Commentary

Hypertonic saline resuscitation in sepsis

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Abstract

The review by Oliveira and colleagues on the subject of hypertonic saline resuscitation in sepsis (included in the present issue) suggests possible benefits for hypertonic saline. There is a firm experimental basis for the actions of hypertonic saline/hyperoncotic solutions in hemorrhagic hypotension, which include expansion of blood volume, improvement in cardiac index, favorable modulation of the immune system, and improvement in survival. These actions are presumed to be of benefit in the treatment of sepsis or septic shock. However, there are few experimental data regarding the use of these solutions, and clinical studies are descriptive. The major impact of early administration of hypertonic solutions may be attenuation of tissue injury, sepsis, and septic shock. Early and aggressive fluid resuscitation with hypertonic solutions to clinical end-points should be investigated in patients with systemic inflammatory response syndrome, sepsis, and septic shock.

Keywords hemorrhage, hyperoncotic, immune function, septic shock, shock

The present discussion focuses on the review by Oliveira and coworkers [1] (presented in this issue), and on the use of hypertonic saline resuscitation in sepsis. Early fluid resuscitation of patients with systemic inflammatory response syndrome reduces the incidence of mortality due to septic shock and sepsis [2]. These favorable results have led to consideration of other fluid modalities. In their review, Oliveira and coworkers consider the use of hypertonic saline solutions in the treatment of patients with severe sepsis.

Hypertonic saline has been extensively investigated in animal models with regard to its efficacy in treating hemorrhagic hypotension [3]. Numerous clinical studies of patients with traumatic injuries have been initiated with favorable, but not definitive, results [4]. Limited animal studies have been directed at treatment of septic shock using hypertonic solutions, and clinical studies have been exploratory at best. Hannemann and coworkers [5] studied 21 stable patients with septic shock. Patients were administered 2–4 ml/kg hypertonic saline in hydroxyethyl starch. Following administration there was a small effect on oxygenation by increasing cardiac output and oxygen delivery. There was no control group in this study for comparison. An abstract reported by Oliveira an colleagues [6] described a randomized study of 25 stable patients with sepsis. Administration of 250 ml hypertonic saline in dextran significantly improved cardiac index and pulmonary artery occlusion pressure as compared with administration of an equivalent volume of normal saline. Although favorable, those studies of responses to hypertonic saline solutions in stable patients with sepsis are only descriptive. Furthermore, administration of hypertonic saline solutions during the early stages of septic shock when the patient is not yet hyperdynamic has not been investigated.

The major benefit of hypertonic solutions is the rapid expansion of blood volume for a small volume administered [7]. This advantage is sustained by the addition of colloids such as dextran. In their review, Oliveira and colleagues [1] suggest that the major benefit of resuscitation with hypertonic solutions in models of septic shock is the restitution of blood volume and accompanying improvements in cardiovascular and hemodynamic function.

Hypertonic solutions have been demonstrated to modulate the immune system [8–10]. As pointed out by Oliveira and coworkers [1], hypertonic saline has a pronounced anti-inflammatory effect that could reduce the response to sepsis and attenuate later multiple organ failure. Recently, Shi and coworkers [11] found resuscitation with hypertonic saline to

ameliorate the gut and lung injury seen following use of Ringer's lactate. This lack of injury reduced bacterial translocation, and would presumably reduce the incidence of sepsis.

Comparisons between various resuscitation solutions on outcome have been controversial. However, the work of Rhee and colleagues [12,13] in comparing various solutions suggests pronounced differences in immune modulation. The question that must be addressed is whether the presently available solutions are harmful in conditions in which immune function is challenged, and are thus inappropriate to use. Rhee and coworkers showed that hypertonic solutions, especially when combined with dextran, are superior to 'standard of care' solutions. This leads to the conclusion that presently used solutions may be harmful because they compromise immune function and that hypertonic solutions are of benefit because they do not.

In their review, Oliveira and coworkers [1] discuss the use of hypertonic solutions for treatment of septic shock; however, they do not refer to the possible prophylactic benefit of early use of these solutions. The etiology of sepsis is based on a sustained period of hypoperfusion of vital organs [14]. Rivers and colleagues [2] demonstrated early resuscitation to improve survival. The use of hypertonic solutions as the initial fluid therapy, irrespective of the cause of hypotension or cardiac insufficiency, may be of benefit in blocking the cascade that leads to septic shock. In a study of trauma patients initially resuscitated with hypertonic saline dextran [15], no cases of sepsis occurred in the hypertonic saline group as compared with an incidence of 2% in the standard of care group. Although interesting, this difference was not significant. The favorable preservation of tissues and immune function that occurs following early resuscitation of the hypotensive patient with hypertonic solutions bodes well for a favorable outcome in the treatment of sepsis.

Oliveira and colleagues [1] point out the probable advantages of using hypertonic solutions in patients with sepsis. There is a rapid and sustained expansion of plasma volume, leading to improvement in cardiovascular function, rectification of microcirculatory blood flow, and favorable modulation of immune function. All of these factors may contribute to improved outcomes in patients with sepsis and septic shock. Beyond the scope of the present commentary is the possibility that early resuscitation with hypertonic solutions could contribute to a reduced incidence of sepsis by modulation of immune responses and reduced tissue injury. These improvements following hypertonic saline resuscitation would have a greater impact on the subsequent course of patients admitted to the intensive care unit. At present, although the experimental data are positive and the rationale for use of hypertonic solutions in the care of patients with sepsis or septic shock is reasonable, definitive clinical studies as to the safety and efficacy in this patient population are still required.

Competing interests

CEW is a faculty member of the University of California at Davis, which holds the US patent for hypertonic saline/hyperoncotic solutions. He holds advisory positions in companies developing these solutions and serves as a consultant to other companies.

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