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The effect of 0.9% saline versus plasmalyte on coagulation in patients undergoing lumbar spinal surgery; a randomized controlled trial☆

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HIGHLIGHTS

- Perioperative fluid resuscitation with 0.9% saline is associated with hyperchloremic metabolic acidosis even in amounts of 2–4 L.
- The changes on coagulation function assessed by rotation thromboelastometry are similar between 0.9% saline and plasmalyte.
- Perioperative administration of plasmalyte resulted in greater intraoperative urine output compared with 0.9% saline.

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ABSTRACT

Introduction: In multi-level lumbar spinal fusion surgery yielding a large amount of blood loss, choice of fluid for volume resuscitation is an important issue since it can influence acid-base status, coagulation, and patients' outcome. This study compared the effect of plasmalyte to 0.9% saline on coagulation assessed by rotation thromboelastometry (ROTEM) and acid-base balance in the aforementioned patients.

Methods: Fifty patients were randomly allocated to receive either 0.9% saline or plasmalyte during operation and until postoperative 12 h. ROTEM was performed at 10 min after anesthetic induction and end of surgery. Arterial blood gas analyses were serially performed from 10 min after anesthetic induction until postoperative 12 h. Fluid balance, blood loss, and transfusion requirement were assessed.

Results: ROTEM variables showed sporadic deterioration in both groups after surgery without intergroup differences. Intraoperatively, arterial pH, base excess, and bicarbonate concentrations were lower and serum chloride concentrations were higher in the 0.9% saline group compared with the plasmalyte group. The differences in base excess and bicarbonate concentrations persisted until postoperative 12 h. Fluid balance, blood loss, and transfusion requirement were similar between the groups while urine output was greater in the plasmalyte group compared with the 0.9% saline group (3.2 ± 1.6 ml/kg/h vs. 1.8 ± 1.1 ml/kg/h, $p = 0.001$).

Conclusion: In contrast to plasmalyte, fluid therapy with 0.9% saline resulted in transient hyperchloremic acidosis in patients undergoing multi-level lumbar spinal fusion, while coagulation assessed by ROTEM analysis and the amount of blood loss were similar between the groups.

1. Introduction

Multi-level spinal fusion surgeries frequently yield considerable amount of blood loss and appropriate intraoperative fluid resuscitation is essential for optimizing preload and consequently cardiac output to ensure adequate oxygen delivery to the tissues. On the other hand, large amount of fluid resuscitation inevitably results in various degrees of coagulopathy and metabolic derangement

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depending on the type of fluid used [1].

For over 50 years, 0.9% saline has been widely used for perioperative fluid therapy due to its simple composition and low cost. However, the electrolyte composition of 0.9% saline, sodium and chloride at 154 mmol/l each, is less physiologic compared with balanced salt solutions such as lactated Ringer's solution. Accordingly, fluid resuscitation using 0.9% saline has been reported to be associated with hyperchloremic metabolic acidosis, even at amounts of 2–3 L [2–4]. Of note, a number of experimental studies suggested that hyperchloremic metabolic acidosis may impair coagulation, as well as myocardial contractility, and renal function [5]. Disturbances in coagulatory function may be deleterious to patients undergoing major surgeries with significant blood loss and fluid shifts requiring large amount of fluid resuscitation. Indeed, 0.9% saline use on the day of major abdominal surgery was associated with more frequent blood transfusion and dialysis compared with balanced salt solution [6].

Large amount of fluid resuscitation alone causes coagulatory dysfunction as a result of hemodilution. Further deterioration in coagulatory function as a result of metabolic acidosis related to the specific type of crystalloid used would be especially detrimental to patients undergoing closed-space surgeries, which are frequently accompanied by large amount of blood loss as in multi-level spinal fusion. As yet, the influence of 0.9% saline on coagulatory function in relation to metabolic acidosis in this subset of patients had not been addressed heretofore.

Contrary to the assessment of hard clinical endpoints such as the amount of blood loss or transfusion requirement, comparison of coagulatory function using sophisticated measurements according to the type of resuscitation fluid is readily feasible and may impose clinical relevance. In that context, rotation thromboelastometry (ROTEM) enables monitoring of multiple parameters of coagulation as a point-of-care test by measuring clotting time and clot strength [7].

