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Association between Serum Potassium Ion Abnormalities and Clinico-Radiologic Parameters in Severe Traumatic Brain Injury

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Abstract

Background: Severe Traumatic Brain Injury, is a major cause of mortality and disability worldwide. Inflammatory and biochemical cascades initiated by the primary injury insult to the brain lead to electrolyte dysfunctions that contribute to secondary brain injury. This study aimed at determining the incidence of serum potassium ion abnormalities and their association with specific clinical and radiologic parameters. **Methodology:** This was a prospective cross-sectional study of 117 patients with severe head injury admitted in our hospital between November 2019 and February 2020. Data collected included patient demographics, mechanisms of injury, prehospital interventions, clinical examination findings, CT Scan head findings, serum potassium ion levels (at admission and 48hrs later), and outcome (30 days). The data gathered was entered into the Statistical Package for Social Sciences for analysis. **Results:** Hypokalemia was the most common potassium ion abnormality, noted in 25(21.4%) and 21(23.9%) of cases at admission and 48hrs post-admission assays respectively. Hypokalemia was associated with the presence of epidural hematoma (p=0.005) while increased pulse rate (p=0.007) and traumatic SAH (p=0.045) were mainly seen in patients with hyperkalemia. Hypokalemia was associated with significantly increased risk of mortality OR 4.12(95% CI: 1.14-14.83, p=0.031) and OR 5.12 (95% CI: 1.08-24.25, p=0.039) at admission and 48hrs post-admission respectively. **Conclusion:** Hypokalemia is the commonest potassium ion abnormality seen in severe head injury, and is associated with significant increased risk of mortality.

Keywords: *Traumatic brain injury, hypokalemia, hyperkalemia*

Introduction

Severe Traumatic brain injury (TBI), defined as Glasgow Coma Scale ≤ 8, is a major cause of death and disability worldwide and is associated with huge direct and indirect costs to the public (1–3). Traumatic Brain Injury (TBI) is more in developing nations because of the increasing number of road traffic accidents (4–6). In our setup, most hospital-based studies have revealed that severe head injury is associated with mortality of >50% and poor functional outcomes (7–9). These bad outcomes may be associated with secondary brain insults such as electrolyte abnormalities that arise from inflammatory and biochemical cascades initiated by the primary injury insult to the brain (2,10).

Serum potassium abnormalities are common following trauma (11). Both hypokalemia and hyperkalemia can occur, and each is associated with poor outcomes. Post-traumatic hyperkalemia, defined as potassium level >5 mmol/l, is caused by extensive tissue damage, aggressive transfusion and hemorrhagic shock (12). Hypokalemia which is defined as potassium level <3.5mmol/l is postulated to arise from intracellular shift of potassium ions caused by epinephrine released during stress response to trauma (13–15). Both hypokalemia and hyperkalemia are associated with life-threatening cardiac arrhythmias which may

lead to death (11,16). There is paucity of local data on the incidence of potassium ion abnormalities following traumatic brain injury. This study aimed at determining the incidence of serum potassium ion abnormalities in severe TBI patients, and their association with clinico-radiologic parameters and 30-day outcome.

Materials and methods

Study design and site

An analytic cross-sectional study carried out over 4 months (1st November 2019 to 28th February 2020). The study site was the Kenyatta National Hospital Accident and Emergency Unit and Intensive Care Unit. Kenyatta National Hospital is located in Nairobi, Kenya and is the largest hospital and the main referral centre for neurotrauma cases countrywide. The Hospital serves patients from different regions and socioeconomic backgrounds.

Study population

One hundred and seventeen patients presenting with severe head injury defined by Glasgow Coma Scale ≤ 8 and whose next of kin had given informed consent were recruited into the study. Patients with known pre-existing chronic illness were excluded from the study.

