Journal of Critical Care 42 (2017) 168–177

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.jccjournal.org

Hypertonic saline in critical illness - A systematic review

Carmen Andrea Pfortmueller, MD *, Joerg C. Schefold, MD

Department of Intensive Care, Inselspital, Bern University Hospital, University of Bern, Freiburgstrasse 10, 3010 Bern, Switzerland

ARTICLE INFO

Keywords:
Critical illness
Saline
Resuscitation
Crystalloid
Fluid

ABSTRACT

Introduction: The optimal approach to fluid management in critically ill patients is highly debated. Fluid resuscitation using hypertonic saline was used in the past for more than thirty years, but has recently disappeared from clinical practice. Here we provide an overview on the currently available literature on effects of hypertonic saline infusion for fluid resuscitation in the critically ill.

Methods: Systematic analysis of reports of clinical trials comparing effects of hypertonic saline as resuscitation fluid to other available crystalloid solutions.

A literature search of MEDLINE and the Cochrane Controlled Clinical trials register (CENTRAL) was conducted to identify suitable studies.

Results: The applied search strategy produced 2284 potential publications. After eliminating doubles, 855 titles and abstracts were screened and 40 references retrieved for full text analysis. At total of 25 scientific studies meet the prespecified inclusion criteria for this study.

Conclusion: Fluid resuscitation using hypertonic saline results in volume expansion and less total infusion volume. This may be of interest in oedematous patients with intravascular volume depletion. When such strategies are employed, renal effects may differ markedly according to prior intravascular volume status. Hypertonic saline induced changes in serum osmolality and electrolytes return to baseline within a limited period in time. Sparse evidence indicates that resuscitation with hypertonic saline results in less perioperative complications, ICU days and mortality in selected patients. In conclusion, the use of hypertonic saline may have beneficial features in selected critically ill patients when carefully chosen. Further clinical studies assessing relevant clinical outcomes are warranted.

Contents

* Corresponding author at: Department of Intensive Care, Inselspital, Bern University Hospital, University of Bern, Freiburgstrasse 10, 3010 Bern, Switzerland.
E-mail addresses: carmen.pfortmueller@insel.ch (C.A. Pfortmueller), joerg.schefold@insel.ch (J.C. Schefold).

http://dx.doi.org/10.1016/j.jcrc.2017.06.019
0883-9441/

1. Introduction

The optimal approach to fluid management in the critically ill is highly debated [1]. Different crystalloid fluid solutions are currently available with varying electrolyte compositions and thus different impact on acid-base and electrolyte status, as well as on other organ systems, such as the cardiovascular and renal systems (Fig. 1) [2].

Hypertonic saline contains supra-physiological quantities of sodium and chloride with varying concentrations (Table 1) [3,4]. Sodium may trigger vasopressin secretion through stimulation of the osmotic hypothalamic receptors [5,6] and may exert preload-independent effects on myocardial contractility [7]. Importantly, as in most clinical conditions associated with intravascular fluid expansion and activation of the renin- angiotensin-aldosterone system (RAAS) (e.g. heart failure or renal failure), iatrogenic sodium loading induces direct effects on end-organs [8]. Renal compensatory mechanisms may be of particular importance resulting in renal vasodilatation and temporary GFR increase [8,9]. The GFR increase is attributed to the increased natriuresis and reduced tubular reabsorption [8,9]. However, over time, the increase in GFR may diminish due to compensatory mechanisms mediated by natriuretic peptides and vasopressin [4,8-11].

Importantly, hypertonic sodium solutions contain equal parts of chloride ions to ensure electroneutrality [12] and increased chloride levels may result in hyperchloremic metabolic acidosis [12]. Most studies on so called "physiological" saline solutions (0.9%, 154 mmol/l sodium, 154 mmol/l chloride) demonstrate development of hyperchloremic metabolic acidosis [13-16], which may be under recognized in current clinical practice.

However, in critically ill patients these effects may be of particular importance as most patients receive considerable quantities of intravenous fluids over the ICU stay [3]. Additionally, changes in vascular permeability and oncotic pressure may contribute to "third spacing" [2,3]. Nevertheless, despite common perception, fluid overload is not a benign occurrence; it was consistently linked to prolonged ICU- and hospital length of stay and increased mortality rates [17,18]. In addition, it was associated with increased perioperative complications [19,20] and decreased gastrointestinal function [3,21].

Fluid resuscitation using bolus or continuous infusion of hypertonic saline was used for more than thirty years [3,22]. Hypertonic saline expands intravascular volume by shifting fluid from the extravascular space [1,5], thus increasing preload [4,23]. Compared to conventional "plasma expanders", it is considered inexpensive, rapidly available, and without risk for anaphylaxis or transmission of infectious disease [23]. Hypertonic saline was evaluated in particular in patients with traumatic brain injury [24-27]. Current evidence on use of hypertonic saline for treatment of increased intracranial pressure is controversial and some authors conclude that administration of hypertonic saline does not result in reduced cerebral edema formation, reduced intracranial pressure, or decreased mortality when compared to other solutions [28]. Hypertonic saline was also studied in additional indications in critically ill patients such as hemorrhagic and cardiogenic shock, and burns [1,22,23,29], but results on relevant patient-centered outcomes were inconsistent. Moreover, some authors postulate effects of hypertonic saline on diverse immune functions, but respective results are inconsistent and await further clarification [29-33].

Despite potential physiological advantages, hypertonic saline was less used in recent years, which may at least partially be due to previous use of combination solutions (e.g. hypertonic saline with colloids). Importantly, mounting data indicating adverse clinical outcomes of critically ill patients treated with colloid solutions when compared to recipients of crystalloid solutions [34]. Nonetheless, fluid resuscitation with hypertonic saline infusion may provide benefits in selected critically ill patients. The aim of this review is to provide an overview on the currently available literature addressing effects of hypertonic saline infusion for fluid resuscitation (and respective comparison to other crystalloid infusates) in critically ill patients.

2. Methods

2.1. Eligibility

Clinical trials on adult ICU patients with the primary objective of comparing effects of hypertonic saline as resuscitation fluid to other crystalloid solutions are reported. The following studies were excluded: trials in pediatric patients, pregnant women, studies investigating crystalloid versus other colloid solutions or hypertonic saline-colloid mixtures, studies investigating hypertonic solutions other than hypertonic sodium-chloride, and trials comparing hypertonic NaCl versus other hypertonic solutions, trials investigating the management of increased intracranial pressure, and hypertonic saline for inhalation therapy, and trials on the therapy of hyponatremia. Only reports available in English or German were considered for inclusion.

2.2. Information sources

A systematic MEDLINE search (www.pubmed.org) and the Cochrane Controlled Clinical trials register (CENTRAL) were conducted to identify suitable investigations. In addition to searching electronic databases, previous respective studies were searched for further references.

2.3. Search strategy

The following search terms were used: "hypertonic saline volume therapy", "hypertonic saline volume replacement", "hypertonic saline resuscitation", "hypertonic saline volume expansion", "hypertonic saline volume overload", "hypertonic saline fluid overload", "hypertonic saline capillary leak". No date restriction was applied.

2.4. Methodological quality of included studies

Methodological quality of included studies was assessed using previously established criteria described [35]. In detail, the Jadad scale proposes methods used for randomization, blinding and patient management in clinical trials. The range of possible scores is 0 (lowest quality) to 5 (highest quality). Studies were not excluded based on Jadad scores.