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Original Research Article

Comparison of normal saline and balanced crystalloid solution on acid-base and electrolyte balance in emergency neurosurgical trauma patients: A prospective randomised controlled trial

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Abstract

Background: Maintaining cerebral perfusion, controlling brain volume, and providing adequate substrate delivery are the goals of fluid therapy in patients with Traumatic Brain Injury (TBI). While Normal Saline (NS) is frequently used, Balanced Crystalloid Solutions (BCS) like Plasmalyte (PL) offer potential benefits due to their electrolyte composition and decreased risk of hyperchloremic acidosis. This study compares the effects of NS versus BCS on acid-base and electrolyte status in emergency neurosurgical trauma patients.

Materials and Methods: A prospective, randomised, double-blinded study was conducted at a tertiary care trauma centre October 2020 to September 2021. One hundred TBI patients undergoing decompressive craniotomy were randomly assigned to receive either NS (Group N) or BCS (Group B) as maintenance fluids. Fluid management was guided by intraoperative needs and arterial blood gases, electrolytes, and urine output were measured pre-operatively, immediately post-operatively, and 6 hours post-operatively. Statistical analysis included ANOVA, paired t-tests, and un-paired t-tests, with a significance level set at $p < 0.05$.

Results: Demographic characteristics and Glasgow Coma Scale (GCS) scores were comparable between groups. Post-operatively, patients in Group B showed a significantly higher pH (7.42 vs. 7.39, $p = 0.02$) and more stable bicarbonate levels compared to Group N. Lactate levels were closer to normal in Group B. Sodium and chloride levels were higher in Group N, while potassium and calcium levels were more stable in Group B. Urine output was significantly greater in Group B (1341.40 ± 232.70 mL) compared to Group N (1091.0 ± 253.45 mL, $p < 0.001$). Mortality rates were similar between groups on Day 1.

Conclusion: Balanced Crystalloid Solutions as maintenance fluids during the peri-operative period in traumatic brain injury patients result in less electrolyte and acid-base disturbance compared to Normal Saline. However, this did not translate into improved survival outcomes. Further research is needed to confirm these findings and assess long-term impacts on patient recovery.

Keywords: Normal saline (NS), Balanced salt solution (BSS), Trauma patients, Neurosurgical patients, Electrolyte, Acid base.

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1. Introduction

An essential component of surgical care is the delivery of perioperative fluids. Optimising the circulatory system to guarantee adequate oxygen delivery to organs is the ultimate objective of fluid management. Maintenance of normal intravascular volume, management of blood or fluid loss from wounds, diuresis from drains, third-space losses, and increased systemic requirements due to fever and hypermetabolism all depend on it.[1] Optimising cardiac output and oxygen supply through goal-directed fluid therapy (GDT) has been demonstrated to enhance outcomes for high-risk surgical patients.[2] Fluid therapy is crucial for maintaining cerebral perfusion, regulating brain volume, and ensuring

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appropriate substrate delivery in patients with traumatic brain injury (TBI).

The most commonly utilised crystalloid in TBI patients is normal saline.[3] It is a universal fluid for trauma resuscitation because of its perceived safety and similar osmolarity to plasma. Ringer's lactate is a common substitute for isotonic saline in the U.S. However, in patients with brain injury, its hypo-osmolarity (273 mmol/L) may result in an increase in intracellular space volume, which could raise intracranial pressure. The strong ion difference (SID) of Ringer's lactate is 26 mmol/L, whereas that of isotonic saline is 0 mmol/L. Dr. Hartmann's lactated Ringer solution formulation results in less hyperchloremic acidosis than isotonic saline because a solution with a SID lower than that of plasma (40 mmol/L) induces hyperchloremic acidosis. A connection between intravenous chloride load and mortality in intensive care has been documented, and excessive chloride delivery may have negative consequences on the kidneys.[4]

As substitutes for normal saline, balanced crystalloid (BC) solutions such as Kabilyte and Plasma-Lyte (PL) have been used. BC shares similarities with plasma[5] in terms of osmolality, pH, and electrolyte concentration. Compared to normal saline, PL has been linked to fewer negative effects and complications related to metabolic and renal systems.[6] There is a dearth of literature on the use of balanced crystalloid solutions as maintenance fluids in patients with traumatic neurosurgical emergencies. However, critical care patients have demonstrated positive outcomes when resuscitated with balanced crystalloid solutions. One of the key goals was to compare normal saline and balanced crystalloid solutions as perioperative maintenance fluids regarding acid-base balance and electrolyte status in emergency neurosurgery trauma patients.

