

Anti-oxidant Supplementation in Critically Injured Patients

INTRODUCTION

The profound oxidative stress that occurs following injury results in an early depletion of many endogenous antioxidants. Several studies have documented lower circulating levels of both ascorbic acid and α -tocopherol in association with increased levels of oxidized glutathione in the plasma of critically ill patients. One of the main scavenger systems responsible for cleavage of free radicals is the selenium-dependent glutathione peroxidase, with protective action against membrane-damaging lipid peroxidation. Selenium levels have also been shown to be lower in patients with severe illnesses, including sepsis and SIRS, compared with controls.

Given the role of oxidative –mediated tissue injury in the development of ARDS and multiple organ dysfunction (MOD), supplemental antioxidants may augment endogenous defenses and serve to prevent the development of organ dysfunction. In addition, there is increasing evidence that anti-oxidants such as ascorbic acid and α -tocopherol may reduce infectious complications in the critically ill patient by restoring neutrophil function and cellular-mediated immunity. As well, selenium replacement has been shown to improve phagocytosis, natural killer cell activity, and immunoglobulin synthesis, in addition to its apparent ability to attenuate organ dysfunction after hemorrhagic shock.

PURPOSE

To standardize the supplementation of antioxidants in the acutely injured patient, by which we may be able to attenuate the maladaptive inflammatory responses that lead, or at least expedite, the development of ARDS and/or MOD. In addition, this anti-oxidant replacement strategy may improve immune function among our most critically ill patients, thereby decreasing their potential for development of nosocomial infections.

INTERVENTION

Who receives anti-oxidant supplementation

- A. All adult trauma patients will receive seven (7) day course of high dose supplemental anti-oxidant therapy.
- B. Excludes pregnant patients (ascorbic acid & selenium= pregnancy category C)
- C. Excludes patients with creatinine > 2.5 mg/dL

Supplement administration

- A. Ascorbic acid 1,000 mg PO/PT/IV q 8 hours
- B. α -tocopherol 1,000 IU PO/PT q 8 hours
- C. Selenium 200 mcg IV qd

All vitamin supplements will be stopped upon discharge from the hospital

BIBLIOGRAPHY

1. Metnitz PG, Barteus C, Fischer M, et al. Antioxidant status in patients with ARDS. *Int Care Med* 1999; 25:180-5.
2. Borrelli E, Roux-Lombard P, Gran GE, et al. Plasma concentrations of cytokines, their soluble receptors, and antioxidant vitamins can predict the development of multiple organ failure in patients at risk. *Crit Care Med* 1996; 24: 392-7.
3. Schorah CJ, Downing C, Piripitsi A, et al. Total vitamin C, ascorbic acid, and dehydroascorbic acid concentration in plasma of critically ill patients. *Am J Clin Nutr* 1996; 63: 760-5.
4. Goode HF, Cowley HC, Walker BE, et al. Decreased antioxidant status and increased lipid peroxidation in patients with septic shock and secondary organ dysfunction. *Crit Care Med* 1995; 23: 646-51.
5. Nathens AB, Neff MJ, Jurkovich GJ, et al. Randomized, controlled trial of antioxidant supplementation in critically ill surgical patients. *Ann Surg* 2002; 236(6): 814-822.
6. Howe KP, Clochesy, JM, Politis J, et al. Antioxidant supplementation to facilitate ventilator weaning. Presented at the Society of Critical Care Medicine's 34th Critical Care Congress, Phoenix, AZ, January 15-19, 2005.
7. Angstwurm MW, Schottdorf J, Schopohl J, et al. Selenium replacement in patients with severe systemic inflammatory response syndrome improves clinical outcome. *Crit Care Med*. 1999;27:1807-1813.

8. Urban T, Jarstrand C. Selenium effects on human neutrophilic granulocyte function *in vitro*. *Immunopharm* 1986; 12: 167-172.
9. Goode HF, Webster NR. Free radicals and antioxidants in sepsis. *Crit Care Med* 1993; 21:1770-17751
10. Porter JM, Ivatury RR, Azimuddin K, et al. Antioxidant therapy in the prevention of organ dysfunction syndrome and infectious complications after trauma. *Am Surg* 1999; 65(5): 478-83.
11. Baeuerle PA, Henkel T. Function and activation of NF-kB in the immune system. *Ann Rev Immunol* 1994; 12:141-179
12. Bertrand Y, Pincemail J, Hanique G, et al. Differences in tocopherol-lipid ratios in ARDS and non-ARDS patients. *Intensive Care Med*. 1989; 15:87-93.
13. Richard C, Lemonnier F, Thibault M, Couturier M, Auzepy P. Vitamin E deficiency and lipoperoxidation during adult respiratory distress syndrome. *Crit Care Med* 1990; 18: 4-9.
14. Schorah CJ, Downing C, Piripitsi A, et al. Total vitamin C, ascorbic acid, and dehydroascorbic acid concentrations in plasma of critically ill patients. *Am J Clin Nutr*. 1996; 63: 760-765.
15. Demling R, LaLonde C, Ikegami K, Picard L, Nayak U. Alpha-tocopherol attenuates lung edema and lipid peroxidation caused by acute zymosan-induced peritonitis. *Surgery* 1995; 117: 226-231

16. Bulger EM, Helton WS, Clinton CM, Roque RP, Garcia I, Maier RV. Enteral vitamin E supplementation inhibits the cytokine response to endotoxin. *Arch Surg.* 1997; 132:1337-1341
17. Deitch EA, Bridges W, Baker J, et al. Hemorrhagic shock-induced bacterial translocation is reduced by xanthine oxidase inhibition or inactivation. *Surgery.* 1988; 104:191-198
18. Yamakawa Y, Takano M, Patel M, Tien N, Takada T, Bulkley GB. Interaction of platelet activating factor, reactive oxygen species generated by xanthine oxidase, and leukocytes in the generation of hepatic injury after shock/resuscitation. *Ann Surg.* 2000; 231: 387-398
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