Study variables

Data collected included patient demographics, mechanisms of injury, prehospital interventions, clinical examination findings, CT Scan head findings, serum potassium levels (at admission and 48hrs later), and outcome (30 days). The Injury Severity Score (ISS) was used to quantify the severity of injury to the patient (17). The serum potassium tests were done using Biolis 50i Superior Chemistry Analyser (Tokyo Boeki Medisys – Japan). Daily internal quality control checks were done to ensure that the results were valid. In addition, external quality control checks were done through the Randox International Quality Assessment Scheme (RIQAS). The reference range for serum potassium from our laboratory is 3.5-5.0mmol/L.

Statistical analysis: Data gathered was entered into Statistical Package for Social Sciences (SPSS) version 20.0 for analysis. Metric data are shown as means and standard deviation, nominal data as frequency and valid percent. Variables were tested for normal distribution using the Kolmogorov-Smirnov test in addition to histograms. If the assumption of normality was violated, Mann-Whitney U and Kruskal-Wallis tests were performed to test for differences between groups, instead of student's t-test and ANOVA (Analysis of Variance) tests respectively. Admission and 48hrs post admission variables were compared using the paired t-test. Categorical data was analysed by Pearson's Chi-square test. Correlation between the serum potassium and the study variables (clinical, radiologic) was determined using Pearson's correlation coefficient (r). Odds ratio were calculated for each electrolyte abnormality to determine its associated risk of mortality (30-day mortality). A p-value of <0.05 was considered as significant.

Ethical considerations: We conducted this study in compliance with the principles of the Declaration of Helsinki. The study's protocol was reviewed and approved by the Kenyatta National Hospital-University of Nairobi Ethics and Research Committee (P723/08/2019). Written informed consent was obtained from the next of kin of the patients as the patients could not consent in view of their low GCS.

Results

General information

The study recruited 117 patients out of which 111(94.9%) were male. The mean age was 32.41±14.59 years. Prehospital use of intravenous normal saline and mannitol solutions were reported in 65(55.6%) and 16(13.7%) of the patients respectively. The mean Glasgow Coma Score and Injury Severity Scores at admission were 6.41±1.69 and 21.06±7.74 respectively.

Prevalence of serum potassium ion abnormalities

The mean serum potassium ion level was 3.936±0.63mmol/l (n=117) and 3.99±0.81mmol/l (n=88) at admission and 48hrs after admission respectively. Paired T-test did not reveal any statistically significant differences between the potassium levels at admission and those at 48hrs post admission (p=0.461). The predominant abnormality was hypokalemia which was noted in 25(21.4%) and 21(23.9%) of cases at admission and 48hrs post admission assays respectively (Figure 1). Hyperkalemia was noted in 8(6.8%) cases at admission and in 6(6.8%) patients 48hrs post-admission.

Association between serum potassium and clinical parameters

The only parameter that displayed a statistically significant difference among the three groups, as well as significant correlation with admission serum potassium levels, was the heart rate (Table 1 and Table 2).

Association between serum potassium & radiologic parameters

Epidural hematoma was mostly associated with hypokalemia at admission (p=0.005) while traumatic SAH was mainly seen in patients with hyperkalemia (p=0.045) 48hrs post admission (Table 3). These variables displayed statistically significant correlations with the 48hr post admission potassium levels (Table 4). Other radiologic parameters did not display any significant associations with the serum potassium ion levels.

Association between serum potassium & 30-day mortality

Hypokalemia was associated with significantly increased risk of mortality OR 4.12(95% CI: 1.14-14.83, p=0.031) and OR 5.12 (95% CI: 1.08-24.25, p=0.039) at admission and 48hrs post admission respectively. Although hyperkalemia was also associated increased risk of mortality, the risks were not statistically significant OR 0.34(95% CI: 0.06-1.50, p=0.154) and OR 2.20 (95% CI: 0.41-11.64, p=0.36) at admission and 48hrs post admission respectively.

