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Effect of Normal Saline versus PlasmaLyte on Coagulation and Metabolic Status in Patients Undergoing Neurosurgical Procedures

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Abstract

Background The choice of intraoperative fluid in neurosurgical patients is important as we need to maintain adequate cerebral perfusion and oxygenation and also avoid cerebral edema. Normal saline (NS) is commonly used in neurosurgeries, but it leads to hyperchloremic metabolic acidosis, which may result in coagulopathy. Balanced crystalloid with physiochemical composition akin to that of plasma has favorable effects on metabolic profile and may avoid the problems associated with NS. Against this background, the present study aimed to compare the effects of NS versus PlasmaLyte (PL) on coagulation profile in patients undergoing neurosurgical procedures.

Methods This prospective, randomized, double-blinded study was conducted in 100 adult patients scheduled to undergo various neurosurgical procedures. Patients were randomly allocated in two groups of 50 each to receive either NS or PL intraoperatively and postoperatively till 4 hours after the surgery. Hemoglobin, hematocrit, coagulation profile (PT, PTT, and INR), serum chloride, pH, blood urea, and serum creatinine were measured prior to induction (baseline) and 4 hours after completion of surgery.

Results Demographic characteristics were statistically similar between the two groups. Coagulation profile parameters were comparable between the two groups at baseline as well as 4 hours after surgery. pH was significantly lower in the NS group as compared to the PL group at 4 hours after surgery. Postoperatively blood urea, serum creatinine, and serum chloride levels were significantly raised in the NS group as compared to the PL group. Hemoglobin and hematocrit values were similar between the two groups.

Conclusion Coagulation profile parameters were normal and statistically similar with intraoperative infusion of NS versus PL in patients undergoing neurosurgical procedures. However, use of PL was associated with a better acid–base and renal profile in these patients.

Keywords
- coagulopathy
- crystalloid
- PlasmaLyte
- normal saline
- neurosurgery

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Introduction

Neurosurgeries are frequently associated with prolonged duration and increased losses requiring significant fluid resuscitation intraoperatively, which results in hemodilution and consecutive coagulopathy. The type of fluid used may have further implications on coagulation.

Normal saline (NS) is the most frequent used crystalloid but may lead to coagulopathy due to hyperchloremic metabolic acidosis and renal dysfunction.[1–4] Recently balanced crystalloid (BC) solutions such as PlasmaLyte (PL) and Kabilyte having composition akin to that of plasma have come into use. The osmolality of BC is 295 mOsm/kg and its pH is 7.4.[3] Each 1,000 mL of PL contains 5.26 g sodium chloride, 370 mg KCl, 300 mg magnesium chloride, 3.68 g sodium acetate, and 5.02 g sodium gluconate, which equates to 140 mmol/L sodium, 5 mmol/L potassium, 1.5 mmol/L magnesium, 98 mmol/L chloride, 27 mmol/L acetate, and 23 mmol/L gluconate. PL, being a more physiological solution, has favorable effects on metabolic and renal profile.[3]

Against this background, the present study aimed to compare effects of NS versus PL on coagulation profile in patients undergoing neurosurgical procedures.

Materials and Methods

The present prospective, randomized, double-blinded study was carried out in the Department of Anesthesiology and Critical Care in a tertiary care institute following approval from Institutional Ethics Committee (IEC). Study participants included 100 adult patients (18–45 years of age) of either sex belonging to American Society of Anesthesiologists (ASA) classes I to II, undergoing neurosurgeries for various conditions (infratentorial tumors, supratentorial tumors, and traumatic brain injury patients).

Patients having dyselectrolytemias, preoperative Glasgow Coma Scale (GCS) less than 13, hemodynamic instability, preexisting renal failure (serum creatinine > 2), coagulation abnormalities, and diabetes mellitus were excluded from the study.

