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High Blood Osmolality is Associated with Poor Neurological Status in Acute Ischemic Stroke Patient on Admission

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Abstract

Purpose: The purpose of this study is to evaluate the association between high blood osmolality and neurological status in acute ischemic stroke.
Methodology: This is a cross-sectional study. Subjects of this study are acute ischemic stroke patients admitted at Dr. Sardjito Hospital. Subjects who met the inclusion and exclusion criteria were analysed mainly the blood osmolality and NIHSS score at the time of admission.
Results: The study involved 58 participants, with 29 (50%) exhibiting blood osmolality exceeding 300 mOsm/kg. A bivariate analysis revealed several factors significantly linked to poor neurological condition upon admission. These included elevated blood osmolality (OR=5,296, p=0,014, 95% CI, 1,29-21,7), presence of infection (OR=11,67, p=0,007, 95% CI, 1,95-6,99), increased white blood cell count (OR=4,750, p=0,028, 95% CI, 1,21-18,5), and an ASPECT Score below 7 (OR=14, p<0,001, 95%CI, 3,34-59). Multivariate analysis revealed that high blood osmolality (p=0,031) significantly associated with poor neurological status at the time of hospital admission.
Applications: This study highlighted the importance of evaluating blood osmolality in acute ischemic stroke patients as it is associated with neurological deficit.

Introduction

Brain ischemia may be preceded by and potentially caused by a lack of hydration (Rowat et al., 2012). In cerebral infarction, dehydration increases blood viscosity and reduces cerebral blood flow due to decreased intravascular volume (Schrock et al., 2012). Dehydration elevates the hematocrit level and is linked to a more extensive infarct size, consequently worsening the neurological impairment (Rowat et al., 2012). Dehydration reduces the volume of plasma and cardiac output, which leads to a decrease in blood pressure. This, in turn, impairs collateral blood flow and cerebral perfusion pressure.

Other studies have also reported an association between dehydration and poor functional outcome in acute ischemic stroke patients (Li et al., 2016). Dehydration has been shown to be an independent predictor of neurological deterioration in acute ischemic stroke patients (Lin et al., 2014; Schrock et al., 2012). Many parameters are used to assess dehydration but no parameter has been established as the gold standard (Bhalla et al., 2000). One of objective parameter and is often used in assessing dehydration is a haematological parameter by measuring blood osmolality (Hooper et al., 2015). Blood osmolality measures hydration status better than urea and blood creatinine levels (Bhalla et al., 2000). Dehydration conditions will cause high blood osmolality with a value> 300 mOsm/kg indicating dehydration.

Limited research has investigated the associated between neurological condition and dehydration, as measured by blood osmolality, in patients with acute ischemic stroke. The neurological status parameter that has been shown to have high reliability and is valid in predicting stroke patient outcome is National Institutes of Health Stroke Scale (NIHSS) score (Shah et al., 2014). This study aims to evaluate the association between high blood osmolality and the neurological status of acute ischemic stroke at the time of admission.

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Method

This study was a cross-sectional analytical study. The independent variables of this study were blood osmolality, age, gender, blood pressure, blood Low-Density Lipoprotein (LDL) level, ischemic area, leukocyte count, heart failure, atrial fibrillation and infection. The dependent variable was the neurological status of acute ischemic stroke at admission as measured with the NIHSS score.

Subjects were acute ischemic stroke patients admitted at Dr. Sardjito Hospital. Inclusion criteria are first acute ischemic stroke confirmed by head CT scan with onset <72 hours. The exclusion criteria were posterior circulation stroke, chronic kidney disease, diabetes mellitus (HbA1c > 6,5 %), incomplete electrolyte examination and previous administration of nootropics drug. This study has received approval from the Ethics Committee for Human Research, Faculty of Public Health Medicine and Nursing, Universitas Gadjah Mada.

Subjects who met the criteria were then analysed based on age, sex, blood osmolality, blood pressure, lipid profile, ischemic area, leukocyte count, heart failure, atrial fibrillation and infection as well as the NIHSS score. Blood osmolality is calculated using formula:

$$2\,(Na+K)+(\text{Blood Urea Nitrogen (BUN)})/2{,}8+(\text{Blood Glucose})/18 \quad (1)$$

Data for all these parameters were the first examination when the patient was admitted to the hospital. Measurement of blood pressure is measured in mmHg, levels of BUN, creatinine, LDL, and blood glucose are measured in mg/dL, the number of leukocytes is measured in units of mc/L based on blood tests at the Clinical Pathology Laboratory, Dr. Sardjito. The diagnosis of atrial fibrillation and heart failure was based on an assessment by cardiologist, a diagnosis of upper respiratory tract infections, pneumonia and Urinary Tract Infection (UTI) based on an assessment by internist. The extent of the ischemic area was assessed using the Alberta Stroke Program Early CT (ASPECT) score based on the CT scan of the head performed at the Radiology of Dr. Sardjito Hospital. The NIHSS score was assessed by a neurologist who examined the patient at hospital admission.