Plasmalyte is a balanced salt solution which has similar electrolyte composition and osmolarity to plasma, which has been shown to elicit less hyperchloremic metabolic acidosis compared with 0.9% saline [8]. This study investigated the effect of plasmalyte or 0.9% saline administration on acid-base balance and coagulation profile measured by ROTEM in patients undergoing multi-level lumbar spinal fusion expected to yield considerable amount of blood loss.

2. Material and methods

2.1. Study population

This study was approved by the Institutional Ethics Committee, and registered with clinicaltrial.gov (unique identifier: NCT01855542). Fifty patients between 20 and 65 years of age with ASA physical status I or II and undergoing multi-level posterior lumbar spinal fusion were enrolled and written informed consent was obtained from all patients. Patients were excluded if they had preexisting acid-base disturbance, electrolyte abnormalities (plasma sodium concentration >145 mmol/l or <135 mmol/l, plasma potassium concentration >5.5 mmol/l or <3.5 mmol/l), anemia (preoperative hematocrit <27%), coagulation abnormalities, renal insufficiency, pulmonary disease, psychiatric disease, pregnancy, drug or alcohol abuse, or were taking diuretics preoperatively. A written informed consent was secured from all of the enrolled patients.

2.2. Study design

Patients were randomly allocated to either the 0.9% saline or plasmalyte group with a block size of two according to a computer-generated random number sequence. The group assignment was concealed by opaque envelopes until anesthetic induction. Intraoperative anesthetic management was conducted by anesthesiologists who were not involved in the study, and investigators including outcome assessors were blinded to the group assignment. Anesthesia was induced by intravenous bolus of propofol 1.5 mg/kg and remifentanil 1 μg/kg. Neuromuscular blockade was facilitated with rocuronium 0.8 mg/kg. Anesthesia was maintained with inhaled sevoflurane in 40% oxygen and continuous infusion of remifentanil at 0.1–0.2 μg/kg/min. Body temperature was maintained above 36 °C using forced-air warming blankets and intravenous fluid warmers. Each group received 0.9% saline or plasmalyte during surgery and until postoperative 12 h. Intraoperative crystalloid solutions were administered at a rate of 6 ml/kg/h, and increased at the discretion of the attending anesthesiologists according to the estimated blood loss. In case of estimated blood loss greater than 500 ml, a colloid solution (6% hydroxyethyl starch 130/0.4 in 0.9% saline) was administered to replace blood loss. Allogeneic packed red blood cell (pRBC) was transfused when the hematocrit value was decreased below 24%.

2.3. Data collection

After anesthetic induction, a radial arterial catheter was placed for continuous monitoring of arterial blood pressure and sampling of blood. ROTEM was performed 10 min after anesthetic induction and at the end of surgery by an anesthesiologist who was blinded to the group assignment. Three ROTEM assays including INTEM, EXTEM and FibTEM were performed according to the standard protocols by the manufacturer. The INTEM, EXTEM and FibTEM assays represent the intrinsic and extrinsic coagulation pathways, and fibrinogen activity, respectively. Ellagic acid and tissue factor activation were used to trigger coagulation pathways in INTEM and EXTEM assays, respectively. In FibTEM assay, coagulation was triggered by tissue factor following inhibition of platelets by Cytochalasin D. Assessed ROTEM variables include clotting time (CT) which represents the onset of coagulation, clot formation time (CFT) and α angle which represent the initial fibrin polymerization rate, and maximum clot firmness (MCF) which measures the strength of the clot. Arterial blood gas analyses were serially performed at following time points; 10 min, 1 h, 2 h, 3 h and 4 h after anesthetic induction, at the end of surgery, and postoperative 12 h. Hemodynamic variables including arterial blood pressure and heart rate were also recorded at the same time. The amounts of crystalloid and colloid administered, pRBC transfusion, urine output and blood loss during surgery were recorded. Blood urea nitrogen (BUN) and serum creatinine (Cr) concentrations were measured at postoperative 24 h.