Informed witnessed consent for participation in the study was obtained from all the patients. Findings of computed tomography (CT) scan (brain) and magnetic resonance imaging (MRI; brain) were noted. Preoperative fasting of 6 hours prior to surgery was ensured. The patients were randomized into two groups on the basis of computer-generated randomization numbers with the help of https://www.random.org. The NS group ($n = 50$) received NS and the PL group ($n = 50$) received isotonic BC (PL) intraoperatively and postoperatively till 4 hours after the surgery.

In the operating room, all routine monitors such as heart rate (HR), electrocardiography (ECG), noninvasive blood pressure (NIBP), and pulse oximetry (SpO_2) were attached. Intravenous (IV) access was obtained and a blood sample was sent for hemoglobin, hematocrit, coagulation profile (prothrombin time [PT], partial thromboplastin time [PTT], and international normalized ratio [INR]), serum chloride, blood urea, and serum creatinine to record baseline values. Left radial artery cannulation was done to monitor invasive blood pressure (BP). Arterial blood gas (ABG) analysis was done to record the baseline pH. IV fluid was administered as per group allocation.

Preoxygenation was done and standard induction protocol comprising of fentanyl 2 mcg/kg, propofol 2 mg/kg, and vecuronium 0.1 mg/kg was followed in all patients. After tracheal intubation, patients were ventilated with volume control mode with tidal volume = 7 mL/kg, flow rate = 2.5 L/min, and inspiratory:expiratory (I:E) ratio = 1:2, and frequency was titrated to keep $EtCO_2$ between 28 and 32 mm Hg. Under all aseptic precautions, the right subclavian vein was cannulated using a 7-Fr triple lumen central venous cannula. Temperature probe (nasopharyngeal) and Foley's catheter were also secured.

Maintenance of anesthesia was done with oxygen (40%) and nitrous oxide (60%) in isoflurane (0.8–1.2 minimum alveolar anesthetic concentration [MAC]). For intraoperative analgesia, fentanyl 1 mcg/kg and for neuromuscular relaxation, vecuronium 1 mg were given hourly. Mannitol 1 g/kg was administered to all the patients before opening of the dura. Fluid was administered as per the CVP guidance, which was maintained between 8 and 12 cmH_2O. Blood transfusion was carried out in accordance to the ASA guidelines.[5] Following completion of surgery, neuromuscular blockade was reversed with glycopyrrolate 0.01 mg/k and neostigmine 0.05 mg/kg. After tracheal extubation, patients were shifted to postanesthesia care unit and the IV fluid was continued as per group allocation at 2 mL/kg/h. Blood samples were sent at 4 hours after extubation for pH (ABG), hemoglobin, hematocrit, coagulation profile (PT, PTT, and INR), serum chloride, blood urea, and serum creatinine.

All parameters were recorded at baseline and 4 hours after extubation. Total amount of intraoperative crystalloid and blood products transfused, blood loss, urine output, and duration of surgery were also recorded.

Sample Size

The study of Dey et al[3] observed that pH and creatinine in the NS group was 7.43 ± 0.07 and 0.98 ± 0.2, respectively, and 7.47 ± 0.04 and 0.74 ± 0.2, respectively, in the PL group. Taking these values as reference, the minimum required sample size with 90% power and 5% level of significance is 43 patients in each study group. To reduce the margin of error, the total sample size taken was 100 (50 patients per group).

Statistical Analysis

The data entry was done in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software version 25.0 (IBM, Chicago, Illinois, United States). The quantitative data with normal distribution were presented as the mean ± SD and the data with non-normal distribution as median with the 25th and 75th percentiles (interquartile range). The quantitative variables were analyzed using Mann–Whitney

