Original Research Article

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A Comparison of the Effect of 0.9% Saline versus Balanced Salt Solution (Plasma Lyte-A) on Acid Base Equilibrium, Serum Osmolarity and Serum Electrolytes in Supratentorial Neurosurgical Procedures Requiring Craniotomy

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Abstract

Background: The most commonly used isoosmolar fluid in neurosurgery is 0.9% saline, which is known to produce hyperchloraemic metabolic acidosis. A balanced salt solution, like PlasmaLyte A, is not only isoosmolar, but also maintains acid –base balance and is stated to produce less serum chloride changes. Our aim was to study the effects of PlasmaLyte-A on acid base balance, serum osmolarity and serum electrolytes in neurosurgical procedures. *Methodology:* 70 patients posted for elective supratentorial craniotomies were randomly allocated to two groups, to receive either 0.9% saline or PlasmaLyte A as the sole intravenous fluid. Arterial Blood Gas Samples were analysed at regular intervals and the variables noted were: serum osmolarity, pH, base deficit or excess, serum chloride, serum lactate, serum sodium, serum potassium, serum calcium, and glucose levels. Intergroup data was analysed statistically by student's T test (continuous) and chi-square test (categorical) while repeated ANNOVA and post-hoc Tukey Kramer test was used to analyze data within each group using NCSS statistical software version 9.0. *Results:* Towards the end of the surgery, pH was found to be low in the normal saline group (7.334±0.05 and 7.275±0.05) as compared to the plasmalyte group (7.402±0.03 and 7.406±0.03), this difference being statistically highly significant ($p<0.0001$). The difference in base deficit was also highly significant at the same time intervals. Chloride levels were significantly higher in the normal saline group in comparison to the study group at different time intervals (112.8±8.002 and 103.63±6.17) and (115.77±9.84 and 103.15±2.95) (p value<0.0001) while serum electrolytes and serum osmolarity was found to be comparable in both the groups. *Conclusion:* We conclude that 0.9% saline when used as sole intravenous fluid in neurosurgical procedures, causes significantly higher chloride levels and significant acidosis when compared to plasmalyte A used for the same purpose.

Keywords: Neurosurgery; Craniotomy; Acid-Base Equilibrium; Osmolarity; Electrolytes; Fluid Therapy.

Introduction

Fluid therapy in neurosurgical procedures poses a challenge to the attending anaesthesiologist. A majority of these patients receive perioperative diuretic therapy which causes a lot of electrolyte imbalance. In addition to these changes, peripheral vasodilatation due to general anaesthesia, excessive blood loss, and inadequate secretion of ADH, complicate the homeostasis of the patient resulting in the need of an ideal intravenous replacement fluid which is iso-osmolar, does not alter the acid base balance and also replenishes lost electrolytes.

In the presence of an intact blood brain barrier, even a small drop in plasma osmolarity (<5%) can potentially increase brain water content and intracranial pressure [1]. The use of hypo-osmolar solutions like 0.45% saline and 5% glucose, for the same reason is avoided in neurosurgical procedures to ensure a better postoperative outcome [2]. Thus, the necessity to preferably choose only an iso-osmolar fluid for perioperative use arises, leaving the anaesthesiologist with only a few options.

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The most commonly used intravenous fluid in craniotomies is 0.9% saline which is iso-osmolar (308 mosm/l), has a high chloride content (154meq/l), is documented to produce acidosis [3] and does not contain potassium. A balanced salt solution, e.g. Plasmalyte A (multiple electrolytes injection, Type 1, USP, Baxter healthcare India Pvt Ltd) on the other hand, is not only isoosmolar (294mosm/l), but also contains additional electrolytes (potassium 5meq/l, magnesium, acetate, gluconate), has chloride content same as in plasma (98meq/l) and has been reported to produce less acid base disturbances [4,5]. Sodium hydroxide and other acid buffers are used in this product to maintain a physiologic pH of 7.4 [6].

