Intensive Care Med (2002) 28:1574–1581
DOI 10.1007/s00134-002-1509-x

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Acute haemodynamic effects of a hypertonic saline/dextran solution in stable patients with severe sepsis

Received: 29 January 2002
Accepted: 4 September 2002
Published online: 1 October 2002

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Abstract *Objective:* To study the haemodynamic effects of a hypertonic saline/dextran solution compared with a normal saline solution in patients with severe sepsis.
Design: Prospective double blind and control-randomised study.
Setting: Adult intensive care unit in a university hospital.
Patients: Twenty-nine patients with sepsis with a pulmonary artery occlusion pressure (PAOP) lower than 12 mmHg. *Interventions:* Patients were randomised to receive 250 ml of blinded solutions of either normal saline (SS group, n=16) or hypertonic saline (NaCl 7.5%)/dextran 70 8% (HSS group, n=13) solutions.
Measurements and results: Haemodynamic, blood gas, and sodium data were collected at the following time points: baseline, 30 min, 60 min, 120 min, and 180 min. PAOP was higher in the HSS group at 30 min (10.7±3.2 mmHg vs 6.8±3.2 mmHg) and 60 min (10.3±3 mmHg vs 7.4±2.9 mmHg); P<0.05. The cardiac index increased in the HSS group and it was greater than the SS group at 30 min (6.5±4.7 l min^{-1} m^{-2} vs 3.8±3.4 l min^{-1} m^{-2}), 60 min (4.9±4.5 l min^{-1} m^{-2} vs 3.7±3.3 l min^{-1} m^{-2}), and 120 min (5.0±4.3 l min^{-1} m^{-2} vs 4.1±3.4 l min^{-1} m^{-2}); P<0.05. The stroke volume index followed a comparable course and it was higher at 30 min [53.6(39.2–62.8) ml m^{-2} vs 35.6(31.2–49.2) ml m^{-2}] and 60 min [46.8(39.7–56.6) ml m^{-2} vs 33.9(32.2–47.7) ml m^{-2}]; P<0.05. Systemic vascular resistance decreased in the HSS group and became significantly lower at 30 min (824±277 dyne s^{-1} cm^{-5} m^{-2} vs 1139±245 dyne s^{-1} cm^{-5} m^{-2}), 60 min (921±256 dyne s^{-1} cm^{-5} m^{-2} vs 1246±308 dyne s^{-1} cm^{-5} m^{-2}), and 120 min (925±226 dyne s^{-1} cm^{-5} m^{-2} vs 1269±494 dyne s^{-1} cm^{-5} m^{-2}). Sodium levels increased in the HSS group (P=0.056) and were higher than in the SS group at 30 min (145±3 mEq l^{-1} vs 137±7 mEq l^{-1}), 60 min (143±4 mEq l^{-1} vs 136±7 mEq l^{-1}), 120 (142±5 mEq l^{-1}vs 136±7 mEq l^{-1}), and 180 min (142±5 mEq l^{-1} vs 136±8 mEq l^{-1}).
Conclusion: Hypertonic saline/dextran solution may improve cardiovascular performance in severe sepsis without significant side effects. The haemodynamic effect appears related mainly to a volume effect.

Keywords Sepsis · Hypertonic saline · Small volume · Hemodynamics · Dextran · Clinical trial

Introduction

Sepsis and septic shock are associated with a mortality rate of 30–80% despite the progress in pathophysiology, diagnosis, and therapeutics over the last four decades [1]. It has been demonstrated that patients with severe sepsis experience marked cardiovascular disturbances that can compromise oxygen delivery to the tissues and consequently are in part responsible for the organ dysfunction and the high mortality rate observed in patients with sepsis [2, 3].

The haemodynamic management of severe sepsis includes a prompt restoration and maintenance of intravascular volume. Isotonic crystalloids and colloids have been used to restore intravascular volume in sepsis. However, there is still a debate concerning which is the best type of fluid to use in sepsis due to the complex alterations in the myocardial function and microcirculation [4, 5].