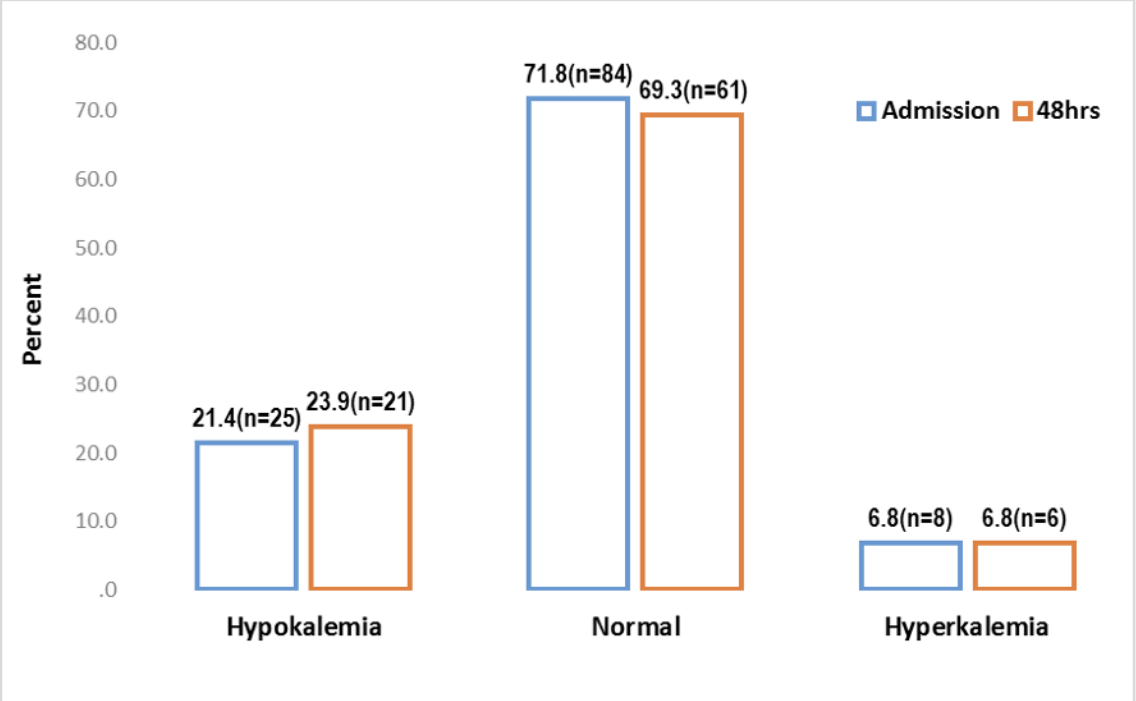

Figure 1: Serum potassium levels at admission and 48hrs post admission

Table 1: Association between serum potassium and clinical parameters

Variable		Hypokalemia	Normal	Hyperkalemia	P value
Age (yrs)	*Admission*	37.5±10.2	31.0±15.4	31.3±15.7	0.168
	48hrs post admission	35.0±16.4	33.9±13.5	24.8±14.7	0.353
Time from injury to presentation (hrs)	*Admission*	18.1±41.1	23.9±46.6	34.1±34.8	0.664
	48hrs post admission	31.2±47.1	23.4±38.3	9.3±7.1	0.469
Pre-hospital use of IV fluids	*Admission*	42.3%	60.0%	25.0%	0.066
	48hrs post admission	61.9%	57.4%	66.7%	0.871
Pre-hospital use of Mannitol	*Admission*	7.7%	15.6%		0.305
	48hrs post admission	19.0%	13.1%		0.485
Systolic BP (mmHg)	*Admission*	131.4±27.2	126.3±25.5	126.8±13.1	0.657
	48hrs post admission	135.5±26.8	129.2±22.7	116.3±7.3	0.194
Diastolic BP (mmHg)	*Admission*	78.3±19.1	75.5±18.0	72.4±14.2	0.662
	48hrs post admission	76.3±14.3	76.4±17.2	66.0±11.1	0.323
Heart rate (/min)	*Admission*	80.8±19.9	98.4±25.4	100.1±30.1	***0.007****
	48hrs post admission	91.9±30.5	93.4±24.0	83.2±23.6	0.644
Respiratory rate (/min)	*Admission*	19.5±3.9	21.3±4.9	20.5±3.7	0.257
	48hrs post admission	19.5±2.6	20.4±4.1	21.5±4.0	0.513
Saturation O2	*Admission*	92.3±7.8	90.6±10.3	93.0±6.1	0.698
	48hrs post admission	90.7±8.8	92.8±7.1	93.3±6.5	0.577
Total GCS Score	*Admission*	6.0±1.7	6.4±1.7	7.3±1.0	0.197
	48hrs post admission	5.9±1.8	6.6±1.5	6.7±2.0	0.180
ISS Score	*Admission*	21.4±7.9	21.2±7.9	18.1±5.5	0.540
	48hrs post admission	23.2±9.2	20.0±7.1	21.5±8.1	0.248