Plasmalyte A has been used and compared before with other iso-osmolar fluids in trauma care, diabetic ketoacidosis, and abdominal surgery [7-9]. Its use in neurosurgery has not been reported in the available literature so far.

We carried out this prospective randomized study with the primary objective to determine whether balanced salt solution (plasmalyte A) produces any changes in acid base balance when compared to 0.9% saline as the sole intravenous fluid in neurosurgical procedures requiring craniotomy. The secondary objectives were to compare changes in serum osmolarity and serum electrolytes after using the two intravenous fluids.

Methodology

After approval from the institutional ethics committee, a prospective, randomized, clinical investigation was carried out in 70 adult consenting patients scheduled to undergo elective supratentorial craniotomies within a period of 12 months.

Sample Size Calculation

A total sample size of 70 (35 in each group) was calculated on the basis of a similar study conducted by Hafizah M , Liu C, Ooi J, et al in 2015, considering changes in pH as the study parameter (mean values of 7.44±0.2 for plasmalyte and 7.39±0.8 for 0.9% normal saline). We used the software G power 3.1 (Universitat Dusseldorf, Germany) to derive the sample size using an effect size of 0.85, α error of 0.05 and power (1-β error probability) of 0.90.

An informed consent was taken, a routine preanaesthetic checkup done and preoperative investigations were carried out which included haemogram and serum electrolytes in particular. History related to treatment with diuretics, coagulopathy, and blood transfusion was taken into account and noted.

Our exclusion criteria were extremes of ages (<20years and >60 years), those with renal dysfunction, patients with severe electrolyte imbalance, a haematocrit of <30 or haemoglobin <10g/dl, and those with known hypersensitivity to plasmalyte. Surgeries involving excessive blood loss (>1.5 liters), longer surgeries (> 6hours), raised intracranial pressure or tense brain/bulging brain, and cases with haemodynamic instability requiring use of intraoperative vasopressors were also excluded from this study.

All the remaining ASA grade 1 or 2 patients were randomly divided into two groups of 35 each using a computer generated randomization table (Microsoft excel 2010, Microsoft corporation, Washington USA).

The two groups received

Group N (n=35): 0.9% saline as the sole intravenous fluid (exclusive of blood and blood products)

Group P (n=35): Plasmalyte-A as the sole intravenous fluid (exclusive of blood and blood products)

The rate of infusion of either fluid was maintained at a range of 8 -10 $ml.kg^{-1}.hr^{-1}$ in both the groups.

Routine neuroanaesthetic management as per our institutional protocol was carried out in each patient which included Fentanyl citrate(2µg/kg), glycopyrrolate (4mcg/kg), pantoprazole (0.8mg/kg) as premedication, thiopentone (5-7mg/kg) and atracurium besylate (0.4mg/kg) for induction, scalp nerve block with bupivacaine 30 ml of 0.25% for suppression of haemodynamic response during Mayfield pin holder insertion, fentanyl-atracurium infusion (both at 0.3mg/kg/h) and sevoflurane at a MAC of 0.8 -1.2% for maintenance, ondansetron (8mg) and dexamethasone (0.08mg/kg) as antiemetics and phenytoin as per requirement. The dose of mannitol was kept constant for all the patients at 0.4g/kg intravenously over 10 minutes. Acetaminophen (15mg/kg) intravenous infusion was given to reduce postoperative pain.

Invasive monitoring (arterial blood pressure and central venous pressure) was carried out along with other noninvasive monitors, including capnography, pulse oximetry, electrocardiography, end tidal exhaled gases, MAC, spirometry, systolic pressure variation, core temperature, urine output, and blood loss. A mean arterial pressure between

50-70mm Hg, Central venous pressure (8-13 mmHg) etCO2 (28-32 mm Hg), and SPV <12 was maintained in all the cases. Total intravenous fluids infused, total blood loss, urine output, number of blood transfusions given if any, and total duration of surgery was noted at the end of each case.