Patients with shock can be resuscitated equally when either crystalloid and colloid solutions are titrated to the same level of filling pressures [6, 7]. Shoemaker and coworkers have stressed the superiority of colloids over crystalloids in the effective restoration of plasma volume and oxygen availability in critical conditions [8, 9]. On the other hand, Metildi et al. observed that the haemodynamic effects and volume requirements after a fluid challenge with albumin 5% or ringer lactate were not different [10]. Several artificial colloids solutions have also been compared and no clear advantage was found over albumin in critically ill patients in terms of total volume infused, haemodynamic effects, and side-effects [6, 7, 11].

Arguments in favour of the use of isotonic crystalloids include expansion of the extracellular compartment with minimal risk of anaphylactoid reactions and low cost. However, volume resuscitation with crystalloids requires two to four times more volume than colloids and more time to achieve the same haemodynamic end points with a greater risk of oedema formation, which interferes with tissue oxygen exchange. Colloid resuscitation requires less volume and time but is more expensive and, when artificial, carries the risk of anaphylactoid reactions and dose-dependent coagulation abnormalities [12].

Alternatively, hypertonic saline solutions can act in all levels. Experimental studies of haemorrhage, trauma, and sepsis have shown that hypertonic saline solutions can improve myocardial contractility and microcirculation by an instantaneous mobilisation of endogenous fluid and an increase in pre-load, direct myocardial stimulation, peripheral vasodilatation, redistribution of blood flow – in particular the mesenteric flow–, and reduction of tissue and endothelial oedema, improving blood viscosity through haemodilution and reduction in erythrocytes size [13, 14, 15]. Controlled clinical studies in trauma and haemorrhage have shown that small-volume resuscitation is feasible and effective in pre-hospital volume resuscitation and in the emergency room [16, 17, 18]. Experience with hypertonic saline solutions in sepsis is limited. Hannemann et al. prospectively studied – in a non-controlled study – the haemodynamic effects of a hypertonic saline/hydroxyethylstarch solution in patients with sepsis [19]. They observed a transitory increase in oxygen transport, cardiac output, and pulmonary capillary wedge pressure.

To test an improve cardiovascular performance in patients with severe sepsis, we studied the haemodynamic effects of a hypertonic saline/dextran solution compared with a normal saline solution in a prospective double blind and randomised study.

Patients, material and methods

Patient criteria

With approval of the institutional ethics committee, 29 patients with severe sepsis admitted to a clinical-surgical ICU over a period of 23 months were enrolled in a double blind, randomised (random numbers table), and prospective study. At the time of enrolment, all patients included had to be newly admitted to the ICU, had to have clinically suspected infection, and had to fulfill at least two criteria of systemic inflammatory response syndrome (SIRS) along with the presence of perfusion abnormalities that may have included oliguria (<0.5 ml/h) or elevated blood lactate levels (>2 mmol/l) or acute alteration of mental status [20]. Clinically suspected infection was defined as an explicit statement by the attending physician indicating the suspicion of an ongoing infection, combined with the initiating of a diagnostic work-up to rule out infection and the prescription of antimicrobial therapy [21]. All patients required invasive monitoring with a pulmonary artery catheter and were haemodynamically stable with a pulmonary occlusion pressure equal to or less than 12 mmHg (no catecholamine requirement or no modifications in infusion dosages for at least 1 h). All patients were 18 years old or over and expected to stay alive for more than 1 day. Patients were entered in the study as soon as they fulfilled the inclusion criteria, and were treated according to our standard treatment protocol. Exclusion criteria included: (1) adjustment of catecholamine doses or aggressive volume resuscitation (fluid administration >200 ml within 30 min) during the 180-min study period; (2) coma after pulmonary-cardio-cerebral-resuscitation; (3) renal failure (blood creatinine >3.0 mg/dl); (4) hypernatremia (Na^+ >145 mEq/l); and (5) pregnancy. Disease severity was scored with the Acute Physiology and Chronic Health Evaluation (APACHE) II scoring system [22].