2.4. Statistical analysis

It was assumed that difference of CT of EXTEM between the 0.9% saline and plasmalyte group would be 10 s with a within group standard deviation of 10 s (mean difference of 1 standard deviation derived from preliminary institutional data). Twenty two patients for each group were needed to have a power of 90% at an α level of 0.05. The size of each group was set to 25 patients considering a possible 10% drop-out rate. Data were expressed as mean ± SD or median [interquartile range], or number of patients (percentage). Continuous data were analyzed by independent t-test. Transfusion requirements and length of hospital stay were analyzed by Mann–Whitney U test. Categorical data were analyzed by χ2 test or Fisher's exact test as appropriate. Repeatedly measured data including ROTEM and arterial blood gas analysis were analyzed by mixed model, and p values for multiple comparisons were adjusted by Bonferroni's method. SAS software (version 9.1.3, SAS Institute, Inc., Cary, NC, USA) was used for statistical analysis. A p value less than 0.05 was considered to be statistically significant.

3. Results

3.1. Patients' characteristics and intraoperative data

Compositions of each fluid are summarized in Table 1. All enrolled patients completed the study (Fig. 1). Preoperative patients' characteristics were similar between the groups (Table 2). Mean intraoperative blood loss was 1848 ± 1000 ml and 2129 ± 1250 ml in the 0.9% saline and plasmalyte group, respectively ($p = 0.388$). There were no significant differences in the amount of infused crystalloid and colloid solution, and pRBC transfusion requirement between the groups (Table 2). Intraoperative urine output was greater in patients who received plasmalyte compared with those who received 0.9% saline (3.2 ± 1.6 ml/kg/h vs. 1.8 ± 1.1 ml/kg/h, $p = 0.001$). Hematocrit values at the end of the surgery were 27 ± 4% and 27 ± 3% in the plasmalyte group and 0.9% saline group, respectively, and were significantly decreased compared to their corresponding baseline values in both groups ($p < 0.05$). Serum Cr concentrations at postoperative 24 h were similar between the two groups (0.62 ± 0.18 mg/dl vs. 0.65 ± 0.29 mg/dl, $p = 0.663$, 0.9% saline vs. plasmalyte, respectively). The lengths of hospital stay was not different between the groups (10.5 [7–18.5] vs. 11 [7–19.5], $p = 0.852$, 0.9% saline vs. plasmalyte, respectively). Hemodynamic data including arterial blood pressure and heart rate were similar between the groups (data not shown).

3.2. Rotation thromboelastometry

ROTEM analyses revealed that values of MCF in FibTEM, CFT, α angle and MCF in INTEM, CT, CFT, α angle and MCF in EXTEM at the end of surgery were changed towards a hypocoagulable state compared to their corresponding baseline values in both groups (Table 3, $p < 0.05$). However, there were no significant differences in FibTEM, INTEM and EXTEM analysis between the groups (Table 3).

3.3. Perioperative acid-base balance and electrolytes

Perioperative acid-base balance is shown in Fig. 2. Arterial pH measured at 1, 2, 3, 4 h after anesthetic induction and at the end of surgery were lower in the 0.9% saline group compared with the plasmalyte group ($p < 0.05$). Base excess measured at 2, 3, 4 h after anesthetic induction, end of surgery, and postoperative 12 h were lower in the 0.9% saline group compared with the plasmalyte group ($p < 0.05$). Serum bicarbonate concentrations measured at 2, 3, 4 h after anesthetic induction, end of surgery, and postoperative 12 h were also lower in the 0.9% saline group compared with the plasmalyte group ($p < 0.05$). Arterial carbon dioxide tension was similar between the groups throughout the study period. The number of patients with perioperative arterial pH < 7.35 was 11 (44%) in the 0.9% saline group and 2 (8%) in the plasmalyte group ($p = 0.005$).

Electrolyte and lactate concentrations are shown in Table 4. Serum chloride concentrations were higher in the 0.9% saline group compared with the plasmalyte group at 2, 3, 4 h after anesthetic induction and end of surgery ($p < 0.05$). Serum magnesium concentrations measured at 4 h after anesthetic induction and end of surgery were higher in the plasmalyte group compared with the 0.9% saline group ($p < 0.05$). Serum lactate concentrations and other electrolytes including sodium and potassium showed no differences between the two groups.