Serial Arterial Blood Gas Samples were analysed at the following time intervals

1. Baseline (T1)
2. At the time of dural opening (T2)
3. One hour after dural opening (T3)
4. At skin closure (T4)
5. One hour postoperatively (T5)

The following observations were made at these five time intervals, serum pH, Serum sodium, serum potassium, serum calcium, serum chloride, serum osmolarity, base deficit, serum lactate, haemoglobin, and glucose. All the deviations in these parameters outside the normal range were meticulously treated. Serum pH values of less than 7.35 were promptly treated with intravenous sodium bicarbonate after careful calculation of the requirement from the base deficit values.

The observations were analyzed statistically using student's T test (continuous data), chi-square test (categorical data) and repeated ANOVA test with post-hoc Tukey Kramer for data within the group and in between the two groups, using NCSS software version 9.0. All values have been expressed in mean±SD, and ratio for categorical data. Probability values of less than 5% were taken as significant.

Results

No patient was excluded. Both the groups were comparable and found to be normally distributed in terms of age, weight, height, gender distribution, total intravenous fluids infused, total blood loss, duration of surgery, and total urine output (Table 1).

pH values were seen to be comparable in both the groups at time intervals T1,T2 and T3. However, at T4 (skin closure) and T5 (1 hour postoperatively), there was a highly significant difference in pH between the groups, with the values in the control group being on the lower side. Similar observations were seen with changes in base deficit, where the groups were comparable at T1and T2, but had highly significant difference in mean base deficit at T3, T4 and T5. (Table 2) (Graph 1)

Intragroup data analysis (ANOVA with post – hoc Tukey kramer) revealed a significant fall in mean ph value and base deficit from baseline (T1) in Group N at T3, T4 and T5 with no significant change at all time intervals in group P. (p value for change from baseline (T1) in control group were T3 (0.02)*, T4 (0.00)** T5 (0.00)** .

Serum chloride levels were similar in both groups at T1 and T2, however there was a highly significant increase in mean chloride levels in the normal saline group towards the end of surgery (at T4 and T5) (Table 3) (Graph 2). Intra-group analysis showed a highly significant rise in mean serum chloride level in Group N at T3 (0.002**)T4 (0.001**)T5 (0.00**) from baseline (T1).

An overall rise in serum lactate was seen in both the groups from baseline group N p=0.04* (T2), p=0.04*(T3) p=0.02*(T4) p=0.01**(T5), and group P p=0.02* (T2), p=0.032*(T3) p=0.02*(T4) p=0.01**(T5) which was comparable between the groups at all time intervals except at T3 (1 hour after dural opening) where the difference was significant (p=0.02*).

Changes in serum sodium, potassium, calcium, blood glucose, serum lactates and serum osmolarity were comparable in both the groups (Table 5). Intragroup comparison of mean values from

Table 1: Demographic and intraoperative data

	Demographic and Intra-operative Data		
	Group N	Group P	P value
Age (years)	50.25±13.73	46.88±10.95	0.5
Weight (kg)	62.48±9.39	58.42±8.70	0.325
Gender (M:F)	15:20	19:16	0.5
BMI (kg/m²)	22.08±0.9	24.03±2.2	0.8
Height (cm)	159.91±5.88	159.14±6.09	0.20
Fluids infused(ml)	2437.14±525.9	2271.42±320.27	0.69
Blood loss (ml)	551.42±212.99	372.57±22.26	0.54
Urine output (ml)	82±64.52	72.87±61.27	0.78
Duration (min)	275.71±87.22	248.11±117.29	0.07

n=35, values in mean±SD, p<0.05=significant*, p<0.01=highly significant**

Table 2: Changes in pH and base deficit (BD)