Measurements and study protocol

Arterial pressure, pulmonary arterial pressure, pulmonary artery occlusion pressure, right atrial pressure, cardiac output (Bese, Belo Horizonte, MG, Brazil), haemoglobin (Technicon H.3 RTX, Bayer, Leverkussen, Germany), sodium concentration (selective ion electrode, Hitachi 917 Roche, Japan), and arterial and mixed venous blood gases (gas analyser 278, Ciba-Cornning, San Diego, Calif., USA) were obtained at baseline, and 30 min, 60 min, 120 min, and 180 min later. Arterial blood lactate concentration was determined by an enzymatic technique (Coba Mira Plus, Roche, Indianapolis, Ind., USA) at baseline and 180 min later. Cardiac output was determined by the thermodilution technique

(the mean of five injections of 10 ml of cooled water (0–5 °C) with injection performed at the end of inspiration). Oxygen-derived parameters were calculated using standard formulas. Immediately after baseline measurements patients were randomised to receive a 10-min infusion of 250 ml of saline (0.9% NaCl) or hypertonic saline/dextran (7.5% NaCl, 2,400 mosmol/l, in dextran 8% 70) solution via a central venous catheter.

Statistical analysis

One-way repeated measures analysis of variance (ANOVA) was used for normally distributed variables (Kolmogorov-Smirnov normality test) with a Student-Newman-Keuls test for post hoc analysis. Kruskal-Wallis one-way ANOVA on ranks was used for those variables non-normally distributed and a Dunn's test was performed whenever treatments varied significantly. To test whether there was association between APACHE II score and haemodynamic variables, a Pearson product-movement correlation (parametric statistic) or a Spearman rank order correlation (non-parametric) tests were performed. A P value of 0.05 was considered statistically significant. Data are reported as mean±SD for normally distributed variables and median (25–75th percentiles) for non-normally distributed variables.

Results

Twenty-nine patients with severe sepsis (18 male, 11 female, median age 43 years) were included in this study. All patients were mechanically ventilated. APACHE II score was calculated for 26 patients and the mean value was 16.7±5.3. Patients' characteristics are shown in Table 1. Sixteen patients were randomised to receive saline solution (SS group) and 13 patients to hypertonic saline/dextran solution (HSS group). Eleven patients received vasoactive drugs in the SS group and four in the HSS group. The SS group had a higher APACHE II score than the HSS group (18.7±4.5 vs 14.1±5.2, P=0.027). The mortality rate was 31% (4/13) for the HSS group and 64% (10/16) for the SS group (P=NS).

The course of haemodynamic parameters on both groups is shown in Table 2, and Figs. 1, 2, and 3. Heart rate and mean arterial pressure were unchanged in both groups. Both study solutions induced a significant increase in PAOP during the study period. PAOP was higher in the HSS group with the differences being significantly greater at 30 min and 60 min (Fig. 1). The cardiac index increased only in the HSS group with differences being significantly greater at 30 min, 60 min, and 120 min (Fig. 1). During fluid infusion the systemic vascular resistance decreased in the HSS group and became lower at 30 min, 60 min, and 120 min (Fig. 1). The reduction in systemic vascular resistance (>10%) was consistent for all but two HSS patients. On the con-

Table 1 Patient's characteristics. (*F* female, *M* male, *HSS* hypertonic saline solution, *SS* saline solution, *Dopa* dopamine, *Dobu* dobutamine, *NA* non-available)