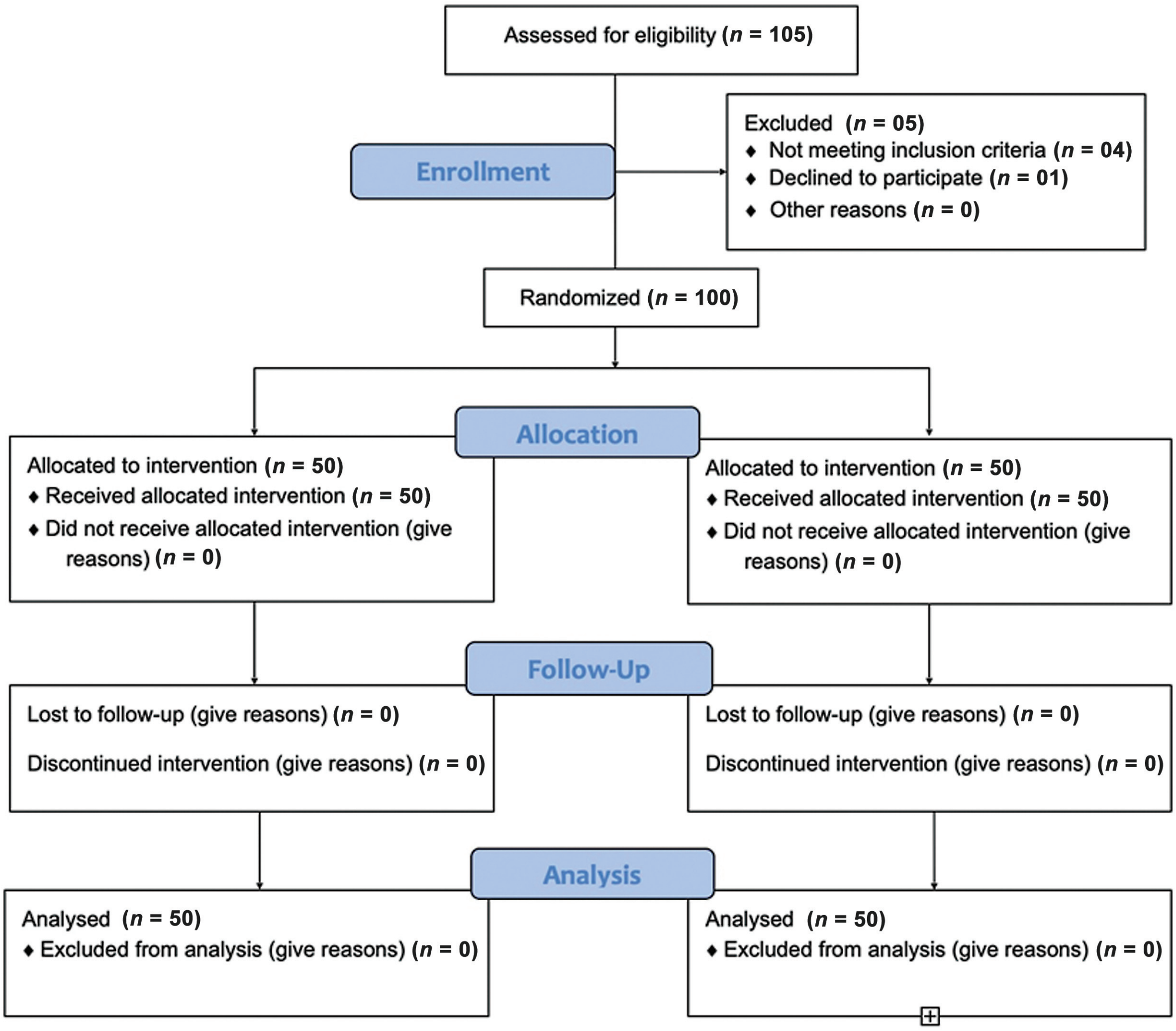

Fig. 1 Consort diagram.

and independent *t*-test, while qualitative variables were analyzed by the chi-squared test and Fisher's exact test. A *p*-value of less than 0.05 was considered statistically significant.

Results

A total of 100 patients were randomized into two groups of 50 each (►**Fig. 1**). The two groups were comparable in terms of demographic parameters, ASA grade, diagnosis, and duration of surgery (►**Table 1**).