Data and statistical analysis were carried out using SPSS. All variables were grouped into 2 categories. High blood osmolality if >300 mOsm/kg and a poor neurological outcome if the NIHSS score is >8. Bivariate analysis analysed with Chi-Square/Fisher's Exact. After the bivariate analysis, variables with a p-value <0.05 were analysed into the multivariate analysis using logistic regression.

Results and Discussion

This study included 58 participants (Table 1), comprising 30 males (51.7%) and 28 females (48.3%), with an average age of 64.79±12.5 years. The mean systolic blood pressure of the subjects at admission was 157.6±28.4 mmHg, the mean diastolic blood pressure at admission was 90.1±17.6 mmHg.

The mean leukocyte count at admission was 9,068±3,341 mc/L. The mean LDL levels of the subjects were 137.25±46.37 mg/dL. The ASPECT score has a median value of 9 with a minimum value of 1 and a maximum value of 10. The subject's NIHSS score has a median value of 4 with a minimum value of 1 and a maximum value of 33. Subjects with comorbid heart failure were 6 (10.3%), atrial fibrillation 6 (10,3%), infection 7 (12.1%) with the most types of infection were pneumonia. Subjects with high osmolality were found to be 29 (50%).

Table 1. Subjects Characteristics.

Variable	N (%)	Average ± SD	Median (min-max)
Gender			
Male	30 (51,7)		
Female	28 (48,3)		
Heart Failure	6 (10,3%)		
Atrial Fibrillation	6 (10,3%)		
Infection	7 (12,1%)		
Age		64,79±12,5 y.o	
Onset			14,5 (1-120) hours
Blood Pressure			
Systole		157,6±28,4 mmHg	
Diastole		90,1±17,6 mmHg	
Leucocyte Count		9.068±3.341 mc/L	

LDL		137,25±46,37 mg/dL	
ASPECT Score			9 (1-10)
NIHSS			4 (1-29)
Osmolality			
>300 mOsm/kg	29 (50%)		
≤300 mOsm/kg	29 (50%)		

SD: Standard Deviation, y.o: years old

In the bivariate analysis (Table 2), high blood osmolality (OR=5.296, p=0.014, 95% CI, 1.29-21.7), infection (OR=11.67, p=0.007, 95% CI, 1.95-6.99), high leukocyte count (OR=4.750, p=0.028, 95% CI, 1.21-18.5), ASPECT score <7 (OR=14, p <0.001, 95% CI, 3.34-59) were significantly related to poor neurological outcome at hospital admission.

Table 2. Statistical Analysis Variables on Neurological Outcome.

Variable	Good Neurological Outcome (%)	Poor Neurological Outcome (%)	OR	95% CI	*p*
Osmolality					
>300	11(37,9)	18(62,1)	5,296	1,29-21,7	0,014*
≤300	3 (10,3)	26 (44,8%)			
Age					
≥65 y.o	9(30)	21(70)	1,971	0,57-6,83	0,28*
< 65 y.o	5(17,9)	23(82,1)			
Gender					
Male	5 (16,7)	25 (83,3)	0,422	0,12-1,47	0,169*
Female	9 (32,1)	19 (67,9)			
Blood Pressure					
>180/120	3 (30)	7 (70)	1,442	0,32-6,5	0,453*
≤180/120	11 (22,9)	37 (77,1)			
Heart Failure					
Yes	3 (50)	3 (50)	3,7	0,65-21	0,145*
No	11 (21,2)	41 (78,8)			
Atrial Fibrillation					
Yes	2(33,3)	4(66,7)	1,667	0,27-10,2	0,45*
No	12(23,1)	40(76,9)			
Infection					
Yes	5 (71,4)	2 (28,6)	11,67	1,95-6,99	0,007*
No	9 (17,6))	42 (82,4)			
Leucocytes					
>11000	6 (50)	6 (50)	4,750	1,21-18,5	0,028*
≤11000	8 (17,4)	38 (82,6)			
LDL					
≥100	13 (27,7)	34(72,3)	3,82	0,44-32,9	0,186*
<100	1 (9,1)	10(90,9)			
ASPECT Score					
≤7	9 (64,3)	5 (35,7)	14	3,34-59	<0,001*
>7	5(11,4)	39(88,6)			