Time interval	Changes in pH and base deficit (BD) Group N	Group P	P value
T1 (pH)	7.432±0.04	7.406±0.06	0.0652
T1 (BD)	-0.871±0.80	-0.954±0.140	0.672
T2 (pH)	7.407±0.05	7.403±0.04	0.753
T2 (BD)	-1.36±1.092	-1.023±0.625	0.063
T3 (pH)	7.393±0.05	7.394±0.03	0.915
T3 (BD)	-2.028±1.004	-0.974±0.706	0.00**
T4(pH)	7.334±0.05	7.402±0.03	0.00**
T4(BD)	-2.474±1.169	-1.046±0.831	0.00**
T5 (pH)	7.275±0.05	7.406±0.03	0.00**
T5 (BD)	-3.682±2.124	-1.438±1.093	0.00**

n=35, values in mean±SD, p<0.05=significant*, p<0.01=highly significant**

Table 3: Changes in serum chloride

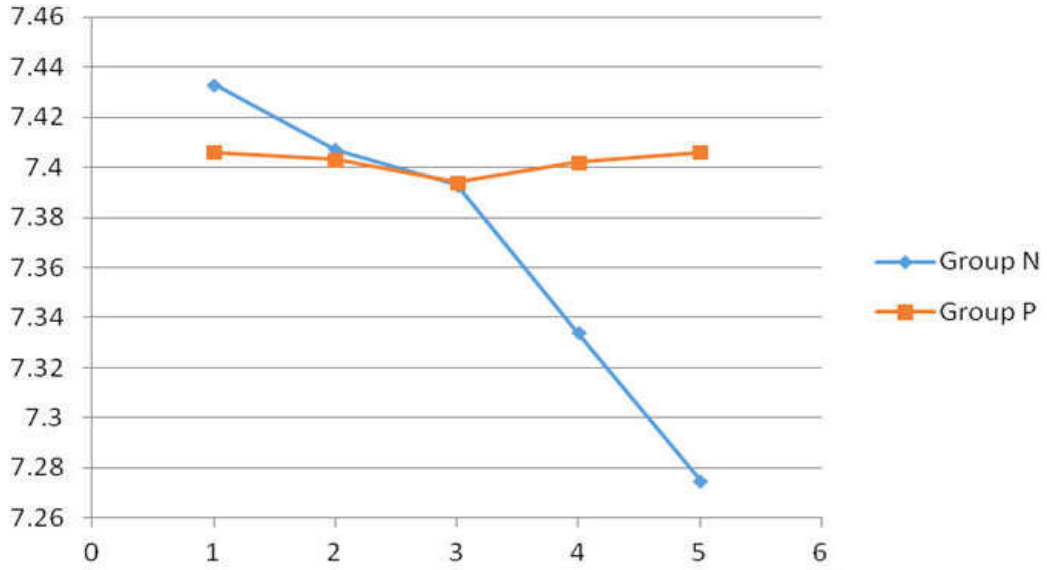
Time interval	Changes in serum chloride Group N	Group P	P value
T1	107.5±3.32	102.8±6.06	0.472
T2	105.228±6.188	100.348±6.625	0.063
T3	109.8±1.008	102.571±5.202	0.062
T4	112.8±8.002	103.63±6.17	0.00**
T5	115.77±9.849	103.151±2.952	0.00**

n=35, values in mean ±SD, p<0.05=significant*, p<0.01=highly significant**

Table 4: Changes in serum lactate

Time interval	Changes in serum lactate Group N	Group P	P value
T1	1.097±0.632	1.108±0.595	0.372
T2	1.941±0.772	2.06±0.625	0.631
T3	2.527±1.008	2.362±0.815	0.02*
T4	3.198±1.201	2.905±0.977	0.267
T5	3.598±0.923	4.054±1.141	0.07

