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Original Article

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Use of a Novel Buffered Hypertonic Saline Solution for Fluid Replacement and Resuscitation During Spinal Surgery in Adolescents

Maria Lysandrou[a], Julie Rice-Weimer[b], Sibelle Aurelie Yemele Kitio[b], Islam Elmitwalli[b], Allen Kadado[c], Walter Samora[c], Marco Corridore[c, d], Joseph D. Tobias[c, d, e]

Abstract

Background: During major orthopedic procedures, such as posterior spinal fusion (PSF), isotonic fluids, colloids, starches, or gelatins are commonly used to replace the preoperative fluid deficit and provide ongoing fluid resuscitation. Given recent concerns regarding the potential adverse physiologic effects of albumin solutions, we have modified our intraoperative practice to include the use of a novel 2% buffered hypertonic saline solution during major orthopedic procedures. We present our preliminary clinical experience with this novel fluid for intraoperative resuscitation and its impact on limiting the use of 5% albumin.

Methods: A retrospective review was performed to identify patients who received 2% buffered hypertonic saline during PSF. The intraoperative course of these patients was compared to case-matched control patients who received standard care with isotonic fluids plus 5% albumin as an adjunct for intravascular resuscitation.

Results: The study cohort included 23 patients who received 2% buffered hypertonic saline and 25 in the case-matched control group. There was no difference in the volume of intraoperative isotonic crystalloid fluids, estimated blood loss, and urine output between the two groups. In the control cohort, 19 of 25 patients (76%) received 5% albumin compared to only six of 23 patients (26%, P = 0.0005) in the 2% buffered hypertonic saline group. The final pH was higher in the patients that received 2% buffered hypertonic saline than in the control group (7.40 ± 0.03 versus 7.36 ± 0.06, P = 0.0131). Additionally, the starting and final serum sodium values were higher in the patients that received 2% buffered hypertonic saline, although no difference was noted in the mean change from the starting value (average increase of 2 mEq/L in both groups).

Conclusion: Use of a novel 2% buffered hypertonic saline solution for intraoperative resuscitation during major orthopedic procedures decreases the need for 5% albumin while avoiding the development of hyperchloremic metabolic acidosis which may occur with standard sodium chloride solutions.

Keywords: Posterior spinal fluid; Blood loss; Resuscitation; Anesthetic care; Hypertonic saline; Albumin

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[a]The Ohio State University College of Medicine, Columbus, OH, USA
[b]Department of Anesthesiology & Pain Medicine, Nationwide Children's Hospital, Columbus, OH, USA
[c]Division of Pediatric Orthopedic Surgery, Nationwide Children's Hospital and The Ohio State University, Columbus, OH, USA
[d]Department of Anesthesiology & Pain Medicine, The Ohio State University College of Medicine, Columbus, OH, USA
[e]Corresponding Author: Joseph D. Tobias, Department of Anesthesiology & Pain Medicine, Nationwide Children's Hospital, Columbus, OH 43205, USA. Email: Joseph.Tobias@Nationwidechildrens.org

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Introduction

During major orthopedic procedures such as posterior spinal fusion (PSF), intraoperative fluid resuscitation is required to replace the preoperative fluid deficit and treat hemodynamic changes caused by third spacing and blood loss. In addition to isotonic fluids, colloids such as 5% albumin are frequently administered as a means of increasing intravenous volume and potentially decreasing the need for allogeneic transfusions. Over the past 5 - 10 years, there has been increasing scrutiny and assessment of clinical information regarding the impact of colloids on perioperative outcomes. The analysis suggests that 5% albumin, and other colloids, may have adverse physiologic effects, including activation of the inflammatory cascade which may lead to increased perioperative morbidity and mortality [1-5]. Additionally, the impact of COVID and supply chain issues led to decreased availability of albumin solutions for clinical use, thereby necessitating investigation of other options for intraoperative resuscitation.