Table 2: Correlations between serum potassium and clinical parameters

		K^+ levels at admission	K^+ levels 48hrs post admission
Age	Pearson Correlation	-0.144	-0.097
	Sig. (2-tailed)	0.134	0.393
Time from injury to presentation (hrs)	Pearson Correlation	0.107	-0.088
	Sig. (2-tailed)	0.243	0.420
Pre-hospital use of Normal saline	Pearson Correlation	0.024	-0.007
	Sig. (2-tailed)	0.792	0.950
Pre-hospital use of Mannitol	Pearson Correlation	-0.005	0.156
	Sig. (2-tailed)	0.960	0.147
Mechanism of injury	Pearson Correlation	0.059	-0.128
	Sig. (2-tailed)	0.516	0.234
Systolic BP	Pearson Correlation	-0.140	-0.185
	Sig. (2-tailed)	0.121	0.085
Diastolic BP	Pearson Correlation	-0.106	-0.023
	Sig. (2-tailed)	0.240	0.831
Heart rate	Pearson Correlation	***0.327****	-0.058
	Sig. (2-tailed)	***<0.001***	0.601
Respiratory rate	Pearson Correlation	0.105	0.096
	Sig. (2-tailed)	0.288	0.409
Temperature	Pearson Correlation	0.006	-0.076
	Sig. (2-tailed)	0.956	0.521
Pupil examination	Pearson Correlation	-0.078	-0.049
	Sig. (2-tailed)	0.388	0.648
Total GCS Score	Pearson Correlation	0.068	0.155
	Sig. (2-tailed)	0.453	0.149
Injury Severity Score (ISS) Score	Pearson Correlation	-0.101	-0.045
	Sig. (2-tailed)	0.264	0.678

Table 3: Association between serum potassium and radiologic parameters

		Hypokalemia	Normal	Hyperkalemia	P value
Midline shift (mm)	Admission	11.4±5.7	8.3±6.2	7.5±7.6	0.223
	48hrs post admission	12.5±6.3	9.5±5.8	5.0±5.0	0.126
Compressed/absent basal cisterns	Admission	92%	71%	77.5%	0.552
	48hrs post admission	90.5%	91.8%	66.6%	0.149
Presence of epidural hematoma	Admission	44%	14.3%	12.5%	***0.005****
	48hrs post admission	23.8%	23.0%	-	0.411
Presence of subdural hematoma	Admission	40%	34.5%	37.5%	0.878
	48hrs post admission	38.1%	41.0%	33.3%	0.920
Presence of traumatic SAH	Admission	40%	38.1%	12.5%	0.332
	48hrs post admission	19.0%	37.5%	50.0%	***0.045****
Presence of contusion hemorrhages	Admission	56%	39.3%	50%	0.312
	48hrs post admission	38.1%	42.6%	50%	0.861
SDH Thickness (mm)	Admission	9.4±4.2	12.2±4.4	6.7±2.9	0.059
	48hrs post admission	11.1±3.5	11.7±5.1	7.5±3.5	0.500
Rotterdam CT Score	Admission	3.9±1.3	3.8±1.1	3.5±1.2	0.726
	48hrs post admission	3.9±1.0	3.9±1.1	3.7±1.4	0.842