*Pearson's Chi-Square test, OR: Odd Ratio, y.o: years old

Logistic regression test was performed on blood osmolality, leukocyte count, infection and ASPECT score (Table 3). Two variables were significantly associated with poor neurological outcome, blood osmolality (B=2.180, p=0.031) and ASPECT score (B=2.396, p=0.006).There was no statistically significant association between age, sex, blood pressure, heart failure, atrial fibrillation and LDL and poor neurological outcome at admission.

Table 3. Statistical Analysis Variables on Neurological Outcome.

Variabel	B	p
Blood Osmolality	2,180	0,031*
Leucocytes	1,515	0,112*
Infection	2,341	0,066*
ASPECT Score	2,396	0.006*

*Logistic Regression Test

These results showed that 50% of the subjects had high blood osmolality (> 300 mOsm/kg). This result was in accordance with Liu et al., (2014) who found almost half of acute ischemic stroke patients were admitted with dehydration. Dehydrated Ischemic stroke patients face multiple physiological challenges. The lack of adequate hydration increases blood viscosity, reduces the heart's ability to pump effectively, and lowers overall blood pressure. Furthermore, it hampers collateral blood flow and diminishes the brain's blood supply. These combined effects intensify the ischemic state, leading to more pronounced neurological impairments (Liu et al., 2014).

Several factors were known to influence hydration status. The subjects in this study were in the elderly with a mean age of 64.79±12.5 years. Elderly individuals experience a decline in thirst perception. This reduced sensitivity to thirst can result in delayed fluid intake for compensation. Consequently, dehydration in older adults may precipitate brain ischemia (Rodriguez et al., 2009).

Insufficient intravascular fluid, resulting from dehydration, can reduce cerebral perfusion and potentially trigger brain infarction. This risk is heightened in cases where blood vessels are occluded or stenotic, making these areas more vulnerable to decreased blood flow (Rodriguez et al., 2009). Thrombus formation can also result from dehydration. Dehydration increases blood viscosity and increase the risk of thromboembolic event, which is linked to more severe stroke outcomes (Swerdel et al., 2016). This is supported with this study result that found high blood osmolality was significantly associated with poor neurological outcome on logistic regression.

The logistic regression analysis revealed that the ASPECT score was a significantly associated with poor neurological status. The ASPECT score serves as an anatomical indicator of ischemic stroke damage in the anterior circulation. A lower ASPECT score indicates a greater extent of ischemic lesions. Extensive ischemic damage typically results in more severe neurological deficits associated with stroke (Zanzmera et al., 2012).

Infection was significantly associated with poor neurological status of ischemic stroke at admission in bivariate analysis although the logistic regression was not significant. These results were consistent with the results of research by Grabska et al. (2011) which found that infection in acute ischemic stroke predicted poor short-term and long-term outcomes (Grabska & Członkowska, 2011). When an infection occurs, the immune system releases inflammatory mediators, including cytokines, which exacerbate the inflammatory response in ischemic stroke. This increased inflammation can potentially aggravate mitochondrial dysfunction, that has been clinically linked to the degree of neurological deficit observed in acute ischemic stroke patients (Westendorp et al., 2011).

The leukocyte count on the bivariate analysis was significantly associated with the poor neurological outcome of acute ischemic stroke at admission. It is known that ischemic brain tissue will experience an acute inflammatory response characterized by leukocyte infiltration in the post-ischemic tissue and susceptible to damage (Scherbakov et al., 2015). Migration of leukocytes into the penumbra region can exacerbate excitotoxicity-induced neuronal death, potentially leading to a deterioration in neurological function and increasing the overall severity of ischemic stroke (Scherbakov et al., 2015). Atrial fibrillation and hypertension were not significantly associated with neurological outcome of stroke ischemic stroke on hospital admission in this study probably because some subjects had been taking anti-hypertensive and anti-coagulant drugs routinely that may affect the neurological condition. The results of studies regarding the relationship between lipid profiles and stroke were inconsistent. Research has demonstrated that LDL is atherogenic and contributes to the formation of atherosclerotic lesions. Elevated LDL have also been correlated with additional vascular risk factors, including hypertension, diabetes, and obesity. The presence of atherogenic plaque, combined with these vascular risk factors, results in more severe strokes in high LDL levels (Xing, 2016).