4. Discussion

In the current randomized controlled study, fluid resuscitation with 0.9% saline to compensate for a large amount of blood loss (>40% of estimated blood volume) in multi-level posterior spinal fusion resulted in intraoperative hyperchloremic metabolic acidosis, which was resolved at postoperative 12 h. In contrast, patients who received plasmalyte, a balanced salt solution, did not exhibit metabolic acidosis. Yet, the disturbance in acid-base balance observed in the 0.9% saline group was not associated with any specific coagulatory dysfunction as assessed by ROTEM analysis when compared with the plasmalyte group.

In surgeries, which are accompanied by a large amount of blood loss, the type of fluid for volume resuscitation should be selected regarding its impact on coagulation and metabolism in addition to its volume expanding capacity. Among various crystalloids, 0.9% saline has been widely used for perioperative fluid resuscitation due to its simple composition and low cost. In the perioperative management of neurosurgical patients, the use of 0.9% saline had been rather unconditional for its purported beneficial influence on cellular edema due to the misbelief of its tonicity. However, 0.9% saline is less physiologic compared with balanced salt solutions, especially because of its higher chloride composition than the extracellular fluid compartment. In conjunction, it was reported to be associated with hyperchloremic metabolic acidosis [2–4], which could negatively influence on the activity of coagulation enzymes, besides its well-known adverse effects on the cardiovascular system. In a previous study, patients who received 6% hydroxyethyl starch in balanced salt solution had more favorable thromboelastographic profile compared to those who received 6% hydroxyethyl starch in 0.9% saline [9,10]. Gan et al. [9] also reported that estimated blood loss was greater in patients who received 6% hydroxyethyl starch in 0.9% saline compared with those who received 6% hydroxyethyl starch in balanced salt solution in a subgroup analysis of patients who required intraoperative transfusion.

Undoubtedly, there exists a close relation between the amount of 0.9% saline administered and the degree of ensuing hyperchloremic metabolic acidosis. Multi-level spinal fusion surgeries pose a specific entity in terms of bleeding as it is not only associated with considerable amount of blood loss, but is also a closed-space surgery, in which hematoma formation may yield deleterious neurologic outcome. Still, despite the theoretical association between metabolic acidosis and coagulatory function, the influence of commonly used crystalloid solution on coagulation in relation to acid-base disturbance in patients undergoing spine surgeries expected to yield large amount of blood loss has not been elucidated

Table 1
Electrolyte composition of 0.9% saline and plasmalyte.

	Sodium (mmol/l)	Chloride (mmol/l)	Potassium (mmol/l)	Magnesium (mmol/l)	Acetate (mmol/l)	Gluconate (mmol/l)	Osmolarity (mOsmol/l)
0.9% saline	154	154					308
Plasmalyte	140	98	5	1.5	27	23	294