Table 4: Correlations between serum potassium and radiologic parameters

		K^+ levels at admission	K^+ levels 48hrs post admission
Rotterdam CT head Score	Pearson Correlation Sig. (2-tailed)	-0.024 0.797	-0.005 0.967
Midline shift (mm)	Pearson Correlation Sig. (2-tailed)	-0.009 0.922	-0.093 0.389
Basal cisterns	Pearson Correlation Sig. (2-tailed)	-0.065 0.486	-0.115 0.284
Presence of Epidural Hematoma	Pearson Correlation Sig. (2-tailed)	***0.270*** ***0.003****	0.024 0.826
Presence of Subdural hematoma	Pearson Correlation Sig. (2-tailed)	0.005 0.956	0.002 0.989
Presence of Intracerebral hematoma	Pearson Correlation Sig. (2-tailed)	-0.020 0.831	-0.054 0.614
Presence of Traumatic Subarachnoid hemorrhage	Pearson Correlation Sig. (2-tailed)	-0.117 0.208	***0.213**** ***0.047***
Presence of Contusion hemorrhages	Pearson Correlation Sig. (2-tailed)	0.081 0.387	-0.103 0.338
Epidural Hematoma volume (ml)	Pearson Correlation Sig. (2-tailed)	0.104 0.723	-0.265 0.431
Subdural hematoma Thickness (mm)	Pearson Correlation Sig. (2-tailed)	-0.036 0.835	-0.213 0.258
Intracerebral hematoma Volume (ml)	Pearson Correlation Sig. (2-tailed)	0.225 0.593	-0.393 0.383

Discussion

The most common serum potassium abnormality reported in the current study was hypokalemia, seen in 21.4% and 23.9% of cases at admission and 48hrs post-admission respectively. Previous studies have also reported that hypokalemia is the most common potassium abnormality in head injury patients. The prevalence rate of hypokalemia in TBI is 21.5-68.3% (18–20). The main mechanism of post-traumatic hypokalemia is postulated to result from

potassium shifts into the intracellular compartment due to epinephrine surge caused by injury 1. The post-traumatic surge in catecholamines leads to β-2-adrenergic receptor stimulation and activation of the sodium-potassium pump, causing an intracellular K+ shift (21). Studies have also revealed that following head injury, there is an increase in cardiac output, blood pressure, pulse rate and pulmonary shunting along with decreased or normal systemic and pulmonary vascular resistance, consistent with increased circulating catecholamines (22). This may explain the observation in the current study that admission heart rate had a statistically significant correlation with serum potassium levels.

Although not observed in the present study, a previous study demonstrated a strong correlation between [K+] and GCS. In that study of 46 patients, the degree of hypokalaemia was found to be proportional to the fall in GCS (23) Serum catecholamine concentration is related to ICP in the setting of brain injury and the relationship between the two is dynamically dependent on ICP (24). Insulin, known to cause hypokalaemia, is not elevated in patients with a traumatic brain injury (13). Hypokalemia is associated with life-threatening cardiac arrhythmias and is a major risk factor for death in TBI patients (11,16). In the present study, hypokalemia was associated with 4-fold and 5-fold increased risk of mortality at admission and 48hrs post admission respectively.

Hyperkalemia in the present study was reported in 6.8% of the cases at admission and 48hrs post-admission. Previous studies have reported a prevalence rate of 0.9-17.7% (18–20). Post-traumatic hyperkalemia is induced by extensive tissue damage and aggressive transfusion (11). Additionally, prolonged hemorrhagic shock theoretically leads to hyperkalemia due to alterations in the cellular membrane function. Other causes of hyperkalemia in TBI include mannitol and anaesthetic agents such as succinylcholine and barbiturates (21,25–28). Although hyperkalemia is rare in TBI, it should be timely managed as it is also associated with life-threatening cardiac arrhythmias which may lead to death 1,5. In the present study, hyperkalemia was associated with risk of mortality of OR 0.34 and OR 2.20 at admission and 48hrs post admission respectively.

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