Nutrition as Medical Therapy

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KEYWORDS

• Selenium • Sepsis • Insulin • Lipid • L-Carnitine • Valproic acid • Toxicity • Overdose

KEY POINTS

- Intravenous selenium may be a useful therapy for treating severe sepsis; a deadly syndrome for which limited treatment options exist.
- Lipid emulsion therapy has emerged as a viable treatment modality for various toxic drug exposures, including local anesthetic toxicity.
- High-dose insulin therapy has been used successfully to improve cardiac function in patients with acute calcium channel blocker overdose.
- L-Carnitine, which is required for metabolic energy production, has been found to be useful in treating encephalopathy associated with valproic acid toxicity.

INTRODUCTION

Selenium, lipid emulsion, insulin, and L-carnitine are often seen as ingredients in parenteral nutrition formulations. Recent evidence suggests that these agents can also be used to treat various medical conditions that may be encountered in the critical care setting. The indications for these nutritional compounds, the clinical rationale for their use, and the supporting evidence for these therapies are presented in this article.

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SELENIUM FOR SEPSIS

Selenium is an essential nutrient for human health. Selenoproteins are responsible for many of the important physiologic actions of selenium. For example, glutathione peroxidases are a group of antioxidant selenoproteins that protect biomembranes and DNA against damage caused by reactive oxygen species (eg, hydrogen peroxide). Iodothyronine deiodinases, another group of selenoproteins, are responsible for converting thyroxine (T4) to the active thyroid hormone triiodothyronine (T3). Selenoproteins also support the immune system by enhancing the activity and proliferation of T cells and natural killer cells.[1,2]

Deficiency in selenium has been shown to negatively affect health. Increased rates of cancer-associated mortality have been associated in countries where dietary intake of selenium is low. Certain viral infections, including human immunodeficiency virus, similarly may be more likely to lead to clinical deterioration in the setting of low plasma selenium levels.[1,2]

In recent years, there has been a growing body of research showing that high-dose selenium supplementation may have a positive impact on clinical outcomes in sepsis syndromes.[3–5] Although it is not currently known whether the low serum selenium levels observed in sepsis are pathogenic or simply a marker of disease severity, it has been hypothesized that intravenous selenium supplementation, in superphysiologic doses, may provide beneficial antioxidant and antiinflammatory activity that may improve morbidity and mortality from sepsis.[2–5]

Sepsis is defined as the presence of probable infection with systemic manifestations of infection, and severe sepsis is defined as sepsis plus resultant organ dysfunction or tissue hypoperfusion.[6,7] In the United States, severe sepsis accounts for nearly 10% of all intensive care unit admissions, and it is associated with a mortality between 20% and 30%.[7] There is currently no recommended drug therapy that targets the systemic inflammatory response syndrome (SIRS), which is associated with sepsis.[7] An intravenous formulation of selenium, sodium selenite, has recently been investigated as a potential therapeutic option to help to improve clinical outcomes in patients with severe sepsis and septic shock.

Angstwurm and colleagues[4] evaluated the effects of selenium supplementation in patients with SIRS, sepsis, and septic shock in a prospective, randomized, placebo-controlled, multicenter study. This trial enrolled 249 patients, and randomized them to receive 1000 μg of sodium selenite as a 30-minute bolus injection, followed by 1000 μg per day delivered as continuous intravenous infusion for 14 days. Although 28-day mortality did not differ between placebo-treated patients and selenium-treated patients, there were several patients in whom the study protocol was severely violated. Among the 189 patients who received treatment as per protocol, adjuvant selenium was associated with a significant reduction in 28-day mortality compared with placebo (42.4% vs 56.7%; $P = .049$). In a subgroup analysis, a similar mortality benefit in favor of selenium therapy was noted among patients with septic shock, as well as among the most critically ill patients according to Acute Physiology and Chronic Health Evaluation (APACHE) III scores. Serum selenium levels and glutathione peroxidase activity were noted to be in the upper normal range among treated patients and deficient among patients who received placebo.

Manzanares and colleagues[5] performed a prospective, randomized, single-blinded trial of selenium supplementation in 35 patients with SIRS. Within 24 hours of admission to the intensive care unit, patients were randomized to receive intravenous selenium (as sodium selenite) 2000 μg over 2 hours or placebo, which was then followed by a continuous infusion of 1600 μg per day of sodium selenite or placebo for 10 days.