Various clinical studies have suggested the potential benefits of resuscitation with hypertonic saline solutions (3-7.5%) in various perioperative and trauma scenarios [6-8]. The use of these hypertonic solutions potentially allows for the limitation of total fluid volume with the same impact on intravascular volume. Intraoperative administration of hypertonic saline solutions (3-7.5%) has been shown to have beneficial effects on cardiovascular function, hemodynamic parameters, and intracranial pressure (ICP). This has led to our use of a novel 2% buffered hypertonic saline solution for intraoperative re-

suscitation during major orthopedic procedures. We retrospectively reviewed our experience with this novel fluid during intraoperative care during surgical correction (PSF) in patients with idiopathic scoliosis. The primary objective was to evaluate the impact of buffered hypertonic saline on 5% albumin administration. Secondary objectives included the impact of the 2% buffered hypertonic saline solution on acid-base status, prevention of hyperchloremic acidosis and other laboratory parameters.

Materials and Methods

This retrospective study was approved by the Institutional Review Board of Nationwide Children's Hospital (Columbus, Ohio) and was conducted in compliance with the ethical standards of clinical research on human subjects and the Helsinki Declaration. As a retrospective study, the need for individual written informed consent was waived. To maintain patient confidentiality, only deidentified data were used for the purpose of this study. Data collected during this study were stored in a secure location and only the collaborators directly involved in this study had access. All electronic files were stored on a secure, password-protected network.

Using pharmacy and surgical databases, patients with idiopathic scoliosis undergoing PSF were identified from March 2018 to December 2022. Patients with non-idiopathic scoliosis including neuromuscular, congenital, and traumatic were excluded. Additionally, patients with significant comorbid cardiac, pulmonary, or renal conditions were excluded. There were two groups evaluated in the retrospective review: patients who received 2% buffered hypertonic saline and a control group who were case- and age-matched. The patients received perioperative care following the introduction of 2% buffered hypertonic saline in our operating room. All patients with idiopathic surgery who underwent PSF and received 2% buffered hypertonic saline were included in the treatment group (n = 23). Twenty-five age- and weight-matched patients also undergoing PSF for idiopathic scoliosis over the same time period were selected as a control group. The control patients received standard intraoperative fluid resuscitation with isotonic crystalloids, primarily Normosol®-R. In both groups, 5% albumin was available for resuscitation as deemed clinically necessary by the intraoperative team.

Demographic data obtained included age, gender at birth, race, ethnicity, weight, height, associated comorbid conditions, and date of birth. Procedural information included the type of procedure, surgical duration, and total intraoperative time. Surgical data obtained included the degree of the preoperative and postoperative curve, the levels involved in the PSF, and whether osteotomies were performed or not. Intraoperative times, fluids, and medications administered were collected and analyzed. This included anesthesia start and finish time, procedure start and finish time, total urine output, estimated blood loss, the type and volume of blood products if administered, use of tranexamic acid, type of general anesthesia (volatile-based with desflurane or total intravenous anesthesia with propofol), opioid infusion (remifentanil or sufentanil), and intraoperative fluids including volume of isotonic fluids (Normosol®-R, 0.9% normal saline or lactated Ringers), 2% buffered hypertonic saline, and 5% albumin. Additionally, the use of rescue medications including anticholinergic agents (atropine or glycopyrrolate) or vasoactive agents (epinephrine, phenylephrine, vasopressin, or ephedrine) was noted.

Laboratory and hemodynamic data were also collected. This included the preoperative and postoperative hemoglobin and hematocrit as well as the first and last arterial blood gas (pH, $PaCO_2$, PaO_2, base deficit, and glucose). Intraoperative and postoperative adverse effects including hypotension, bradycardia, respiratory arrest, apnea, or hypoventilation were identified.