Patient	Sex	Age	Underlying condition	Source	Solution	Vasoactive drugs μg kg min	Apache II	Outcome
2	F	43	Cirrhosis	Abdomen	SS	Dopa, 9	17	Died
3	M	33	Cancer	Abdomen	SS	Dobu, 4	16	Survived
4	M	65	Cancer	Abdomen	SS	Dobu, 7	24	Died
5	F	24	Pneumonia	Lung	SS	Dopa, 7	19	Survived
9	M	65	Ulcer	Urinary	SS	Dopa, 6	23	Died
11	M	41	Pneumonia	Lung	SS	No	23	Died
12	M	41	Blood coagulation	Abdomen	SS	No	11	Died
13	F	66	Pancreatitis	Abdomen	SS	Dopa, 5	18	Died
14	M	50	Cancer	Mediastinum	SS	No	11	Survived
15	F	46	Intestinal obstruction	Abdomen	SS	No	24	Survived
17	F	69	Cholangitis	Abdomen	SS	Dopa, 8	20	Died
18	M	39	Trauma	Soft tissue	SS	No	14	Survived
19	M	42	Pneumonia	Lung/abdomen	SS	Dopa, 4; Dobu, 5	19	Died
22	M	44	Pneumonia	Lung	SS	Dopa, 8; Dobu, 5	28	Died
23	M	39	Pneumonia	Lung	SS	Dobu, 5	NA	Survived
28	M	60	Cancer	Mediastinum	SS	Dopa, 7	23	Died
1	M	23	Trauma	Abdomen	HSS	No	11	Died
6	M	60	Cancer	Mediastinum	HSS	No	17	Survived
7	F	46	Appendicitis	Abdomen	HSS	Dopa, 11; Dobu, 6	14	Died
8	M	61	Pancreatitis	Abdomen	HSS	No	12	Survived
10	M	65	Trauma	Bone	HSS	No	20	Died
16	M	44	Cancer	Mediastinum	HSS	Dopa, 7	5	Survived
20	M	43	Pancreatitis	Abdomen	HSS	No	20	Survived
21	F	37	Abortion	Abdomen	HSS	No	13	Survived
24	F	41	Pancreatitis	Blood	HSS	Dopa, 4	NA	Died
25	M	46	Pneumonia	Blood	HSS	No	NA	Survived
26	F	40	Peritonitis	Abdomen	HSS	No	10	Survived
27	F	22	Pneumonia	Lung	HSS	No	11	Survived
29	F	40	Pneumonia	Lung	HSS	Dopa, 7	22	Survived

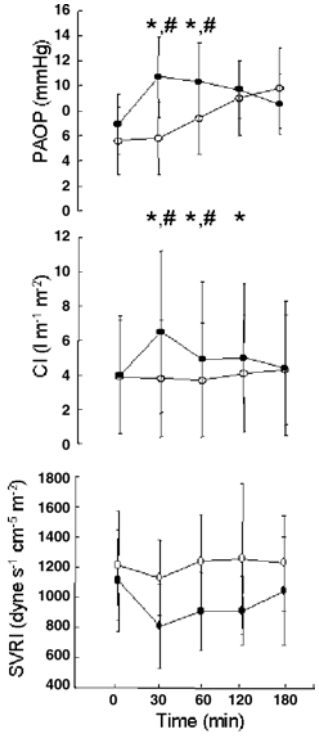

Fig. 1 Time course of pulmonary artery occlusion pressure (PAOP *top*), SVRI, systemic vascular resistance index, cardiac index (CI *bottom*) –, after intravenous administration (250 ml) of hypertonic saline/dextran solution (*n*=13, *closed circle*) and saline solution (*n*=16, *open circle*). **P*<0.05 between the two groups, #*P*<0.05 versus baseline for hypertonic saline/dextran solution group. Data are shown as mean±SD

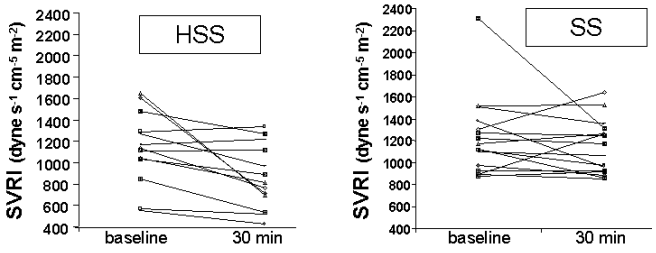

Fig. 2 Individual changes in systemic vascular resistance index at baseline and 30 min after intravenous administration (250 ml) of hypertonic saline/dextran solution (HSS) and saline solution (SS)