n=35, values in mean ±SD, p<0.05=significant*, p<0.01=highly significant**

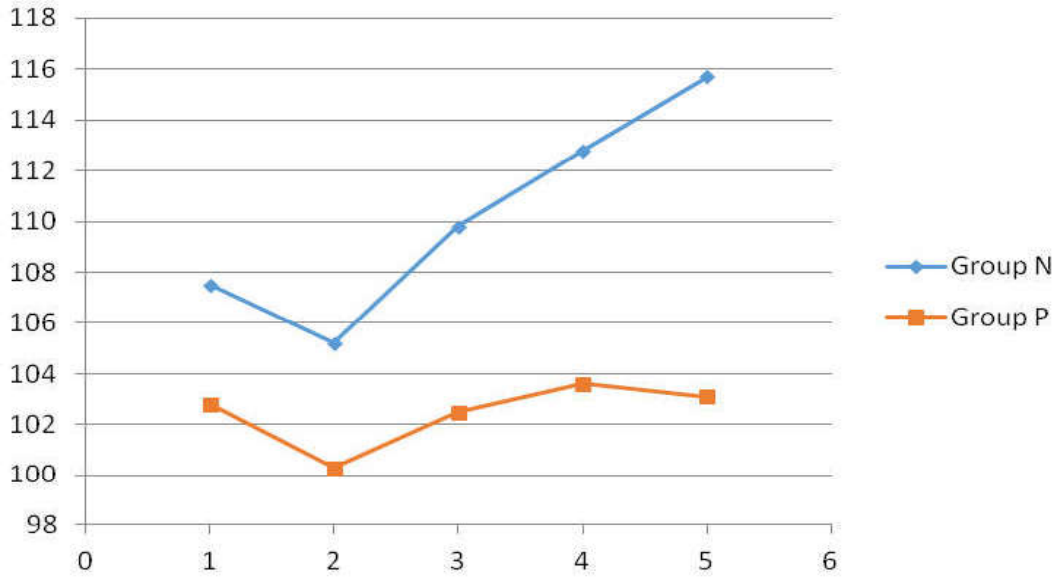


Graph 1: Graph showing changes in ph at different time intervals in both the groups with pH values on y axis and time intervals (T1 to T5) on x axis.

Table 5: Comparison of changes in serum electrolytes, serum osmolarity and blood glucose

Parameter	Time interval	Group N	Group P	P value
Serum sodium	T1	134.97±3.27	135.24±4.05	0.754
	T2	136.12±3.14	136.28±4.04	0.853
	T3	137.21±3.88	137.13±3.82	0.926
	T4	137.2±3.37	137.78±3.55	0.517
	T5	137.11±3.87	138.48±3.47	0.124
Serum potassium	T1	3.58±0.231	3.67±0.261	0.095
	T2	3.68±0.245	3.68±0.356	0.953
	T3	3.67±0.29	3.66±0.321	0.910
	T4	3.72±0.378	3.74±0.339	0.819
	T5	3.75±0.41	3.72±0.389	0.817
Serum calcium	T1	0.85±0.133	0.94±0.144	0.10
	T2	0.90±0.149	0.87±0.134	0.389
	T3	0.89±0.241	0.87±0.117	0.797
	T4	0.98±0.296	0.87±0.138	0.052
	T5	0.95±0.264	0.91±0.130	0.445
blood glucose	T1	106.05±25.246	114.54±27.320	0.181
	T2	123.0±34.534	129.55±43.515	0.289
	T3	134.71±34.119	129.71±48.611	0.11
	T4	141.02±32.482	138.90±52.325	0.07
	T5	151.37±38.677	142.52±45.077	0.06
Serum osmolarity	T1	275.90±3.087	276.82±4.296	0.07
	T2	276.47±5.648	277.81±6.464	0.21
	T3	278.92±4.970	281.22±17.750	0.61
	T4	277.44±5.221	280.31±4.501	0.267
	T5	278.89±5.344	281.33±5.060	0.07

n=35, values in mean±SD, p<0.05=significant*, p<0.01=highly significant**



Graph 2: Graph showing changes in serum chloride levels at different time intervals in both the groups (time intervals T1 –T5 on x axis)

baseline with regards to all the above parameters showed no significant difference p>0.05.

None of the patients in either of the groups presented with any adverse reaction to the intravenous fluid infused. There was no hypersensitivity reaction reported.

