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CORRELATION BETWEEN MANNITOL INTERVENTION AND ELECTROLYTE IMBALANCE IN TRAUMATIC BRAIN INJURY PATIENTS OF REGIONAL GENERAL HOSPITAL OF WEST NUSA TENGGARA PROVINCE

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ABSTRACT

Background: Traumatic brain injury (TBI) is a commonly occurring injury following traffic accident. The most common complication following TBI is electrolyte imbalance and might be happen due to mannitol use. This research aims to know the correlation between mannitol intervention and electrolyte imbalance (natrium, kalium and chloride) in TBI patients of Regional General Hospital of West Nusa Tenggara Province.

Methods: This is a retrospective research with cross–sectional design. This research was done in Regional General Hospital of West Nusa Tenggara Province. Samples were collected by medical records of TBI patients from 2018 to 2019 which had met the inclusion criteria and then tested with correlation comparative test.

Results: From 160 samples that were obtained, 146 samples had electrolyte data, then categorized into those who were given mannitol (73,29%) and those who were not given mannitol (26,71%). The most common electrolyte imbalance was chloride (70,55%) which in hyperchloremia condition, followed by kalium (30,82%) with hyperkalemia and natrium (28,08%) with hyponatremia. Mannitol is most commonly given for one day and has the mean intervention of 2.6 days. Length of mannitol intervention and electrolyte levels were not

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normally distributed. There was no statistically significant difference between mannitol intervention and electrolyte imbalance (p=1.000, p=1.000, p=0.481) and length of stay on patients with no mannitol intervention and electrolyte imbalance (p=0,856, p=0,303, p=0,347). **Conclusion**: This research shows no correlation between the length of mannitol intervention and electrolyte imbalance (represented by natrium, kalium, and chloride) in TBI patients of Regional General Hospital of West Nusa Tenggara Province.

Keywords: mannitol intervention, electrolyte imbalance, traumatic brain injury.

Introduction

Traumatic brain injury is a brain disorder caused by outer mechanical force such as external impact or hit or penetrating injury.[1,2] The prevalence, morbidity and mortality rate of TBI is moderately high with the most common cause is traffic accident. The most common follow up event after traumatic brain injury is electrolyte disturbances. Various suspected etiologies such as intravenous fluid administration, the use of diuretics such as furosemide and mannitol, Syndrome of Inappropriate ADH Secretion (SIADH), and Cerebral Salt Wasting Syndrome (CSW) are said to cause disturbances in serum electrolytes of sodium, potassium, calcium and phosphate.[3,5-7]

Electrolyte disturbances may worsen due to mannitol administration, where mannitol administration in traumatic brain injury patients aims to prevent and treat intracranial hypertension, stabilization of cerebral perfusion pressure and brain oxygenation.[3,7] The use of mannitol can cause polyuresis and is a possible source of loss of various electrolytes in patients.[1,3] Excessive reduction in intravascular fluid volume due to mannitol administration can lead to dehydration and electrolyte disturbances in the form of hyponatremia and hypokalemia.[4]

Materials and Methods

This study was a retrospective unpaired comparative study with a cross sectional design. This study was conducted on traumatic brain injury patients at the Regional General Hospital of West Nusa Tenggara Province. Inclusion criteria were 1) Patients with head trauma who have medical records at Regional General Hospital of West Nusa Tenggara Province, 2) Patients with head trauma and diagnosed with traumatic brain injury, 3) Patients with a diagnosis of traumatic brain injury and accompanied by symptoms of increased intracranial pressure, 4) Patients with traumatic brain injury with increased intracranial pressure and were given

mannitol, and 5) Patients with traumatic brain injuries who had laboratory results of serum electrolytes (sodium , potassium, and chloride). The exclusion criteria were patients with a diagnosis of traumatic brain injury who did not have laboratory data on serum electrolytes and patients with electrolyte balance disorders before administration of mannitol. The minimum sample in this study is 150 samples. This study used a patient's medical record that was taken once. The medical record data recorded were data on the degree of traumatic brain injury measured using Glasgow Coma Scale (GCS), the duration of mannitol administration which was divided into ≤ 7 days and > 7 days, the length of patient care in days, sodium, potassium and chloride levels which were divided into normal and impaired (normal sodium levels 135-145 mmol / L, potassium 3,4-5,4 mmol / L, chloride 95-105 mmol / L) and age divided into 18–24 years, 25–34 years, 35–44 years , 45–54 years, 55–65 years, and the gender of the patient.