The 2% buffered hypertonic saline solution includes sodium acetate which is intended to limit the hyperchloremic acidosis seen following resuscitation with other sodium chloride solutions (0.9-7.5% saline). The final composition of the 2% buffered hypertonic saline solution includes 176 mEq/L of sodium chloride and 120 mEq/L of sodium acetate for a final sodium concentration of 296 mEq/L. The 2% sodium concentration has a low enough osmolarity to be less caustic to peripheral veins and therefore safe to use peripherally. It was administered intraoperative peripherally either via an infusion pump at 50 - 150 mL/h or as a bolus resuscitation fluid through a fluid warmer.

A study by Martin et al outlined our general departmental practice for the provision of intraoperative anesthetic care during PSF including neurophysiological monitoring with motor and somatosensory evoked potentials [9]. Preoperative medications included placement of a scopolamine patch and the oral administration of aprepitant (40 mg) as prophylaxis against postoperative nausea and vomiting (PONV). Oral gabapentin was administered as an adjunct to postoperative analgesia. Techniques to limit the need for allogeneic blood products included control of the mean arterial pressure (MAP), intraoperative blood salvage, and the administration of tranexamic acid (bolus and infusion).

Anesthetic induction included the inhalation of increasing concentrations of sevoflurane or the administration of intravenous propofol. Following anesthetic induction, a neuromuscular blocking agent (rocuronium 0.2 - 0.3 mg/kg) was administered to facilitate endotracheal intubation. Two peripheral intravenous cannulas and an arterial cannula were then placed. Maintenance anesthesia consisted of inhaled desflurane, adjusted to maintain the bispectral index (BIS) at 40 - 60 to ensure amnesia. Methadone (0.1 mg/kg) and an opioid infusion (remifentanil or sufentanil) were then administered. The opioid infusion was adjusted to maintain the MAP at 55 - 65 mm Hg. Clevidipine or labetolol were administered as needed as adjuncts for MAP control. Acetaminophen (15 mg/kg) to a maximum dose of 1,000 mg was administered intraoperatively as an adjunct to postoperative analgesia. Additional prophylaxis against PONV included intravenous ondansetron (4 mg) and dexamethasone (8 mg).

Study data were collected and managed using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at Nationwide Children's Hospital [10, 11]. REDCap is a secure, web-based software platform designed to sup-

Table 1. Demographic Data of the Study Groups

Variables	Hypertonic saline (n = 23)	Control group (n = 25)	Entire cohort (n = 48)
Age (years)	15.4 ± 1.9 (11.5 - 19.0)	14.9 ± 1.9 (12.4 - 19.7)	15.1 ± 1.9 (11.5 - 19.6)
Gender (female/male)	17/6	19/6	36/12
Weight (kg)	60.0 ± 17.3 (34.3 - 97.3)	63.1 ± 30.8 (33.2 - 173.6)	61.6 ± 25.0 (33.2 - 173.6)
Height (cm)	160.3 ± 24.0 (58.2 - 179.3)	155.3 ± 22.2 (57.7 - 177.5)	157.7 ± 22.9 (57.7 - 179.3)
Ethnicity			
Hispanic	1 (4%)	0	1 (2%)
Non-Hispanic	22 (96%)	25 (100%)	47 (98%)
Race			
Caucasian	18 (78%)	18 (72%)	36 (75%)
African American	3 (13%)	4 (16%)	7 (15%)
Asian	1 (4%)	1 (4%)	2 (4%)
Multi-racial	0 (0%)	1 (4%)	1 (2%)
Other	1 (4%)	1 (4%)	2 (4%)

Data are listed as the mean ± SD (range) or number (%). There were no statistically significant differences among the groups. SD: standard deviation.

port data capture for research studies, providing an intuitive interface for validated data capture; audit trails for tracking data manipulation and export procedures; automated export procedures for seamless data downloads to common statistical packages; and procedures for data integration and interoperability with external sources. Data collected during this study were stored in secure, password-protected computer files. Only trained members of the research team and collaborators directly involved with the research project had access to the data. Subjects and their information were closely monitored by study staff. For the purpose of publication, de-identified data are used.