2. Materials and Methods

This prospective, randomised, double-blind study was conducted at the Trauma Centre of a tertiary care hospital affiliated with a medical college, following approval from the Institutional Ethics Committee (No. Dean/2019/EC/1774) and registered with CTRI, India (No. CTRI/2020/10/028620).Written informed consent was obtained from the patient's relative. The study was conducted between October 2020 and September 2021and included 100 traumatic neurosurgery patients aged 18 to 60 years, scheduled for decompressive craniotomy within 24 hours of injury. Patients were selected from the emergency trauma center after initial resuscitation. Exclusion criteria included the use of inotropic or vasopressor support, abnormal baseline electrolyte levels, systemic diseases such as diabetes or hypertension, and end-stage organ damage involving hepatic, renal, or cardiovascular systems.

Initial resuscitation adhered to trauma emergency protocols, with intravenous fluids (ringer lactate or normal saline) administered in the emergency setting. Life-threatening injuries were managed during the primary survey. After stabilization of Airway, breathing, circulation, disability, and exposure (ABCDE), patients were transferred to the trauma emergency operating room (OT). Baseline investigations, arterial blood gas (ABG) analysis, Glasgow Coma Scale (GCS) scores, and urine output were recorded. Patients meeting the inclusion criteria were subsequently enrolled in the study.

The sample size for this study was determined based on the primary objective of comparing the effects of normal saline and balanced crystalloid solutions on acid-base and electrolyte balance in emergency neurosurgical trauma patients. The calculation followed standard statistical principles for continuous outcomes using the formula:

$$n = [2 \times (Z_{\alpha/2} + Z_{\beta})^2 \times s^2] / d^2$$

where n represents the required sample size per group, $Z_{\alpha/2}$is the Z-value for a two-tailed test at a significance level of 0.05 (1.96), Z_{β} is the Z-value for 80% power (0.84), S is the pooled standard deviation, and d is the clinically significant difference between group means.

Based on the assumption of sample size estimation in clinical research,[7] a pooled standard deviation (s) of 3 mmol/L (for bicarbonate levels) was assumed. A clinically significant difference (d) of 2 mmol/L was selected, which was derived from previously published data. Using this information, a minimum sample size of 36 patients per group was determined.

To account for potential dropouts or missing data, the sample size was adjusted to 50 patients per group, resulting in a total of 100 participants.

A computer-generated randomization number was used to divide the 100 patients into two equal groups (n = 50). Group B received a balanced salt solution (kabilyte) as a maintenance fluid, while Group N received reg normal saline. The amount of fluid needed for intraoperative maintenance was determined by taking into account the fluid deficit, blood loss, third space loss, and urine production. ABG was performed again immediately after the procedure and six hours after the procedure (OP). On the same day, urine output was measured. Following surgery, patients were either moved to the intensive care unit (ICU) for additional management with ventilatory support, or extubated on a table and shifted topost-operated ward. Information was gathered from patients' regular medical records in the trauma centre’s triage section. These comprised data on GCS, co-morbidities, diagnosis, and demographic characteristics.

The outcomes measured included arterial blood gas (ABG) analysis, electrolytes, Glasgow Coma Scale (GCS) scores, and urine output. These were assessed at three specific intervals: pre-operatively (before the surgical procedure),

immediately post-operatively (right after the surgery), and six hours post-operatively.

The study utilised SPSS 19.0 for statistical analysis, with Microsoft Word and Excel for creating visual representations. Both descriptive and inferential statistical methods were employed. Descriptive statistics summarised categorical data as numbers and percentages, while continuous data were presented as means and standard deviations. Inferential statistics included paired t-tests for within-group comparisons, ANOVA for analysing differences among group means, and unpaired t-tests for between-group comparisons. The significance level was set at $p < 0.05$.

3. Results

A total of 100 patients were analysed (**Figure 1**). Both groups displayed comparable demographic profiles and Glasgow Coma Scale (GCS) scores (**Table 1**). Compared to baseline, pH increased in both groups, with a significant intergroup difference observed 6 hours postoperatively. The balanced crystalloid solution (BCS) group showed values closer to the alkalotic end of the normal physiological range (7.42), while the normal saline (NS) group trended toward mild acidosis (7.39).