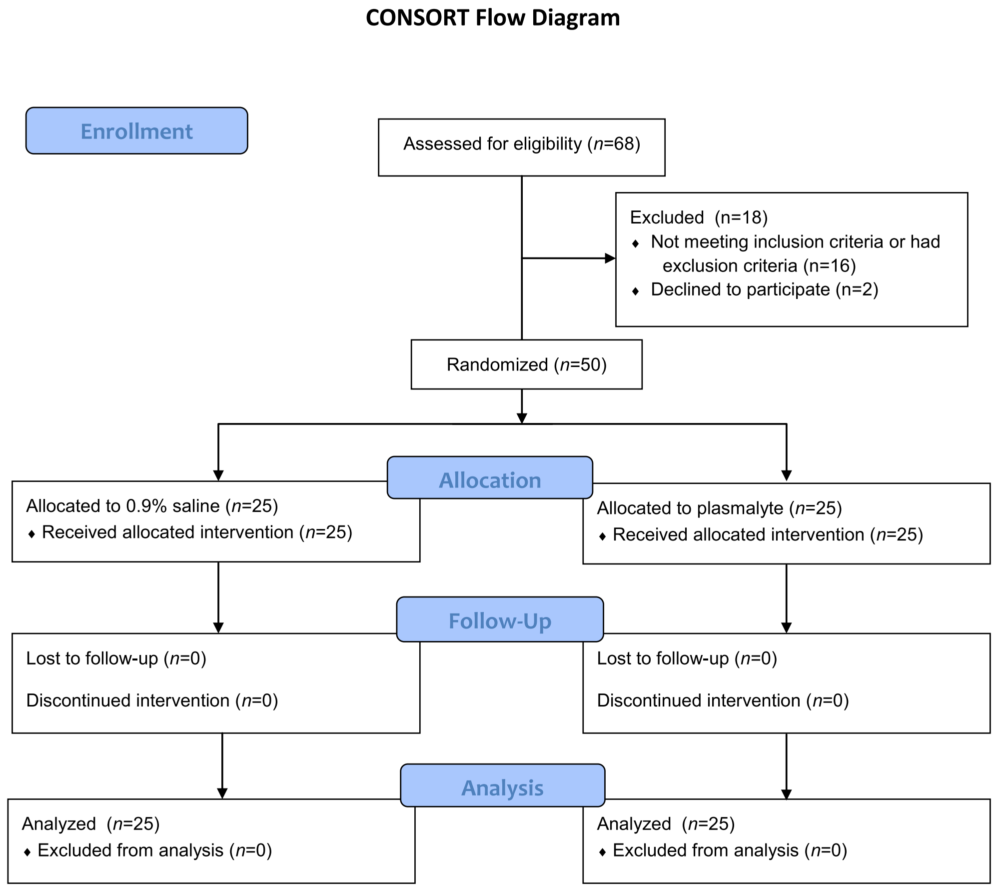

Fig. 1. Patient flow chart.

Table 2
Patients' characteristics and intraoperative data.

	0.9% Saline (n = 25)	Plasmalyte (n = 25)	p
Gender (male/female)	9/16	8/17	0.765
Age (years)	63 ± 10	60 ± 12	0.314
Body mass index (kg/m^2)	24.0 ± 3.2	23.2 ± 3.4	0.359
Preoperative creatinine (mg/dl)	0.92 ± 0.4	0.92 ± 0.3	0.973
Preoperative hematocrit (%)	37 ± 4	38 ± 5	0.351
Duration of surgery (min)	256 ± 91	299 ± 122	0.169
Crystalloid (ml)	3164 ± 1557	3766 ± 1570	0.184
Colloid (ml)	856 ± 339	914 ± 247	0.495
Urine output (ml/kg/h)	1.8 ± 1.1	3.2 ± 1.6	0.001
Blood loss (ml)	1848 ± 1000	2129 ± 1250	0.388
Packed red blood cell transfusion (unit)	1 [0–3]	2 [0.5–3]	0.806

Data are expressed as number of patients, mean ± SD or median [interquartile range].

heretofore.

Even more sophisticated than thromboelastography, ROTEM offers comprehensive tests regarding the coagulation as a point-of-care test by measuring clotting time and clot strength. Accordingly, increasing number of evidence support the adoption of transfusion algorithms based on ROTEM analysis to decrease transfusion requirement [11]. In the current study, both groups exhibited changes towards a hypocoagulable state on ROTEM analysis at the end of the surgery. Although coagulopathy during major surgery has a complex and multifactorial pathophysiology, reduced pro-coagulant factor level resulted from hemodilution and consumption has been thought to play a central role [12]. Our patients were not hypothermic or hypocalcemic, and unlikely to have other factors which can potentially induce coagulopathy including ischemia, infection or intense systemic inflammation. Therefore, the observed trends towards a hypocoagulable state in both groups at the end of the surgery seem to be attributable to hemorrhage and its replacement by intravascular fluid. Indeed, the relatively small changes in CT, prominent increases in CFT of INTEM and EXTEM, and marked decreases in MCF of FibTEM were in accordance with a previous study, which showed that disturbed fibrin polymerization is the main problem underlying dilutional coagulopathy resulted from surgical blood loss and intravascular volume replacement [13]. However, no significant differences in ROTEM analysis were observed according to the administration of plasmalyte or 0.9% saline. The amounts of intraoperative blood loss and transfusion requirements were also similar between the groups. This discordance between the results of previous and current study might be

Table 3
Rotation thromboelastometry.