Discussion

Intravenous fluids with an osmolarity of around 300mosm per liter tend to remain in the intravascular compartment, reducing the possibility of increased brain water and raised intracranial

pressure, with or without an intact blood brain barrier [10,11]. The iso-osmolar fluid most widely used in neurosurgery is 0.9% normal saline (308mosm/L), which is easily available and has a long term safety record as fluid therapy. However large volumes of 0.9% normal saline (NS) tend to cause hyperchloraemic metabolic acidosis (HMA) with a normal anion gap [3]. Significant increases in chloride levels and HMA have been observed in various surgeries like intraabdominalsurgery [9], Gynecological surgery [12], and kidney replacement post-operative fluid therapy [13]. HMA tends to impede recovery [14].

Plasmalyte-A contains organic acid buffers like sodium hydroxide, acetate and gluconate, and is physiologically similar to plasma (pH 7.4) [6]. It is more similar to body fluid composition than NS, making it less likely to lead to HMA.

In our study, we observed that acid base changes with the use of plasmalyte –A and normal saline were initially comparable over a period of time, after which as the duration of infusions prolonged, significant acidosis in the control group started to set in. Similar findings have been reported by other authors in studies where normal saline was compared to plasmalyte-A [7,9,13]. We also observed a significant increase in serum chloride levels with normal saline, towards the end of the surgery, a finding similar to many other authors [4,8,16,17].

A literature search revealed that another iso-osmolar crystalloid stereofundin ISO has also been compared to 0.9% normal saline in neurosurgical procedures [18], where the authors have reported better control of acid base balance, sodium and chloride levels with stereofundin than normal saline. The chloride content in stereofundin (127meq/L) is still higher than plasmalyte-A(98 meq/L), further lowering the possibility of hyperchloraemia with our study fluid.

The available literature so far, indicates that there is very little and inconclusive evidence, as far as the association of acidosis and postoperative outcome is concerned [19]. However, Hyperchloraemia, has been shown to influence renal function in the perioperative period by altering tubular chloride reabsorbtion and renal vasoconstriction [16]. Similarly, hyperchloraemia is also stated to cause coagulation abnormalities which have been studied by thromboelastography and platelet aggregometry [20]. Moreover acidosis following hyperchloraemia is known to increase inflammatory markers in the serum [21]. All these factors when compounded together carry the potential to adversely affect the postoperative outcome of a neurosurgical patient, in whom ,renal function is already affected by the use of diuretics and electrolyte disturbances, and in whom haemostasis is a major determinant of prognosis.

Serum osmolarity did not show any significant change in both groups. Maitenance of serum osmolarity is one of the prime concerns in neurosurgical anaesthesiology as even a small fall in the same can increase brain water content [11]. In our study both the fluids maintained serum osmolarity well, thus indicating that they were comparable in this aspect. Similarly, changes in serum sodium, potassium, calcium and glucose were comparable in both groups, an observation similar to other studies [7,8].

We therefore suggest that the positive effect of plasmalyte A on acid base equilibrium and particularly on chloride levels, and its subsequent prospective effect on patient recovery and outcome marginally outweighs its only disadvantage of being available at a higher cost when compared to normal saline.

Our study was not devoid of limitations. We could not use the benefit of blinding, due to technical reasons, which would have otherwise made our study methodologically stronger. Secondly, we did not continue our study in the postoperative period for more than an hour after extubation. By doing the same we would, perhaps, have also been able to provide evidence related to the effect on postoperative outcome of the patient after using plasmalyte-A. Another reason why we chose to refrain ourselves from commenting on the effect of these changes on postoperative outcome, is the fact that neurological outcome in brain tumour surgery necessarily has a multifactorial causation [22]. Factors like, anatomical site of tumor, its size, structures involved, histopathology, vascularity are only a few of them. Attributing a postoperative outcome only to intraoperative acid-base changes or chloride levels thus, is difficult to justify. Our limitations leave scope for further research in this area.

Conclusion

We thus conclude that, 0.9% normal saline when used as sole intravenous fluid in neurosurgical procedures involving craniotomy, has a potential to cause significant acidosis and significant hyperchloraemia when compared to plasmalyteA used for the same purpose. Hyperchloraemia can

potentially prove to be harmful for neurologic outcome in neurosurgical procedures.

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