼), Hi-AscA (▲).

(Kim et al., 2017)

 Purpose: evaluate the efficacy of combined vitamin C, hydrocortisone, and thiamine in patients with severe sepsis pneumonia

Mortality rate of patients with pneumonia in ICU is 29-47% (Restrepo et al. as cited in Kim et al., 2018)

Treatment Protocol:

- IV vitamin C 1.5 grams every 6 hours for 4 days
- IV hydrocortisone 50 mg every 6 hours for 7 days followed by a taper over 3 days
- O IV thiamine 200 mg every 12 hours for 4 days

- June 2017 January 2018 = treatment group (53)
- June 2016 January 2017 = control group (46)

Admission Data

Variable Upon Admission	Control Group - 46	Treatment Group - 53
Age, mean	74	73
ARDS Upon Admission, # of pts	10	12
SOFA Score, mean	11	11
Day 1 Ventilation Need, # of pts	36	43
Day 1 Vasopressor Need, # of pts	22	33
Day 1 Renal Replacement Need, # of pts	5	19
Lactate, mean	2.2	2.3

Results

Variable	Control Group - 46	Treatment Group - 53
No. of days on vasopressors	7.5	8.2
No. of days on ventilator	18.1	15.7
Length of ICU stay, days	12	9
Hospital mortality, # of pts	14	6

What can this research teach medical professionals?

- There is constantly new research being published
- As medical professionals, we need to be challenging the medications and interventions that we provide
- By researching evidence based practice, we can ensure we are providing the most current, evidenced based care
- This research shows significant improvement in patient conditions

References

- Fowler, A. A., Syed, A. A., Knowlson, S., Sculthorpe, R., Farthing, D., DeWilde, C., . . . Gupta, S. (2014). Phase I safety trial of intravenous ascorbic acid in patients with severe sepsis. *Journal of Translational Medicine*, 12(32). doi:10.1186/1479-5876-12-32
- Kim, W. Y., Jo, E. J., Eom, J. S., Mok, J., Kim, M. H., Kim, K. U., ... Lee, K. (2018). Combined vitamin C, hydrocortisone, and thiamine therapy for patients with severe pneumonia who were admitted to the intensive care unit: Propensity score-based analysis of a before-after cohort study. *Journal Of Critical Care*, 47, 211–218.https://doi.org/10.1016/j.jcrc.2018.07.004
- Marik, P. E., Khangoora, V., Rivera, R., Hooper, M. H., & Catravas, J. (2017). Hydrocortisone, Vitamin C, and Thiamine for the Treatment of Severe Sepsis and Septic Shock: A Retrospective Before-After Study. *Chest*, *151*(6), 1229–1238. https://doi.org/10.1016/j.chest.2016.11.036

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