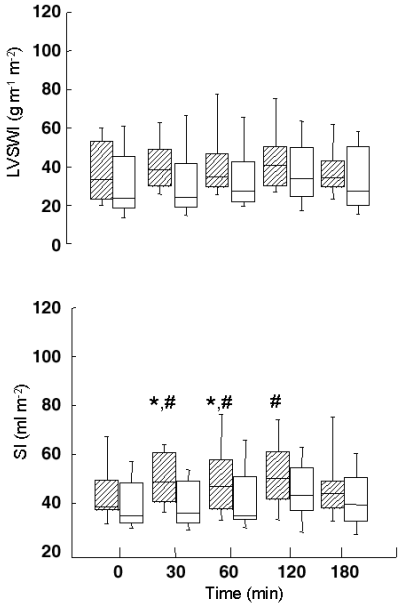

Fig. 3 Time course of left ventricular stroke work index (LVSWI *top*) and stroke index (SI *bottom*) after intravenous administration (250 ml) of hypertonic saline/dextran solution (*n*=13, *filled box*) and saline solution (*n*=16, *hollow box*). **P*<0.05 between the two groups, #*P*<0.05 versus baseline for hypertonic saline/dextran solution group. The *box plot lines* indicate the median and the 25th and 50th percentiles and *error bars* indicate the 10th and 90th percentiles

trary, the reduction in systemic vascular resistance was observed in only seven out of 17 patients in the SS group (Fig. 2). The stroke volume followed a comparable course and it was substantially higher at 30 min and 60 min (Fig. 3). Although the left and right ventricular stroke work index increased in HSS group (*P*=NS) there were no differences between groups (Fig. 3 and

Table 2 Time course of hemodynamic parameters. Data are reported as mean±SD or median (25–75th percentiles). (*HSS* hypertonic saline/dextran solution, *SS* saline solution, *MAP* mean arterial pressure, *HR* Heart rate, *CVP* central venous pressure, *LVSWI* left ventricular stroke work index, *RVSWI* right ventricular stroke work index, *PVRI* pulmonary vascular resistance index)

		0 min	30 min	60 min	120 min	180 min
MAP	SS	70(57–80)	66(57–82)	70(60–77)	72(63–80)	72(60–90)
(mmHg)	HSS	63(52–70)	72(65–77)	70(63–76)	70(60–78)	67(60–77)
HR	SS	111±22	111±20	104±19	106±20	103±19
(beats/min)	HSS	112±25	117±18	116±20	109±18	106±17
CVP	SS	6(4–7.5)	7(5–8.5)	8(7–9)	9(7.5–11)	7.5(7–12)
(cmH_2O)	HSS	8(4–10.5)	11.5(9.5–14)	8(7.8–10.3)	8(7–11.5)	7(5.5–10.5)
RVSWI	SS	5.5(4.3–8)	6.5(4.6–9.6)	5.9(3.9–9)	6.1(5–8.7)	8(5.5–9.7)
($g\ m^{-1}\ m^{-2}$)	HSS	6.2(4.8–8)	8.8(7–9.6)	7.6(4.7–10.7)	9(8–10.7)	7.5(6–10)
PVRI	SS	207(182–341)	260(150–314)	215(150–361)	230(158–379)	318(154–381)
($dyne\ s^{-1}\ cm^{-5}\ m^{-2}$)	HSS	228(150–305)	166(100–240)	149(96–222)*,**	147(121–270)	238(127–267)

**P*<0.05 vs baseline; ***P*<0.05 between groups

Table 3 Metabolic variables. Data are reported as median (25–75% percentiles). (PaO_2 arterial oxygen tension, PvO_2 mixed venous oxygen tension, SaO_2 arterial oxygen saturation, SvO_2 mixed venous oxygen saturation, *Hb* haemoglobin, DO_2 oxygen delivery, VO_2 oxygen consumption, O_2ER oxygen extraction ratio)