Statistical analysis

Statistical analysis was initiated with a descriptive approach to gain comprehensive insights into the dataset. Continuous variables were summarized using mean ± standard deviation (SD), and group differences were assessed using the *t*-test. Categorical variables were presented as counts and percentages, and statistical tests such as Chi-square test or Fisher's exact test were employed as appropriate. To evaluate disparities in albumin usage between the hypertonic saline group and the control group, a Chi-squared analysis was performed. Meanwhile, differences in intraoperative fluids volume and intraoperative laboratory values between the two groups were assessed using non-paired *t*-test. All statistical analyses were conducted using SAS (Statistical Analysis System) 9.4, and the threshold for determining statistical significance was set at a P-value less than 0.05.

Results

The study cohort included 48 American Society of Anesthesiologists physical classification 1 or 2 patients who received intraoperative care during PSF for idiopathic scoliosis. There were 23 patients who received 2% buffered hypertonic saline and 25 patients in the case- and age-matched control group who received standard care with isotonic fluids. The demographic data are listed in Table 1. There were no statistically significant differences in the demographic data between the two groups. Intraoperative anesthetic and surgical data are listed in Table 2. There was no difference between the two groups in respect to performance of osteotomies as part of the surgical procedure, anesthesia time, surgical time, intraoperative urine output, and estimated blood loss.

Intraoperative fluid administration including isotonic fluids (Ringers lactate, Normosol®-R, and 0.9% normal saline),

Table 2. Intraoperative Anesthetic and Surgical Data

Variable	Hypertonic saline (n = 23)	Control (n = 25)	Entire cohort (n = 48)
Osteotomy performed (yes/no)	17 (74%)/6	16 (64%)/9	33 (69%)/15
Total anesthesia time (min)	398 ± 79 (271 - 519)	370 ± 48 (270 - 459)	383 ± 60 (270 - 519)
Total surgical time (min)	282 ± 66 (180 - 409)	251 ± 45 (159 - 336)	265 ± 58 (159 - 409)
Urine output (mL)	619 ± 415 (110 - 1,655)	504 ± 343 (110 - 1,500)	559 ± 380 (110 - 1,655)
Estimated blood loss (mL)	411 ± 290 (50 - 1,200.00)	523 ± 225 (150 - 1,100)	471 ± 261 (50 - 1,200)

Data are listed as the mean ± SD (range) or the number (%). There were no statistical differences between the two groups. SD: standard deviation.

Table 3. Intraoperative Fluid Administration

Fluids	Hypertonic saline (n = 23)	Control (n = 25)	Entire cohort (n = 48)	P value*
Albumin used (number and %)	6 (26%)	19 (76%)	25 (52%)	0.0005
Volume of albumin (mL)[a]	91 ± 164 (0 - 500)	370 ± 271 (0 - 1,000)	-	< 0.0001
Crystalloid fluids (mL)[b]	1,484 ± 678 (320 - 3,113)	1,652 ± 522 (645 - 2,535)	1,571 ± 602 (320 - 3,113)	0.3392
2% hypertonic saline (mL)	646 ± 402 (233 - 2,000)	-	-	-

Data are listed as the mean ± SD (range) or the number (%). *P value for hypertonic saline versus control group. [a]Volume of albumin administered is calculated using a denominator of 23 in the hypertonic saline cohort and 25 in the control cohort. Volumes were equivalent if the calculation is completed using only those patients that received albumin (333 ± 129 mL in the 2% buffered hypertonic saline cohort versus 487 ± 195 mL in the control cohort). [b]Volume of crystalloid includes all intraoperative fluids including normal saline, lactated Ringer's, and Normosol®-R. SD: standard deviation.

5% albumin, and 2% hypertonic saline are listed in Table 3. There was no difference in the volume of isotonic crystalloid fluids between the two groups. Twenty-six percent of patients (six of 23) in the 2% buffered hypertonic saline cohort received albumin compared to 76% (19 of 25, P = 0.0005) of patients in the control cohort. The volume of 5% albumin was also lower in the patients that received 2% hypertonic saline (91 ± 164 mL versus 370 ± 271 mL, P < 0.0001). In the entire cohort of 48 patients, three received an allogeneic transfusion including one in the 2% buffered hypertonic saline group and two in the control group.