The coagulation profile parameters, that is, PT, PTT, and INR, were comparable between the two groups at baseline as well as at 4 hours after surgery. Hemoglobin and hematocrit values were also statistically similar at both the observed timepoints. The pH was statistically similar and within normal physiological range in both the groups at baseline. However, the values were significantly lower (acidosis) in the NS group as compared to the PL group at 4 hours after surgery. Serum chloride values were comparable in the two groups at baseline. Intraoperatively, it increased in the NS group with time, while it decreased/slightly increased in the PL group, and the levels were statistically higher in the NS group as compared to the PL group at 4 hours after surgery. Blood urea and serum creatinine values were similar in the two groups at baseline but were significantly increased in the NS group as compared to the PL group at 4 hours after surgery (►**Tables 2** and **3**).

Total crystalloid transfused was 4,050 (2,500–6,175) mL in the PL group and 3,750 (2,425–6,587.5) mL in the NS group ($p = 0.555$). Blood loss was 675 (400–1,048.75) vs. 612.5 (250–800) mL in the PL and NS groups, respectively. Total blood transfused was 750 (387.5–1,050) and 650 (325–975) mL in the PL and NS groups, respectively ($p > 0.05$). Urine output was 1,100 (912.5–2,350) mL in the PL group and 925 (800–1,337.5) mL in the NS group ($p = 0.006$).

Discussion

The pathophysiology of coagulopathy is multifactorial. Fluid resuscitation leads to coagulopathy by dilution of circulating concentration of clotting factors. Coagulation is impaired when the induced hemodilution reaches 40%.[6] However, there may be also some direct effect owing to an interaction

Table 1 Comparison of demographic characteristics between group PL and NS

Demographic parameters		PL ($n=50$)	NS ($n=50$)	p-Value
Gender	Female	12 (24%)	17 (34%)	0.271[a]
	Male	38 (76%)	33 (66%)	
Body mass index, kg/m^2 (mean ± SD)		22.46 ± 2.88	22.51 ± 2.47	0.93[b]
ASA grade	I	30 (60%)	35 (70%)	0.295[a]
	II	20 (40%)	15 (30%)	
Diagnosis	Infratentorial tumor	7 (14%)	8 (16%)	0.876[c]
	Supratentorial tumor	18 (36%)	17 (34%)	
	Traumatic brain injury	25 (50%)	25 (50%)	
Age (y)		36.5 (30–42.75)	37 (30.25–42.75)	0.876[c]
Duration of surgery (min)		275 (252.5–317.5)	280 (240–327.5)	0.892[c]

Abbreviations: ASA, American Society of Anesthesiologists; NS, normal saline; PL, PlasmaLyte.
[a]Chi-square test.
[b]Independent *t*-test.
[c]Mann–Whitney *U* test.

Table 2 Comparison of parameters at baseline between PL and NS groups

At baseline	PL ($n=50$)	NS ($n=50$)	p value
pH	7.39 ± 0.08	7.36 ± 0.07	0.105[a]
Blood urea (mg/dL)	29 (25–38.75)	32 (26.55–38.825)	0.208[b]
Serum creatinine (mg/ dL)	0.9 (0.748–1)	0.9 (0.8–1.145)	0.146[b]
Serum chloride (mEq/L)	109 (94–112)	111 (104.25–113)	0.242[b]
Hemoglobin (g/dL)	12.55 ± 2.11	12.41 ± 2.26	0.746[a]
Hematocrit (%)	42.1 ± 7.96	39.33 ± 6.99	0.067[a]
PT (s)	14.55 (13.35–15.875)	13.9 (12.6–15.575)	0.147[b]
APTT (s)	36.3 (32.375–40)	36.9 (35.025–40.825)	0.277[b]
INR	1.1 (1.03–1.218)	1.07 (0.932–1.2)	0.164[b]

Abbreviations: APTT, activated partial thromboplastin time; INR, international normalized ratio; NS, normal saline; PL, PlasmaLyte; PT, prothrombin time.
[a]Independent *t*-test.
[b]Mann–Whitney *U* test.