			0.9% Saline (n = 25)	Plasmalyte (n = 25)	p
FibTEM	CT (sec)	10 min after induction	48.8 ± 16.4	43.2 ± 8.3	0.145
		At the end of surgery	54.3 ± 19.1	50.2 ± 15.6	0.449
	MCF (mm)	10 min after induction	18.4 ± 10.8	17.4 ± 8.0	0.724
		At the end of surgery	10.1 ± 8.7*	10.2 ± 5.7*	0.979
INTEM	CT (sec)	10 min after induction	211.4 ± 105.7	206.3 ± 77.1	0.852
		At the end of surgery	214.3 ± 56.6	202.0 ± 65.3	0.504
	CFT (sec)	10 min after induction	81.0 ± 55.7	81.2 ± 36.5	0.990
		At the end of surgery	130.5 ± 63.0*	118.6 ± 46.9*	0.482
	α (°)	10 min after induction	74.6 ± 8.5	74.4 ± 5.7	0.953
		At the end of surgery	67.1 ± 8.4*	68.6 ± 7.5*	0.514
	MCF (mm)	10 min after induction	60.6 ± 13.8	62.4 ± 5.7	0.558
		At the end of surgery	54.0 ± 8.2*	55.8 ± 8.5*	0.481
EXTEM	CT (sec)	10 min after induction	44.8 ± 10.2	44.1 ± 9.8	0.463
		At the end of surgery	60.0 ± 30.3*	55.4 ± 22.6*	0.561
	CFT (sec)	10 min after induction	104.0 ± 36.7	96.6 ± 28.2	0.441
		At the end of surgery	170.4 ± 76.6*	156.5 ± 58.2*	0.497
	α (°)	10 min after induction	70.6 ± 6.7	71.9 ± 5.8	0.463
		At the end of surgery	60.9 ± 9.6*	62.0 ± 9.2*	0.700
	MCF (mm)	10 min after induction	62.9 ± 6.9	65.4 ± 6.2	0.209
		At the end of surgery	54.3 ± 7.1*	54.0 ± 8.7*	0.898

CT, clotting time; CFT, clot formation time; MCF, maximum clot firmness.
Data are expressed as mean ± SD. *$p < 0.05$ vs. 10 min after induction.