$PaCO_2$ decreased in both groups relative to baseline, suggesting respiratory alkalosis. This reduction became statistically significant 6 hours after surgery. Similarly, serum bicarbonate levels diverged markedly between groups at the 6-hour postoperative mark: BCS patients maintained near-normal values, whereas NS patients exhibited progressive decline.

Base excess was significantly more negative in the NS group but remained within normal limits in the BCS cohort. Lactate levels stayed physiologically normal in both groups, though BCS patients demonstrated values closer to baseline 6 hours postoperatively ($p < 0.05$) (**Table 2**).

Sodium levels showed relative hypernatremia in both groups compared to baseline, but the NS group exhibited a significantly greater increase ($p < 0.001$). Plasma chloride rose above baseline in both cohorts, with a more pronounced elevation in the NS group ($p < 0.01$). Potassium decreased marginally from baseline in NS patients ($p < 0.05$), while serum calcium declined slightly in the NS group but increased modestly in BCS patients postoperatively (**Table 3**).

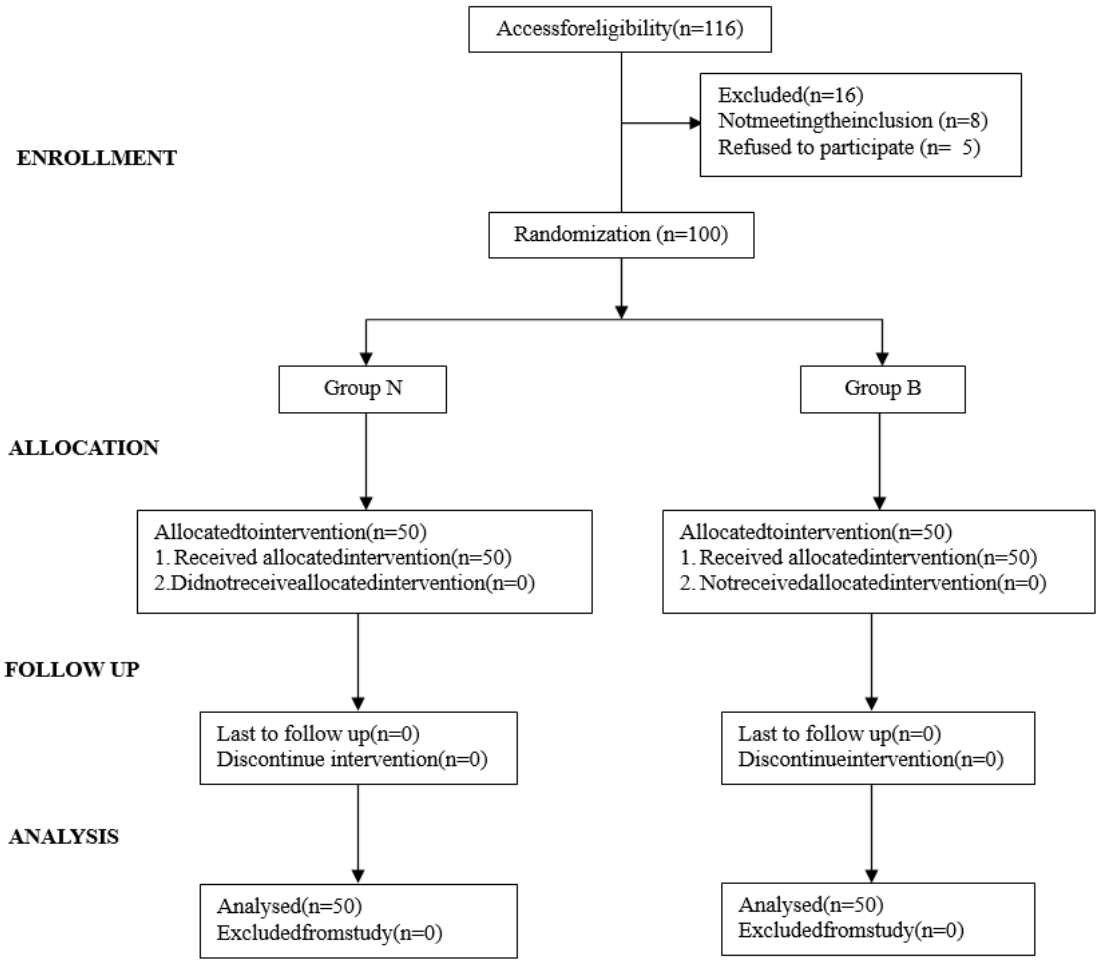

Figure 1: Flowchart of patient studied

Preoperative urine output was similar between groups. However, immediate postoperative and 6-hour outputs were significantly higher in the BCS group ($p < 0.001$ for both intervals) (**Table 4**). Though diuresis increased substantially in both cohorts, the BCS group demonstrated greater enhancement of urinary flow rates. No statistically significant difference in Day 1 mortality rates was observed between groups (**Table 5**).