Intraoperative laboratory values at the start and the end of the case are listed in Table 4. There was no difference in the starting hemoglobin or hematocrit between the two groups. The ending hemoglobin was slightly lower in the control group (11.4 ± 1.4 versus 9.9 ± 1.7 g/dL, P = 0.0042), although there was no statistically significant difference in the ending hematocrit. The final pH was higher in the patients that received 2% buffered hypertonic saline than in the control group (7.40 ± 0.03 versus 7.36 ± 0.06, P = 0.0131). Additionally, the starting and final serum sodium values were higher in the patients that received 2% buffered hypertonic saline, although no difference was noted in the mean change from the starting value (average increase of 2 mEq/L in both groups).

Discussion

Albumin is a natural plasma protein synthesized by the liver with a plasma half-life of 18 - 19 days. It is the primary factor for maintaining colloid osmotic pressure, controlling the transmembrane movement of fluid, and maintaining intravascular volume [12]. Albumin was one of the first human proteins to be identified and extracted from plasma for clinical use with initial solutions available during the 1940s [13, 14]. Improved outcomes during the initial clinical trials with albumin resuscitation in critically ill trauma and burn patients resulted in early acceptance of the use of albumin for volume resuscitation. However, these clinical practices were not driven on clear evidence-based medicine and these practices were challenged by a meta-analysis, published in 1998, and other more carefully controlled studies which reported increased mortality in critically ill patients who received albumin solutions during critical illness or trauma [15-17]. These concerns coupled with the cost of albumin and a recent supply chain shortage during the COVID pandemic led to our re-evaluation of the use of 5% albumin for resuscitation during intraoperative care of patients undergoing major orthopedic surgery including PSF. In an attempt to limit the need for resuscitation with 5% albumin, we introduced a novel 2% buffered hypertonic saline solution as

Table 4. Intraoperative Laboratory Values

Variables	Hypertonic saline (n = 23)	Control (n = 25)	P-value*
First hemoglobin (g/dL)	11.3 ± 2.8	11.6 ± 1.2	NS
Last hemoglobin (g/dL)	11.4 ± 1.4	9.9 ± 1.7	0.0042
First hematocrit (%)	35.7 ± 5.6	35 ± 3	NS
Last hematocrit (%)	33.2 ± 8.5	30 ± 5	NS
First pH	7.43 ± 0.04	7.41 ± 0.04	NS
Last pH	7.40 ± 0.03	7.36 ± 0.06	0.0131
First $PaCO_2$ (mm Hg)	38 ± 4	38 ± 4	NS
Last $PaCO_2$ (mm Hg)	41 ± 4	41 ± 6	NS
First base deficit	1.3 ± 1.2	1.0 ± 1.0	NS
Last base deficit	2.1 ± 4.5	2.6 ± 2.1	NS
First sodium (mEq/L)	141 ± 2	139 ± 2	0.0008
Last sodium (mEq/L)	143 ± 3	141 ± 3	0.0061

Data are listed as the mean ± SD. *P value for hypertonic saline versus control group. SD: standard deviation.

an alternative to 5% albumin for intraoperative fluid resuscitation during major surgical procedures. After the introduction of this solution into our clinical practice and education regarding the potential safety issues and availability of 5% albumin solutions, we saw a significant decrease in the use of albumin with a decrease in albumin use from 76% in the control group to 26% in patients who received 2% buffered hypertonic saline during PSF.

