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

Vandna Arora1 Akanksha Khatri1 Renu Bala1 Vibhuti Kumar1 Rashmi Arora1 Shweta Jindal1

1Department of Anaesthesiology, Pt. B.D. Sharma PGIMS, Rohtak, Haryana, India

Address for correspondence Renu Bala MD, DM, Department of Anaesthesiology, Pt. B.D. Sharma PGIMS, Rohtak, 124001, Haryana, India (e-mail: drvandna4@gmail.com).

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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.
Introduction

Neurosurgical procedures 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 frequently used crystalloid but may lead to coagulopathy due to hyperchloremic metabolic acidosis and renal dysfunction. 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. 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.

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 the 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 neurosurgical procedures 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 fasting and the data with non-normal distribution as median with interquartile range. The quantitative data with normal distribution were presented as the mean ± SD and the data with non-normal distribution as median with 25th and 75th percentiles (interquartile range). The quantitative variables were analyzed using Mann–Whitney
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%. However, there may be also some direct effect owing to an interaction...
### Table 1: Comparison of demographic characteristics between group PL and NS

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

Abbreviations: ASA, American Society of Anesthesiologists; NS, normal saline; PL, Plasmalyte.

<sup>a</sup>Chi-square test.
<sup>b</sup>Independent t-test.
<sup>c</sup>Mann–Whitney U test.

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

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

Abbreviations: APTT, activated partial thromboplastin time; INR, international normalized ratio; NS, normal saline; PL, Plasmalyte; PT, prothrombin time.

<sup>a</sup>Independent t-test.
<sup>b</sup>Mann–Whitney U test.

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

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

Abbreviations: APTT, activated partial thromboplastin time; INR, international normalized ratio; NS, normal saline; PL, Plasmalyte; PT, prothrombin time.

<sup>a</sup>Independent t-test.
<sup>b</sup>Mann–Whitney U test.
between resuscitation fluid molecules and the coagulation
system. The effect of colloids on coagulation has been studied
earlier, but the researches assessing alteration in coagulation
profile due to type of crystalloid are anecdotal. 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. NS has high chloride
content and infusion of large volumes results in hyper-
chloremic metabolic acidosis, which affects the activity of
enzymes involved in coagulation pathway. Hyperchloremia
may induce afferent arteriolar vasoconstriction leading to
reduced glomerular filtration rate and acute kidney
injury.

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 acido-
sis 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. 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 while evaluating the
effects of NS versus PL on coagulation in 50 patients under-
going lumbar spinal surgery. Hematocrit values were signif-
icantly decreased at the end of the surgery as compared to
baseline values (27 ± 4 vs. 27 ± 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 for-
mation 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 there-
fore large multicentric trials are required to ascertain the
safety of NS and other crystalloids with regard to coagulop-
athy 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 sta-
tistically 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.

Funding

None.

Conflict of Interest

None declared.

References

3. Dey A, Adinarayanan S, Bidkar PU, Bangera RK, Balasubramaniyan V. Comparison of normal saline and balanced crystalloid (plas-
file in patients receiving lactated Ringer’s solution, 6% hetastarch in a balanced-saline vehicle, or 6% hetastarch in saline during major