Results

In this study, 160 samples were obtained. This sample consisted of 111 men (69.4%) and 49 women (30.6%). The mean age was 38.5 years and the mode was 18 years. The 18–24-year age group had the greatest prevalence (25%). Of the total sample, 57 of them had severe brain injury (35.6%), 66 had moderate brain injury (41.3%) and 37 had mild brain injury (23.1%). The most frequent cause of injury was traffic accidents (87.5%). Leucocytosis occurred in 148 traumatic brain injury patients (92.5%). There were 27 traumatic brain injury patients who experienced comorbidities (16.9%) and 133 patients who did not experience comorbidities (83.1%). The accompanying injuries were mostly fractures. The average length of stay is 11 days. The condition of patients at the time of discharge from the hospital was still alive as much as 85.6%, so that the mortality rate for traumatic brain injury cases in this study was 14.4%.

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Table 1 Sample Characteristics

Characteristics		**Frequencies (N)**	**Percentage (%)**
Gender	Male	111	69.4
	Female	49	30.6
Severity of brain injury	Severe brain injury	57	35.6
	Moderate brain injury	66	41.3
	Mild brain injury	37	23.1
Cause of trauma	Traffic accident	140	87.5
	Attack	1	0.6
	Hit	2	1.2
	Fall	10	6.2
	Struck by an object	7	4.4
Leukocytosis	Yes	148	92.5
	No	12	7.5
Accompanying trauma	Yes	27	16.9
	No	133	83.1
Conditions on discharge	Dead	23	14.4
	Alive	137	85.6
Age	18 – 24 years	40	25.0
	25 – 34 years	30	18.8
	35 – 44 years	35	21.9
	45 – 54 years	22	13.8
	55 – 65 years	33	20.6
Age (mean)		38.6 years	
Age (modus)		18 years	
Length of stay (mean)		11 days	

In this study, 146 samples had electrolyte data. Of these 146 samples, 107 (73.29%) were given mannitol and 39 (26.71%) were not given mannitol. In patients given mannitol, the electrolyte disturbances

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mostly occurred in chloride as many as 79 people. Disruption to chloride level was dominated by hyperchloremia (72.9%) followed by hypochloraemia (0.9%). The second most common problem is sodium, which happened to 33 people. Disorders of sodium consisted of hyponatremia (23.4%) and hypernatremia (7.5%). Imbalance in potassium occurred in 31 people consisting of hypokalemia (9.34%) and hyperkalemia (19.6%). The average sodium content was 136.89 mmol / L, potassium was 11.73 mmol / L and chloride was 106.74 mmol / L. The highest sodium content was 155 mmol / L and the lowest was 123 mmol / L. The highest potassium content was 50 mmol / L and the lowest was 2.8 mmol / L. The highest chloride content was 134 mmol / L and the lowest was 65 mmol / L.