Hypertonic saline solutions have been used in both experimental and clinical scenarios since the early 1900s with clinical trials regarding its effects on brain volume and ICP in 1919 [18, 19]. Although used primarily for the resuscitation of patients with traumatic brain injury or increased ICP, these solutions have also seen clinical use for intravascular resuscitation in shock of other causes and various other clinical scenarios [6]. Hypertonic fluids contain a higher concentration of sodium and hence solute when compared to the plasma and interstitial fluid. The sodium contents of these solutions vary from 1.8% to 30%, although 3-5% solutions are used most commonly in clinical practice. The osmotic gradient that is created from the higher serum (intravascular) concentration of sodium results in the movement of fluid into the intravascular space and an increase in intravascular volume thereby increasing preload. Cardiac output increases related to increased preload, as well as additional effects on the microvascular circulation with decreased afterload and decreased viscosity [20]. During critical illness and shock, endothelial cell volume can increase due to increased cell membrane permeability leading to an increase in intracellular water and fluid accumulation. The increased tonicity of hypertonic saline reduces intracellular volume and normalizes endothelial cell volume. As a result, capillary diameter increases and resistance to microcirculatory flow decreases, thereby restoring regional blood flow. Additionally, hypertonicity results in arteriolar dilatation, which along with restoration of regional blood flow and microcirculatory flow, decreases afterload and pulmonary vascular resistance. Direct effects on improvement in myocardial performance may also be seen through a reduction of edema and improved calcium handling by myocardial cells. These effects and the restoration of intravascular volume occur with significantly less total fluid than when using isotonic solutions.

In addition to these physiologic benefits, there is a relatively benign adverse effect profile with the administration of hypertonic saline solutions, with the primary concerns being the development of a hyperosmolar state or a hyperchloremic metabolic acidosis related to the administration of large volumes over a protracted period of time [21]. While the exact physiologic and end-organ effects of the hyperchloremic metabolic acidosis remain controversial, adult studies have suggested several potential deleterious effects of hyperchloremia including an increased incidence of mortality, length of hospitalization, and kidney injury [22-24]. Given these concerns, we routinely use balanced isotonic fluids with physiologic chloride concentrations and buffer (acetate and gluconate) such as Normosol®-R for intraoperative care during major surgical procedures [25]. Previous work has demonstrated that patients receiving 0.9% saline compared to Normosol®-R had a greater change in the base deficit and a lower pH during major orthopedic surgical procedures.

When we decided to use hypertonic saline for intraoperative resuscitation, we worked with our pharmacy to develop a unique buffered solution to potentially avoid hyperchloremic metabolic acidosis. This included development of the components of the solution including sodium, chloride, and acetate as well as their concentrations. Additionally, a pathway was developed for compounding the solutions, storing it in the operating room pharmacy, and the addition of an order set for 2% buffered hypertonic saline to the electronic medical record. The solution used for the current study (2% buffered hypertonic saline) contains sodium (296 mEq/L), chloride (176 mEq/L), and acetate (120 mEq/L). Patients in the 2% buffered saline group received an average of 564 mL of the solution during intraoperative care. In those patients, there was no statistically significant change or difference in pH and base deficit when comparing the final laboratory values to the starting values. When comparing the starting pH, there was no difference between the two groups (7.43 ± 0.4 versus 7.41 ± 0.04); however, the final pH was higher in the buffered hypertonic saline group (7.40 ± 0.03 versus 7.36 ± 0.06, $P = 0.0131$) when compared to patients who received balanced isotonic fluids (Normosol®-R) and 5% albumin. There was no clinically significant increase in the sodium values during resuscitation in the 2% buffered hypertonic saline group. Sodium values increased by an average of 2 mEq/L from baselines and were 2 mEq/L greater than the control group. However, the potential for hypernatremia and hyperosmolarity would vary depending on the volume of resuscitation fluid required. Therefore, as resuscitation is achieved with hypertonic saline solutions, ongoing monitoring of serum sodium values is suggested.