Table 1: Comparison of demographic parameters between the two groups

Parameter	Group N	Group B	p value
Age	33.86 ± 12.19	34.72 ± 13.25	0.090[#]
Gender	34/16	40/10	0.171[#]
GCS	5.40 ± 1.85	5.36 ± 1.21	0.898[#]

[#]Statistically not significant

Table 2: Comparison of metabolic parameters between the two groups

Parameter	Group N	Group B	p value
pH			
Preoperative	7.344 ± 0.06	7.340± 0.07	0.76
Immediate post-op	7.376± 0.05	7.377± 0.06	0.92
6 hr postoperative	7.39± 0.08	7.421 ± 0.03	0.02
$PaCO_2$			
Preoperative	38.10 ± 7.44	37.85 ± 7.63	0.87
Immediate post-op	35.69± 6.62	35.63 ± 6.72	0.96
6 hr postoperative	31.06± 6.54	33.83 ± 7.26	0.04
HCO_3			
Preoperative	22.54± 5.21	22.12± 2.77	0.613
Immediate post-op	22.28± 4.56	24.26± 10.06	0.211*
6 hr postoperative	21.29 ± 4.08	24.37 ± 2.72	0.0001*
Base excess			
Preoperative	-2.58 ± 2.96	-1.99 ± 2.16	0.25
Immediate post-op	-3.13± 3.16	-0.53 ± 1.99	0.0001*
6 hr postoperative	3.48± 4.38	0.32 ± 1.91	0.0001*
Serum Lactate			
Preoperative	2.34± 1.4	2.75 ± 0.9	0.1
Immediate post-op	2.46 ± 0.84	2.30 ± 0.85	0.3
6 hr postoperative	2.63 ± 0.86	1.67 ± 0.61	0.0001*

*Statistically significant

Table 3: Comparison of electrolytes between the two groups

Parameter	Group N	Group B	P value
Na-1	137.37 ± 4.96	138.08 ± 5.63	0.50
Na-2	140.20 ± 4.75	139.09 ± 5.14	0.26
Na-3	142.81 ± 5.27	140.00 ± 4.92	0.007
K-1	3.62± 0.42	3.592 ± 0.48	0.72
K-2	3.593 ± 0.32	3.68± 0.38	0.21
K-3	3.41 ± 0.38	3.90 ± 0.30	0.0001
Cl-1	98.88± 4.13	98.37 ± 2.35	0.45
Cl-2	101.04± 3.50	98.93± 1.96	0.0001*
Cl-3	102.77 ± 3.02	99.79 ± 1.71	0.0001*
Ca-1	1.044± 0.08	1.018 ± 0.05	0.06
Ca-2	1.018 ± 0.13	1.001± 0.08	0.46
Ca-3	0.96 ± 0.10	1.06 ± 0.06	0.0001*

*Statistically significant

Na, sodium; K, potassium; Cl, chloride; Ca, Calcium; 1-pre-operatively; 2-Immediate post operatively; 3-6hr post operatively.

Table 4: Comparison of Urine output between the two groups

Urine output	N	Group N (Mean ± SD)	Group B (Mean ± SD)	p-value
Preoperative	50	398.80± 205.90	442.00± 253.90	0.3[#]
Immediate post-op	50	285.20 ± 122.01	406.20 ± 167.53	<0.001*
6 hr postoperative	50	1091.0± 253.45	1341.40 ± 232.70	<0.001*

[#]Statistically not significant *Statistically significant

Table 5: Comparison of mortality between two groups on day 1

Mortality	Group N		Group B		p-value
	Number	Percentage (%)	Number	Percentage (%)	
Survived	45	90	46	92	
Expired	5	10	4	8	
Total	50	100%	50	100%	0.06