Graph 1 Electrolyte Disorders

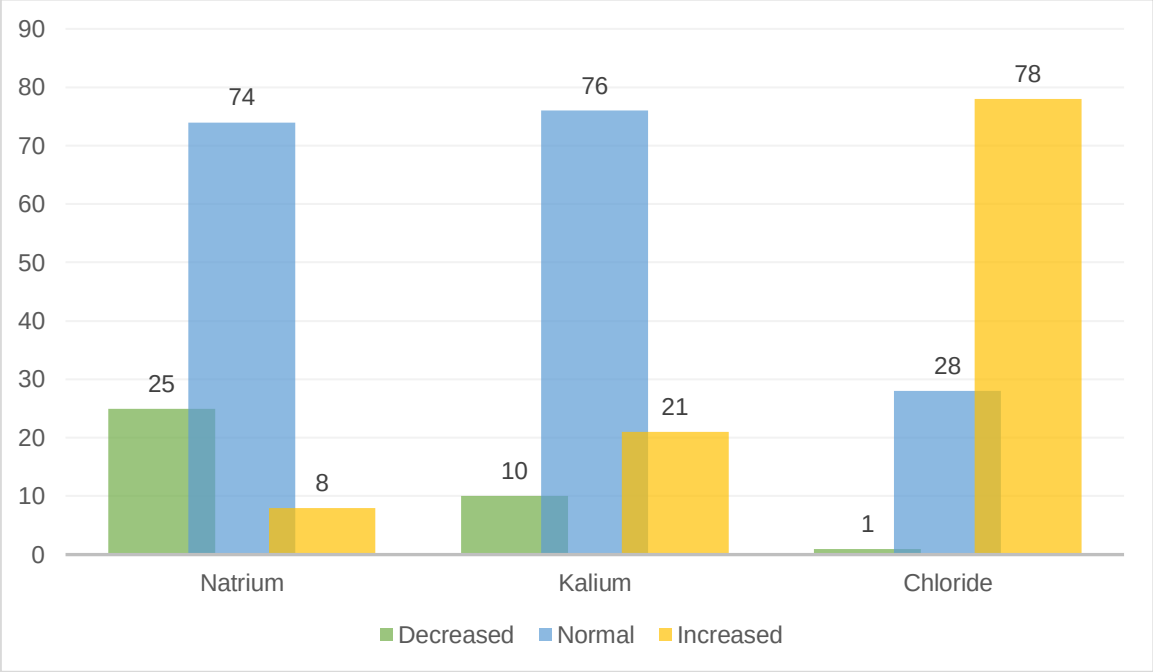

Table 2 Variable analysis test results of the length of treatment for patients who were given mannitol, the length of treatment for patients who were not given mannitol, and the length of mannitol administration

	Length of treatment	**Length of treatment (without mannitol)**	**Length of mannitol administration**
	P value (Mann-Whitney)	P value (Mann-Whitney)	P value (Fisher)
Natrium level	0.080	0.856	1.000
Kalium level	0.440	0.303	1.000
Chloride level	0.941	0.347	0.481

Discussion

In this study, it was found that the gender who experienced most traumatic brain injury were men. This is consistent with several previous studies which found that the incidence of traumatic brain injury was higher in men.[8,9] The median age with traumatic brain injury was 38.5 years. This is similar to a study by Marquez de la plata which found an average age of 36 years.[10] Traffic accident was the main cause of traumatic brain injury in this study. The same thing was found in a study by Dunne et al where they found that traffic accident was the most common cause of traumatic brain injury.[11] The incidence of leucocytosis occurred in 92.5% of the samples. This result is different from Guel's study which found 45.6% of traumatic brain injury patients in his study had leucocytosis.[12] The average length of patient care in days in this study was 11 days. In a previous study by Tardif et al., It was found that the average length of stay was similar, which was 11.7 days.[13]

The mortality rate from traumatic brain injury in this study was 14.4%. Similar results were found in a study by Kourbeti, which found that mortality occurred in 12.8% of the sample.[14] This finding is different from that of Song et al., Which found that 4.7% mortality from traumatic brain injury in 2010–2014.[15] The difference was found in 2013–2017 by a study by Okidi et al which found that the mortality of traumatic brain injury reached 33%. This difference might be due to the

lack of health resources in the African region[16]. Mortality of traumatic brain injury also shows a decreasing trend each year along with the developments in the health sector.[17] Administration of mannitol is often used as a dehydrating agent in cases of traumatic brain injury.[18] The same thing was found in this study where mannitol was used more in cases of traumatic brain injury (107 versus 39). To reduce the increased intracranial pressure (ICP), mannitol is usually given 0.5–2 g / kg intravenously for 30 to 60 minutes where the effect will appear in 5 to 10 minutes and this mannitol is given every six hours.[19] It is similar with this study which found that mannitol was most often given every 4 hours. The effect of mannitol can work for 1.5 to 6 hours on ICP so that if long-term reduction of ICP is needed, mannitol administration can be done every 2 to 6 hours.[20] A study conducted by Tan et al also found that administering mannitol every four hours was effective at reducing ICP during the first four days.[21] Mannitol was most often given for one day. This is consistent with what Tan et al wrote that mannitol should not be given for more than eight days.[21] This is because mannitol can aggravate cerebral oedema. Although mannitol is difficult to cross the blood-brain barrier, it can easily pass-through gaps in the damaged endothelium. Prolonged use of mannitol can cause mannitol leakage across the blood-brain barrier and exacerbate cerebral oedema. This is because the mannitol that has entered the brain draws water into the brain.[19]