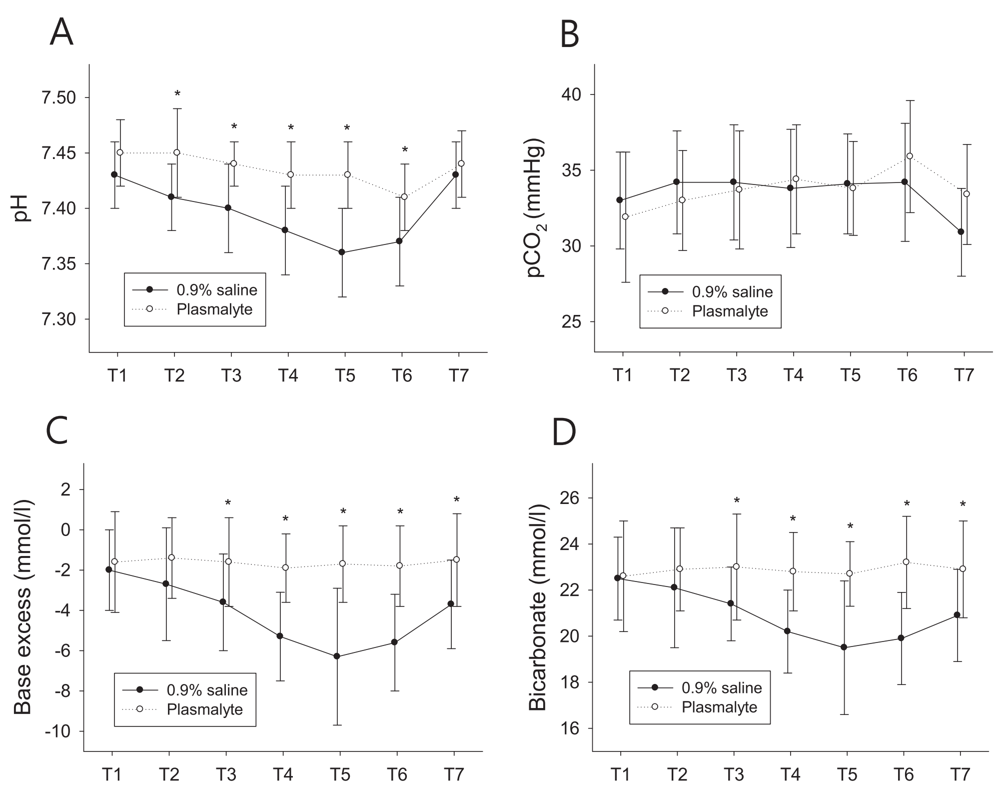

Fig. 2. Perioperative acid-base balance. (A) pH; (B) pCO_2; (C) Base excess; (D) Bicarbonate concentrations; T1, 10 min after induction; T2, 1 h after induction; T3, 2 h after induction; T4, 3 h after induction; T5, 4 h after induction; T6, the end of surgery; T7, postoperative 12 h; Data are expressed as mean ± SD. *$p < 0.05$ vs. 0.9% saline.

based on the differences in ionized calcium concentrations. In the previous studies, the differences in thromboelastographic profile and estimated blood loss were supposed to be attributed to different ionized calcium concentration as well as altered acid-base balance secondary to chloride load. On the contrary, both plasmalyte and 0.9% saline had no calcium ion and intraoperative ionized calcium concentrations were not different in both groups in the current study (data not shown). Taken together, the coagulatory function does not seem to be specifically influenced by large amounts of 0.9% saline infusion alone. Yet, the safety of 0.9% saline administration on coagulation profiles remains elusive in the presence of coexisting coagulopathy and/or pH as low as 7.1 when deleterious effects of acidosis on coagulation become evident [14,15].

In the current trial, arterial pH of patients who received 0.9% saline was significantly lower than those of patients with plasmalyte from 1 h after anesthetic induction until the end of the surgery. Also, significantly more patients exhibited a pH < 7.35 in the 0.9%

Table 4
Perioperative electrolytes and lactate concentrations.

	Sodium (mmol/l)		Potassium (mmol/l)		Chloride (mmol/l)		Magnesium (mg/dl)		Lactate (mmol/l)	
	0.9% Saline (n = 25)	Plasmalyte (n = 25)	0.9% Saline (n = 25)	Plasmalyte (n = 25)	0.9% Saline (n = 25)	Plasmalyte (n = 25)	0.9% Saline (n = 25)	Plasmalyte (n = 25)	0.9% Saline (n = 25)	Plasmalyte (n = 25)
10 min after induction	138 ± 3	138 ± 2	3.8 ± 0.4	3.6 ± 0.4	108 ± 2	108 ± 2	1.40 ± 0.13	1.36 ± 0.14	1.1 ± 0.6	1.1 ± 0.5
1 h after induction	139 ± 2	138 ± 2	3.8 ± 0.3	3.8 ± 0.5	110 ± 2	108 ± 3	1.38 ± 0.13	1.36 ± 0.13	1.0 ± 0.5	1.1 ± 0.5
2 h after induction	138 ± 3	138 ± 2	3.8 ± 0.4	3.8 ± 0.5	112 ± 3	109 ± 3*	1.29 ± 0.10	1.38 ± 0.17	1.1 ± 0.6	1.2 ± 0.6
3 h after induction	138 ± 3	138 ± 2	3.9 ± 0.4	3.8 ± 0.3	114 ± 4	111 ± 2*	1.29 ± 0.14	1.39 ± 0.13	1.1 ± 0.6	1.3 ± 0.8
4 h after induction	138 ± 2	137 ± 2	3.7 ± 0.3	3.8 ± 0.4	115 ± 2	110 ± 2*	1.19 ± 0.10	1.37 ± 0.13*	1.0 ± 0.4	1.2 ± 0.8
At the end of surgery	139 ± 3	137 ± 2	3.9 ± 0.4	3.9 ± 0.4	115 ± 3	111 ± 5*	1.23 ± 0.13	1.37 ± 0.13*	1.2 ± 0.7	1.4 ± 0.7
Postoperative 12 h	135 ± 4	134 ± 3	3.8 ± 0.6	3.8 ± 0.5	109 ± 4	107 ± 3	1.30 ± 0.14	1.35 ± 0.15	1.7 ± 0.8	1.5 ± 0.6

Data are expressed as mean ± SD. *$p < 0.05$ vs. 0.9% saline.

saline group compared with the plasmalyte group. The base excess and bicarbonate concentration still remained slightly lower in patients who received 0.9% saline compared to those who received plasmalyte at postoperative 12 h, while the serum chloride concentration returned to its baseline value. The observed trend towards a lower pCO_2 in patients who received 0.9% saline in the postoperative period implicates respiratory compensation. These findings imply that 0.9% saline infusion induced hyperchloremic metabolic acidosis.