*Statistically significant

4. Discussion

Balanced crystalloid solution is currently being used as the fluid of choice perioperatively as well as in intensive care both in paediatric and adult.[8] The composition of balance crystalloid solution is quite similar to plasma composition in terms of various electrolytes. It contains lower amount of sodium as well as chloride compared to normal saline. It prevents the risk of any iatrogenic derangement in electrolytes and acid-base to a certain extent. A study conducted by Stewart et al. showed, hydrogen ion concentration (pH) is independently influenced by three variables: (1) PaCO2, (2) Total weak acid concentration composed of phosphate and albumin, 3) SID corresponding to the difference between strong cation and strong anions.[9] Various studies have reported that sodium chloride concentration contributes to metabolic acidosis by causing a decrease in SID.[10-12] 0.9% normal saline has high concentration of chloride ions that leads to hyperchloremic metabolic acidosis which has many detrimental effects on patient. Wilkes NJ et al. found that balanced crystalloid solution reduces the risk of hyperchloremic metabolic acidosis to a great extent.[13]

In our study all the demographic data and amount of mannitol given were comparable in both the groups. Therefore, it can be assumed that the electrolyte and acid base status was not confounded by the patient's demographic values and mannitol administration in our study.

pH was found to increase in both groups compared to baseline, with a significant difference observed at 6 hours post-operatively between the two groups. The pH in the balanced crystalloid solution group (7.421) was more towards the alkalotic side of the normal range, while in the normal saline group (7.39), it remained slightly acidotic within the normal range. The relative respiratory alkalosis observed in both groups compared to baseline could be attributed to hyperventilation. In the normal saline group, a gradual drop in bicarbonate ion concentration may have contributed to maintaining an acidotic pH. Conversely, in the balanced crystalloid group, the presence of acetate, which is metabolised to bicarbonate, likely prevented the pH from shifting towards the acidotic side.

$PaCO_2$ value was decreased in both the groups from baseline due to high respiratory rate. But it was significant 6 hours post operatively. As traumatic brain injury patients are shown to hyperventilate leading to respiratory alkalosis. Esnault et al. described the consequences on outcome of spontaneous hyperventilation after severe TBI.[14] They found that severe head injuries (SHV) were common in patients with a persistent coma after severe TBI, with an overall incidence of 69.1%. Patients with SHV were more severely injured and had higher morbidity. The proportion of patients with unfavourable functional neurologic outcome was significantly higher in SHV patients (52.6%). After adjusting for confounders, SHV remains an independent factor associated with unfavourable outcome at 6-month follow-up.

Base excess was found to be more negative in case of normal saline group due to presence of more chloride. In balanced crystalloid solution group of patients, it was in normal range. It was more in the positive side in BCS group of patients. In a study by Kellum conducted in surgical patients which had shown decrease in base excess in NS receiving patients as compared to balanced solution group.[11] Significant difference was seen in both groups with Base excess being more negative in NS group of patients immediately post op and 6 hours post operatively. Wilkes et al. showed balanced crystalloid solution causes significant acid-base stability compared to normal saline in elderly patients.[13]

4.1. Bicarbonate

Six hours after surgery, there was a noticeable difference in the groups' bicarbonate levels. While the mean serum bicarbonate in the balanced crystalloid solution group was more or less close to normal, it gradually dropped in the NS group patients. The NS group's reduced bicarbonate value might be the result of compensating for respiratory alkalosis. The bicarbonate plasma concentration is more stable in the

balanced solution. Acetate serves as a buffer in the kabilyte that we employed for this investigation. Bicarbonate is produced from acetate. According to the Hofmann-Kiefer pilot investigation, acetate-buffered solutions showed marginally better pH and plasma HCO3-stability than lactate-based solutions.[15] Additionally, the metabolism of balanced crystalloid solutions containing acetate is independent of liver function.[11]

4.2. Lactate

In each group, the lactate level was within the normal range. However, a statistically significant difference was observed six hours after surgery in both groups, with the balanced crystalloid solution group's value being closer to normal than the NS group. This suggests that the balanced crystalloid solution may have a more favourable effect on maintaining metabolic stability and preventing lactate accumulation, which is often associated with tissue hypoxia or metabolic disturbances. This observation is supported by findings from a pilot study done by Hofmann-Kiefer pilot et al., that acetate-buffered solutions-maintained plasma effective strong ion differences more stability than lactate-based solutions, potentially leading to better acid-base balance post-operatively.[15]