As a retrospective study, there are specific limitations that must be recognized. Randomization was not controlled and we used age- and weight-matched control patients who did not receive 2% buffered hypertonic as a comparator group. We believe that the impact of this concern was mitigated to some extent by our general practice and the use of a standardized anesthetic approach for intraoperative care of these patients. As a retrospective study, a power analysis was not feasible, although the study did reach statistical significance when comparing 5% albumin use and specific laboratory parameters between the two groups. The availability of specific laboratory parameters for comparison was limited to those laboratory parameters that are routinely obtained during these cases including arterial blood gas analysis, hemoglobin/hematocrit, and sodium. With a limited cohort of 48 patients in both groups, it was not feasible to perform intragroup subset analysis to determine the impact of specific demographic factors on laboratory and clinical outcomes.

In summary, we have found that the use of a unique 2% buffered hypertonic saline solution can limit the clinical need for colloid resuscitation (5% albumin) during major orthopedic surgical procedures such as PSF. This is the first report of the clinical use of this unique fluid as well as demonstration of its impact on intraoperative 5% albumin use and laboratory parameters including pH and serum sodium values. The unique buffered solution avoids the development of hyperchloremic metabolic acidosis which may be seen with standard hypertonic solutions containing only sodium chloride. Additionally, by using a 2% solution, administration via a peripheral intrave-

nous cannula is feasible as the potential for thrombophlebitis or tissue injury with inadvertent extravasation should be less than what may occur with a standard 3% solution. As it is prepared in a sterile environment, it may be stored for up to 30 h for later use. This unique solution may offer an option for intraoperative resuscitation in various other clinical scenarios.

Acknowledgments

None to declare.

Financial Disclosure

None to declare.

Conflict of Interest

None to declare.

Informed Consent

As a retrospective study, the need for individual written informed consent was waived.

Author Contributions

ML: data collection and analysis, preparation of initial and subsequent drafts, review of final manuscript; JRW, IE, and MC: study coordinator and compliance regulation, data collection and analysis, review of drafts and final manuscript; SAYK: data analysis, preparation of tables, review of drafts and final manuscript; AK and WS: surgical care of patients, review of drafts and final manuscript; JDT: study oversight, preparation, review of drafts and final manuscript.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

References

1. Finfer S, Bellomo R, Boyce N, French J, Myburgh J, Norton R, Investigators SS. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. N Engl J Med. 2004;350(22):2247-2256. doi pubmed
2. Vincent JL, Navickis RJ, Wilkes MM. Morbidity in hospitalized patients receiving human albumin: a meta-analysis of randomized, controlled trials. Crit Care Med. 2004;32(10):2029-2038. doi pubmed
3. Melia D, Post B. Human albumin solutions in intensive care: A review. J Intensive Care Soc. 2021;22(3):248-254. doi pubmed pmc
4. Hanley C, Callum J, McCluskey S, Karkouti K, Bartoszko J. Albumin use in bleeding cardiac surgical patients and associated patient outcomes. Can J Anaesth. 2021;68(10):1514-1526. doi pubmed
5. Dingankar AR, Cave DA, Anand V, Sivarajan VB, Nahirniak S, Sheppard C, Hanot J, et al. Albumin 5% versus crystalloids for fluid resuscitation in children after cardiac surgery. Pediatr Crit Care Med. 2018;19(9):846-853. doi pubmed
6. Strandvik GF. Hypertonic saline in critical care: a review of the literature and guidelines for use in hypotensive states and raised intracranial pressure. Anaesthesia. 2009;64(9):990-1003. doi pubmed
7. Wang BW, Chiou YH, Chen WB, Peng TY, Leung HK. Intravenous pretreatment of hypertonic saline can prevent systemic hypotension induced by spinal anesthesia. Acta Anaesthesiol Sin. 1997;35(2):85-90. pubmed
8. Kashefi P, Montazeri K, Hashemi ST. Effect of hypertonic saline on hypotension following induction of general anesthesia: A randomized controlled trial. Adv Biomed Res. 2014;3:183. doi pubmed pmc
9. Martin DP, Bhalla T, Thung A, Rice J, Beebe A, Samora W, Klamar J, et al. A preliminary study of volatile agents or total intravenous anesthesia for neurophysiological monitoring during posterior spinal fusion in adolescents with idiopathic scoliosis. Spine (Phila Pa 1976). 2014;39(22):E1318-1324. doi pubmed
10. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42(2):377-381. doi pubmed pmc
11. Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, McLeod L, et al. The REDCap consortium: Building an international community of software platform partners. J Biomed Inform. 2019;95:103208. doi pubmed pmc
12. Fanali G, di Masi A, Trezza V, Marino M, Fasano M, Ascenzi P. Human serum albumin: from bench to bedside. Mol Aspects Med. 2012;33(3):209-290. doi pubmed
13. Matejtschuk P, Dash CH, Gascoigne EW. Production of human albumin solution: a continually developing colloid. Br J Anaesth. 2000;85(6):887-895. doi pubmed
14. Nicholson JP, Wolmarans MR, Park GR. The role of albumin in critical illness. Br J Anaesth. 2000;85(4):599-610. doi pubmed
15. Cochrane Injuries Group Albumin Reviewers. Human albumin administration in critically ill patients: systematic review of randomised controlled trials. BMJ. 1998;317(7153):235-240. doi pubmed pmc
16. SAFE Study Investigators; Australian and New Zealand Intensive Care Society Clinical Trials Group; Australian Red Cross Blood Service; George Institute for International Health; Myburgh J, Cooper DJ, Finfer S, Bellomo R, Norton R, Bishop N, et al. Saline or albumin for fluid resuscitation in patients with traumatic brain injury. N Engl J Med. 2007;357(9):874-884. doi pubmed