		0 min	30 min	60 min	120 min	180 min
PaO_2 (mmHg)	SS	100(78–167)	108(94–143)	105(87–127)	105(73–120)	99(80–124)
	HSS	132(110–144)	115(86–143)	106(71–138)	115(89–135)	108(89–1460
PvO_2 (mmHg)	SS	39(36–47)	39(37–46)	39(37–43)	39(34–43)	39(35–43)
	HSS	45(41–46)	44(37–50)	43(38–46)	43(39–47)	42(40–44)
SaO_2 (%)	SS	96(94–99)	97(95–98)	97(94–98)	97(93–98)	97(93–98)
	HSS	98(97–98)	98(96–98)	96(93–98)	97(94–98)	97(96–98)
SvO_2 (%)	SS	71(63–79)	71(67–76)	69(66–78)	68(61–74)	68(59–75)
	HSS	74(71–77)	72(57–80)	73(70–77)	72(68–76)	70(67–78)
Hb (mg/dl)	SS	9.3(8.2–9.9)	9.0(7.8–9.7)	8.3(8.1–9.0)	8.2(7.5–9.0)	8.2(7.7–9.0)
	HSS	8.6(7.8–9.1)	7.6(7.3–8.3)*,**	8.0(7.0–8.3)	8.0(7.4–8.8)	8.0(7.0–8.6)
DO_2 (ml min^{-1} m^{-2})	SS	490(402–763)	461(411–726)	426(390–545)	418(367–533)	449(350–632)
	HSS	467(426–706)	689(446–818)	583(478–87)	582(464–804)	513(398–578)
VO_2 (ml min^{-1} m^{-2})	SS	130(113–154)	135(115–155)	119(111–131)	137(105–164)	132(124–166)
	HSS	143(91–172)	121(109–290)	133(111–168)	162(120–203)	145(124–171)
O_2ER (%)	SS	26(17–34)	28(22–31)	28(22–33)	31(23–36)	28(22–39)
	HSS	25(17–26)	29(19–36)	24(18–28)	23(22–28)	28(22–31)
Lactate (mmol/l)	SS	3.5(2.2–4.4)	–	–	–	3.1(2.0–5.5)
	HSS	2.6(2.3–3.4)	–	–	–	2.9(2.1–3.4)
Sodium (mEq l^{-1})	SS	139±7	137±7	137±7	136±7136±8	
	HSS	139±6	145±3	143±4	142±4	142±5

*P<0.05 vs baseline; **P<0.05 between groups

Table 2). Pulmonary vascular resistance decreased in HSS group (P<0.05) and it was lower than the SS group after 60 min (Table 2).

The course of metabolic variables, haemoglobin, and blood oxygenation is shown in Table 3. After fluid challenge, the oxygen delivery increased in the HSS group (P=NS) and it was higher at 60 min and 120 min [583(478–687) vs 426(390–545) ml min^{-1} m^{-2} and 582(464–804) vs 418(367–5339) ml min^{-1} m^{-2}]. The oxygen consumption did not change in both groups. The haemoglobin levels significantly decreased in the HSS group and were significantly lower after 30 min [7.6(7.2–8.2) vs 9.0(7.8–9.7), P=0.045]. The serum sodium levels increased in the HSS group (P=0.056) and were higher in comparison to the SS group at 30 min, 60 min, 120 min, and 180 min. Blood oxygenation variables and blood lactate levels did not change in both groups. Fluid balance was not different between groups (SS group, 1548±790 ml vs HSS group, 1361±993 ml, P=NS) after 360 min.

The state of illness measured by the APACHE II score was not correlated with any haemodynamic variable. The HSS was well tolerated in all patients and no arrhythmia, neurologic dysfunction or metabolic effects were noted.

Discussion

In this series of stable patients with severe sepsis, hypertonic saline/dextran solution induced an increase in cardiac output and DO_2 but VO_2 and O_2ER remained stable. The concurrent increase in cardiac filling pressures indicates that it was mainly due to a volume effect. The doses of vasoactive drugs were kept constant 1 h before the solution infusion and they were not modified during the observation period. The decreased afterload (reduced SVR) also might have contributed to increase cardiac output. As the mean baseline value of systemic vascular resistance was similar in both groups, another explanation for the acute change in vascular resistance could be the regimen of volume resuscitation. Hypertonic solutions can rapidly increase intravascular volume by pulling water from the intracellular space into the interstitial and intravascular spaces due to the osmotic gradient [23, 24]. Initially, the hypertonic saline solution mobilises fluids from the microvascular endothelium and red cells. In addition, by reducing the endothelium oedema, the hydraulic resistance is decreased and tissue perfusion may improve [24].

Experimentally, hypertonic saline solutions may also improve myocardial contractility by a direct effect on myocytes, precapillary vasodilation, decrease in myocardial cell oedema, and restoration of myocardial cell transmembrane potentials [25]. However, our study did

not address myocardial function and our findings does not support this hypothesis.