4.3. Serum sodium

In both groups, the analysis of sodium levels revealed relative hypernatremia relative to baseline. Six hours after surgery, a significant difference between the two fluids was seen, with the normal saline group having a greater difference. The increased sodium burden in NS (154meq/l) relative to plasma is the cause of this. Nonetheless, both patient groups' salt levels were within the usual range. Kolmodin et al. in their study also concluded that hypernatremia is common following traumatic brain injury and is because of different mechanisms such as use of hyperosmotic fluids, limitation of free water, or diabetes insipidus.[16]

4.4. Serum chloride

There was an increase in Chloride level in plasma in both the groups from baseline. However, the increase was more in case of normal saline group of patients as compared to balanced crystalloid solution group.[12] Significant difference was seen immediately postoperative and 6 hours post operatively. NS contains a very high chloride content (154 meq/L) which if infused for prolonged duration rapidly can lead to hyperchloremic metabolic acidosis as well as impairs the renal blood flow and glomerular filtration rate. Our results are in alignment with the study by Yessayan L et al. showed the association between hyperchloremia and occurrence of acute kidney injury in intensive care unit patients.[17] Balanced crystalloid solution contain very less amount of chloride. The mean chloride level was however within normal range in both groups.

4.5. Serum potassium

There was mild decrease in potassium level from baseline in NS group which was statistically significant. This is evident as NS does not contain potassium. Mean serum potassium level was found to be increased from baseline in balanced crystalloid solution group. There was statistically significant difference between two groups 6 hours postoperatively. Balanced crystalloid solution contains potassium that leads to increase in serum potassium level. This rise is due to the potassium content in balanced crystalloids, which helps maintain serum levels and prevent acidosis-driven potassium shifts. In contrast, normal saline lacks potassium and induces hyperchloremic metabolic acidosis, leading to potassium depletion through renal excretion and dilution. Thus, balanced crystalloids support better potassium stability compared to normal saline.

4.6. Serum calcium

There was mild decrease in serum Calcium level in NS group 6 hours postoperatively. However mean serum calcium level increased mildly from baseline in balanced crystalloid solution group patient. There was statistically significant difference in between two groups 6 hours postoperatively. This is evident by the fact that balanced crystalloid solution contains calcium.

The findings of significantly higher mean urine output in Group B at immediate post-operative and after 6 hours ($p<0.001$) compared to Group N can be correlated with existing literature that emphasises the importance of fluid management and its effects on renal function post-surgery.

Previous studies have shown that maintaining adequate urine output is crucial for assessing renal perfusion and function during the postoperative period.[18,19] For instance, a study indicated that a perioperative urine output target of 0.2 mL/kg/h was noninferior to the standard target of 0.5 mL/kg/h, resulting in substantial intravenous fluid sparing while still ensuring adequate renal function.[20] This suggest that careful management of fluid administration can lead to improved urine output without compromising kidney health.

Moreover, it has been documented that transient oliguria may occur postoperatively as a physiological response to tissue injury, which does not always indicate acute kidney injury (AKI).[21,22] In our study, the increased urine output in Group B may reflect effective fluid resuscitation and a better renal response following surgery, aligning with findings that demonstrate how appropriate fluid management can enhance postoperative renal outcomes.[20]

Additionally, postoperative oliguria is often seen as part of the body's adaptive response to surgical stress, where antidiuretic hormone release can influence urine output.[23] The significant increase in urine output observed in Group B could thus indicate a more favourable fluid balance and renal recovery compared to Group N, supporting the notion that

targeted fluid therapy can mitigate the risk of AKI and enhance recovery.

Our study has several limitations. Respiratory parameters were not recorded in either group. Apart from mannitol other drugs administered intraoperatively or postoperatively may alter acid base and electrolyte status of patients. A relatively small sample size in proportion to the burden of problem may influence our finding. Our results may vary from studies done on other ethnic groups owing to variations in body fluid composition, and subjective response to fluid administration. Further large multicentric trails could investigate the benefit of balanced crystalloids over normal saline in emergency neurosurgical patients.

5. Conclusion

The use of a balanced crystalloid solution as a maintenance fluid during the perioperative period in patients with traumatic brain injury results in fewer imbalances in electrolyte levels and acid-base balance compared to normal saline. No significant difference in survival rates is observed between the balanced crystalloid solution group and the normal saline group.

6. Source of Funding

None.

7. Conflict of Interest

None.

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