17. SAFE Study Investigators, Finfer S, McEvoy S, Bellomo R, McArthur C, Myburgh J, Norton R. Impact of albumin compared to saline on organ function and mortality of patients with severe sepsis. Intensive Care Med. 2011;37(1):86-96. doi pubmed
18. Sutherland WD, McCay D. Observations on the inhibitory influence exerted by hypertonic saline solutions and calcium chloride solutions on the action of specific haemolysins, with suggestions as to the therapy of blackwater fever. Biochem J. 1911;5(1-3):1-22. doi pubmed pmc
19. Weed MP, McKibben LH. Experimental alteration of brain bulk. Amer J Phys. 1919;48:531-560
20. Ziai WC, Toung TJ, Bhardwaj A. Hypertonic saline: first-line therapy for cerebral edema? J Neurol Sci. 2007;261(1-2):157-166. doi pubmed
21. Kolsen-Petersen JA, Nielsen JO, Tonnesen E. Acid base and electrolyte changes after hypertonic saline (7.5%) infusion: a randomized controlled clinical trial. Scand J Clin Lab Invest. 2005;65(1):13-22. doi pubmed
22. Neyra JA, Canepa-Escaro F, Li X, Manllo J, Adams-Huet B, Yee J, Yessayan L, et al. Association of hyperchloremia with hospital mortality in critically ill septic patients. Crit Care Med. 2015;43(9):1938-1944. doi pubmed pmc
23. Yunos NM, Bellomo R, Hegarty C, Story D, Ho L, Bailey M. Association between a chloride-liberal vs chloride-restrictive intravenous fluid administration strategy and kidney injury in critically ill adults. JAMA. 2012;308(15):1566-1572. doi pubmed
24. McCluskey SA, Karkouti K, Wijeysundera D, Minkovich L, Tait G, Beattie WS. Hyperchloremia after noncardiac surgery is independently associated with increased morbidity and mortality: a propensity-matched cohort study. Anesth Analg. 2013;117(2):412-421. doi pubmed
25. King M, Martin D, Miketic R, Beebe A, Samora W, Klamar J, Tumin D, et al. Impact of intraoperative fluid management on electrolyte and acid-base variables during posterior spinal fusion in adolescents. Orthop Res Rev. 2020;12:69-74. doi pubmed pmc