Many experimental studies demonstrated the detrimental effects of acidosis. Acidosis was reported to depress myocardial contractility [16,17] and impair the response to catecholamines [18,19]. Moreover, hyperchloremia may induce renal vasoconstriction and impair renal function [5,20,21]. Indeed, difference in intraoperative urine output in our study suggests that hyperchloremia may influence renal function. Administration of 0.9% saline in human volunteers resulted in decreased renal blood flow velocity and renal cortical tissue perfusion compared with plasmalyte [22]. Emerging evidences suggest that use of 0.9% saline may be associated with increased mortality and major morbidity including acute kidney injury and need for renal replacement therapy [6,23].

Despite the development of acidosis, patients who received 0.9% saline showed no differences in intraoperative hemodynamic variables, postoperative serum Cr level and length of hospital stay compared to plasmalyte. Thus, transient, moderate acidemia may not result in significant physiologic disturbances or adverse clinical outcomes in relatively healthy patients as enrolled in this study. Metabolic acidosis, however, could be accentuated or prolonged in critically ill patients, especially in those with respiratory or renal insufficiency. Postoperative respiratory insufficiency might lead to CO_2 retention and disturb respiratory compensation of hyperchloremic metabolic acidosis which could be aggravated to the level of clinical relevance and detrimental postoperative outcome. Similarly, hyperchloremic metabolic acidosis might be troublesome in patients with renal insufficiency, since those patients exhibit reduced ability to handle chloride load and are prone to development of acidosis. Yet, due to a limited sample size, this study does not ensure the safety of 0.9% saline in terms of hard clinical endpoints. Also, it is beyond the scope of this study to draw any conclusions regarding the potential adverse influence of 0.9% saline in critically ill patients as these patients were not addressed in the current trial. Still, the results of the current trial clearly alarms the importance of the choice of isotonic crystalloid solution in patients undergoing extensive surgeries, as increased negative base-excess and lower bicarbonate concentrations persisted up to 12 h postoperatively, merely by the use of 3–4 L of 0.9% saline over a 5 h period, which is common to our daily anesthetic practice.

The limitations of this study are as follows. Patients in both groups received approximately 900 ml of 0.9% saline-based 6% hydroxyethyl starch 130/0.4, because balanced salt solution-based colloid was not available in Korea at the time of study. The amount of infused colloid, however, was limited to 20 ml/kg and was identical between the groups with a crystalloid to colloid ratio of 4:1. Moreover, since the patients in the plasmalyte group did not exhibit any acid-base or electrolyte imbalance, the influence of 0.9% saline-based 6% hydroxyethyl starch 130/0.4 on the observed results should have been negligible. Another limitation is that this study was not double-blinded. While the collection of data including ROTEM was done by a blinded investigator, the fluid type was not blinded to the anesthesiologists who conducted intraoperative fluid management.

5. Conclusion

Although coagulation profiles evaluated by ROTEM and intraoperative blood loss were not different between the patients received plasmalyte or 0.9% saline, intraoperative infusion of 0.9% saline was associated with the development of hyperchloremic metabolic acidosis contrary to plasmalyte in patients undergoing multi-level lumbar spinal surgery. Notwithstanding the negative experimental and clinical allegations with the use of 0.9% saline, a further study for the safety of large amount of 0.9% saline as a perioperative fluid in patients with reduced respiratory or renal compensatory reserve seems to be mandatory.

Ethical approval

This study was approved by the Institutional Ethics Committee of Yonsei University College of Medicine (4-2012-0059).

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Author contribution

Young-Lan Kwak and Jae-Kwang Shim: Conception and design of the study, interpretation of data.

Na Young Kim and Jaewon Jang: Data collection.

Jong Wook Song: Analysis and interpretation of data, drafting of the manuscript.

Conflict of interest

None.

Guarantor

Young Lan Kwak, MD, PhD.

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