The effects of HSS on oxygen-derived parameters suggest that these patients with severe sepsis were haemodynamically resuscitated and no change in VO_2 or O_2ER would be expected [26]. High blood lactate levels at study admission and 180 min later could be explained by mechanisms other than anaerobic metabolism due to tissue hypoxia (accelerated anaerobic glycolysis, hepatic defective clearance, inhibition of pyruvate dehydrogenase) [27].

An important risk when using hypertonic saline solutions is iatrogenically induced hypertonic states. Plasma sodium levels increased transiently in the HSS group but always in the range of normality. There was no evidence that this transient sodium load caused harm to the patients. Nevertheless, HSS was not infused in severe hyponatremic in whom the risk of pontine myelinolysis was possible, or in hypernatremic patients in whom an acute further increase in plasma sodium concentration could have been harmful [28].

The combination of hypertonic saline solution with colloids provides a greater and more sustained haemodynamic improvement than isotonic solutions by increasing plasma volume [29, 30]. The haemodynamic effects of the HSS were greater and more sustained than the SS but returned to baseline levels after 180 min. Although our results are similar to experimental and clinical studies, which show a more sustained haemodynamic improvement of hypertonic solutions when compared to isotonic solution in haemorrhagic and septic shock, the haemodynamic effects of the hypertonic saline/dextran solution were more transient than expected [17, 29, 30, 31]. We chose a saline/dextran solution because this is widely used in our country. Dextran is considered safe and effective in relatively large amounts and is much cheaper than albumin [32]. We used 7.5% NaCl as the hypertonic solution because this concentration appears to induce maximal beneficial effects without overt toxicity in several experimental and clinical studies of traumatic, haemorrhagic, and septic shock [14, 19, 32, 33, 34, 35].

The finding of equivalent fluid balances shows the short timing effect of the hypertonic solution in patients with sepsis. This contrasts with previous experimental and clinical studies of severe hypovolemic shock and some experimental studies of endotoxic shock. However, Armistead et al. showed a similar finding in an endotoxic dog model in which a hypertonic saline/hetastarch solution did not decrease fluid requirements [36]. In addition, we choose a maximum PAOP of 12 mmHg to avoid acute hypervolemia with the HSS and, as in patients with severe sepsis patients the loss of fluids is multi-factorial and continuous, the restoration of the blood volume would be expected to be incomplete and transient.

The total mortality rate was 48%, which was expected for a population with severe sepsis. Interestingly, the mortality rate for the HSS group was lower than for the SS group. However, the two groups of patients were not absolutely comparable. The APACHE II score was lower, baseline PaO_2 was higher, and fewer patients needed vasoactive drugs in the HSS group, and we cannot attribute the difference in mortality to the treatment solution. The differences in severity of illness could have influenced the haemodynamic response. Therefore, a less sick group of patients could better respond to volume infusion independent of the type of volume. This hypothesis seems to be improbable as the APACHE II score was not associated with any haemodynamic variable tested.

The data presented in this study demonstrate that a short infusion of a hypertonic saline/dextran solution seems to be efficacious and safe. The magnitude of the haemodynamic effects was similar to other studies with critically ill patients and patients with sepsis but with a significant lower volume [6, 7, 8, 9, 11, 19]. Nevertheless, the study did not answer the question whether the study solution is better than other isotonic crystalloids or colloids in avoiding complications such as systemic and pulmonary oedema after fully volume resuscitation. However, hypertonic saline solutions have other potentially beneficial effects in the redistribution of blood flow among different organs [14, 37]. Moreover, hypertonic saline solutions may reduce endothelial cell swelling, modulate inflammation, and improve oxygen extraction capabilities [15, 38, 39]. If one considers this therapy for future studies on clinical sepsis – not only as an alternative fluid for acute volume replacement – it would be interesting to test the role of hypertonicity in modulating the inflammatory response as observed in experimental studies [25].

In summary, our results demonstrate that HSS can improve global cardiovascular performance in the resuscitation of patients with severe sepsis due to a volume effect. Hypertonic saline/colloid solutions may help to rapidly improve haemodynamic status in patients with sepsis without significant side effects. The potential effects on the microcirculation or long-term beneficial effects of single or repetitive infusions of a hypertonic saline solution during the course of severe sepsis need further studies.

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