Table 3 Comparison of parameters at 4 hours after surgery between group PL and NS

Parameter	PL ($n=50$)	NS ($n=50$)	p value
pH	7.45 ± 0.07	7.33 ± 0.14	< 0.0001[a]
Blood urea (mg/dL)	29.5 (24–38)	40.5 (32–49.75)	< 0.0001[b]
Serum creatinine (mg/ dL)	0.8 (0.7–0.9)	1.2 (0.952–1.53)	< 0.0001[b]
Serum chloride (mEq/L)	108 (100.5–113.75)	116 (110.25–139.75)	< 0.0001[b]
Hemoglobin (g/dL)	10.49 ± 2.34	10.59 ± 1.9	0.829[a]
Hematocrit (%)	36.31 ± 6.73	33.22 ± 7.21	0.029[a]
PT (s)	14.6 (13.8–16.625)	14.5 (13.2–15.55)	0.256[b]
APTT (s)	40 (29.975–42)	38.7 (35–42)	0.604[b]
INR	1.1 (1.022–1.2)	1.11 (1.08–1.3)	0.141[b]

Abbreviations: APTT, activated partial thromboplastin time; INR, international normalized ratio; NS, normal saline; PL, PlasmaLyte; PT, prothrombin time.
[a]Independent *t*-test.
[b]Mann–Whitney *U* test.

between resuscitation fluid molecules and the coagulation system.[7] Th effect of colloids on coagulation has been studied earlier, but the researches assessing alteration in coagulation profile due to type of crystalloid are anecdotal.[7,8] 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] NS has high chloride content and infusion of large volumes results in hyperchloremic metabolic acidosis, which affects the activity of enzymes involved in coagulation pathway.[1–4] Hyperchloremia may induce afferent arteriolar vasoconstriction leading to reduced glomerular filtration rate and acute kidney injury.[3,4,10]

In our study, we observed significant blood loss and consequent hemodilution to resuscitation. Hemoglobin and hematocrit values decreased significantly at 4 hours after surgery as compared to baseline, although the values were similar between the two groups. Patients in the NS group developed transient hyperchloremic metabolic acidosis after surgery, while no such metabolic abnormality was observed in the PL group. However, the coagulation profile (PT, PTT, and INR) was normal and comparable in both the groups ($p > 0.05$). In contrast to PL, lower urine output and increased blood urea and creatinine values in the NS group after surgery indicate toward renal impairment. Similar results were observed by Song et al[4] while evaluating the effects of NS versus PL on coagulation in 50 patients undergoing lumbar spinal surgery. Hematocrit values were significantly decreased at the end of the surgery as compared to baseline values (27 ± 4 vs. $27 \pm 3\%$ in the PL vs. NS group, respectively) but were statistically similar between the two groups ($p < 0.05$). Hyperchloremic metabolic acidosis and a significantly lower urine output were observed in the NS group. The coagulation parameters (clotting time, clot formation time, fibrin polymerization rate, and maximum clot firmness) and amount of blood loss were statistically similar between the two groups.

To our knowledge, there is no other study comparing the effects of crystalloids on coagulation parameters and therefore large multicentric trials are required to ascertain the safety of NS and other crystalloids with regard to coagulopathy in different kinds of patient population. Thus, the choice of crystalloid is important in patients undergoing major surgeries, critically ill or with renal insufficiency.

The limitation of our study is that the coagulation profile was assessed by PT, PTT, and INR, which constitute only a part of the clotting process. Rotational thromboelastometry (ROTEM) and thromboelastography provide comprehensive point-of-care analysis but were not available during the study duration.

Conclusion

The coagulation profile parameters were normal and statistically similar with intraoperative infusion of NS versus PL in patients undergoing various neurosurgical procedures.

However, use of PL was associated with a better acid–base and renal profile in these patients. Thus, BC, that is, PL, may be preferred over NS in patients undergoing neurosurgeries.

Ethical Approval
Institutional Ethics Committee Approval No.- IEC/Th/19/Anst17.

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None.

Conflict of Interest
None declared.

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