In this study, hyperchloremia, hyponatremia, and hyperkalemia were mostly found in patients with traumatic brain injury. This is in accordance with a study conducted by Lee et al., 2016 which found that hyperchloremia occurred in 24.4% of traumatic brain injury patients. This is due to administration of high chloride fluids such as normal saline which can cause hyperchloremia. This hyperchloremic condition is associated with postoperative complications, acute renal failure and infection.[22] Hyponatremia is common in traumatic brain injury patients. Hyponatremia is the result of a syndrome of abnormal secretion of antidiuretic hormone (Syndrome of Inappropriate Antidiuretic Hormone Secretion / SIADH) and Cerebral Salt Wasting Syndrome (CSWS).[23] Hyponatremia due to SIADH usually occurs after traumatic brain injury and is mild. Chronic hyponatremia due to SIADH can result from damage to the infundibulum or posterior pituitary. This results in inappropriate ADH secretion.[24] CSWS is an electrolyte disorder characterized by hyponatremia and hypovolemia. The

underlying etiology has not been widely studied, but it is hypothesized to be caused by elevated levels of natriuretic peptides and changes in the sympathetic nervous system, renin – angiotensin – aldosterone, and adrenomedullin.[25] Hyperkalemia is the most common potassium electrolyte disturbance found in this study. This is different from the research by Syah et al. who found that hypokalemia was mostly found in traumatic brain injury patients. Hyperkalemia in this study may occur due to catecholamine secretion that accompanies head trauma resulting in stimulation of the Na / K ATPase pump.[26]

In this study, there was no significant difference between length of treatment and electrolyte disturbances, both in patients who were given mannitol or patients who were not given mannitol. Different results were obtained in a study by Ouf et al., 2015 which found that there was a significant relationship between length of treatment and electrolyte disturbances.[27] This difference is due to several confounding factors such as drugs or therapies that affect electrolyte levels such as diuretics and therapy, fluids, as well as dietary changes.[28] In this study, the results of the analysis test showed no significant difference between the duration of mannitol administration and electrolyte disturbances. This is similar to a study conducted by Czupryna in 2018 which examined the effect of mannitol with electrolyte concentrations in encephalitis patients and found that there was no significant difference in electrolyte balance after administration of mannitol.[29] This finding was also similar to the study conducted by Seo in in 2010 which found that there was no difference in hypernatremia and hyponatremia after seven days of mannitol administration.[30]

This insignificant result was caused by several confounding factors. Electrolyte disturbances such as hyperchloremia can occur due to normal saline fluid resuscitation. Resuscitation of large volumes of normal saline can cause excess chloride ions in the blood.[31] Hypochloremia in TBI patients can be caused by the body's response by reducing renal perfusion, resulting in decreased Claudin-2 expression. Decreasing Claudin-2 expression will make it more difficult for chlorine to be absorbed.[32] Another confounding factor is an abnormal body response to trauma. An example is SIADH which occurs in response to trauma and causes hyponatremia. In addition, CSWS can also cause hyponatremia.[23] Hypokalemia occurs in patients with traumatic brain injury due to movement of potassium into cells in response to increased epinephrine after a traumatic event. This is evidenced by a research from

Beal et al who found high epinephrine levels in new traumatic brain injury patients.[33,34] The weakness of this study is the insufficient medical record data. Electrolyte data were only taken for a short period of time, while the data on mannitol administration were quite complete. This caused the researchers to be unable to analyse the exact length of mannitol administration. Another weakness is the incompleteness of medical records to record patient comorbidities such as diabetes mellitus and other diseases that can cause electrolyte disturbances. This study also did not exclude normal saline administration so that electrolyte disturbances can be caused by improper administration of normal saline.

Conclusion

Based on the results of this study, it can be concluded that there is no relationship between the use of mannitol and the condition of serum electrolyte imbalance in Traumatic Brain Injury patients at the Regional General Hospital of West Nusa Tenggara Province.

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