Cholesterol serves a vital structural purpose within cell membranes. As one of the principal lipid elements in the plasma membrane, cholesterol contributes significantly to cellular integrity. Moreover, cholesterol is recognized for its influence on vascular function and maintaining the durability of vascular membranes (Hasibuan et al., 2015). No significant association between heart failure and NIHSS score at admission was likely influenced by severity heart

failure which was not classified in this study. The severity of heart failure has been shown to be a factor that also influences ischemic stroke outcome (Scherbakov et al., 2015).

There are several limitations to this study. No studies have yet assessed the specificity and sensitivity of blood osmolality in assessing dehydration. Other factors that affect blood osmolality such as albumin, anti-diuretic hormone levels have not been analysed.

Conclusions

We conclude that high blood osmolality was associated with poor neurological status in acute ischemic stroke patient on hospital admission.

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References

Bhalla, A., Sankaralingam, S., Dundas, R., Swaminathan, R., Wolfe, C. D. A., & Rudd, A. G. (2000). Influence of Raised Plasma Osmolality on Clinical Outcome After Acute Stroke. 2043–2049.

Grabska, K., & Członkowska, A. (2011). Infections and Ischemic Stroke Outcome. 2011. https://doi.org/10.1155/2011/691348

Hasibuan, A. E., Fitri, A., Surbakti, K. P., & Rambe, A. S. (2015). Hubungan Kadar Low-Density Lipoprotein Cholesterol dengan Kejadian dan Keparahan Stroke Akut. Neurona, 32(July).

Hooper, L., Abdelhamid, A., Ali, A., Bunn, D. K., Jennings, A., John, W. G., Kerry, S., Lindner, G., Pfortmueller, C. A., Sjöstrand, F., Walsh, N. P., Fairweather-Tait, S. J., Potter, J. F., Hunter, P. R., & Shepstone, L. (2015). Diagnostic accuracy of calculated serum osmolarity to predict dehydration in older people: adding value to pathology laboratory reports. BMJ Open, 5(10), e008846. https://doi.org/10.1136/bmjopen-2015-008846

Li, J., Wang, D., Tao, W., Dong, W., Zhang, J., Yang, J., & Liu, M. (2016). Early consciousness disorder in acute ischemic stroke : incidence , risk factors and outcome. BMC Neurology, 1–7. https://doi.org/10.1186/s12883-016-0666-4

Lin, L. C., Lee, J. Der, Hung, Y. C., Chang, C. H., & Yang, J. T. (2014). Bun/creatinine ratio-based hydration for preventing stroke-in-evolution after acute ischemic stroke. American Journal of Emergency Medicine, 32(7), 709–712. https://doi.org/10.1016/j.ajem.2014.03.045

Liu, C. H., Lin, S. C., Lin, J. R., Yang, J. T., Chang, Y. J., Chang, C. H., Chang, T. Y., Huang, K. L., Ryu, S. J., & Lee, T. H. (2014). Dehydration is an independent predictor of discharge outcome and admission cost in acute ischaemic stroke. European Journal of Neurology, 21(9), 1184–1191. https://doi.org/10.1111/ene.12452

Rodriguez, G. J., Cordina, S. M., Vazquez, G., Suri, M. F. K., Kirmani, J. F., Ezzeddine, M. A., & Qureshi, A. I. (2009). The hydration influence on the risk of stroke (THIRST) study. Neurocritical Care, 10(2), 187–194. https://doi.org/10.1007/s12028-008-9169-5

Rowat, A., Graham, C., & Dennis, M. (2012). Dehydration in hospital-admitted stroke patients: Detection, frequency, and association. Stroke, 43(3), 857–859. https://doi.org/10.1161/STROKEAHA.111.640821

Scherbakov, N., Haeusler, K. G., & Doehner, W. (2015). Ischemic stroke and heart failure : facts and numbers. 1–4. https://doi.org/10.1002/ehf2.12026

Schrock, J. W., Glasenapp, M., & Drogell, K. (2012). Elevated blood urea nitrogen/creatinine ratio is associated with poor outcome in patients with ischemic stroke. Clinical Neurology and Neurosurgery, 114(7), 881–884. https://doi.org/10.1016/j.clineuro.2012.01.031

Shah, R., Vyas, C., & Vora, J. (2014). NIHSS Score : A handy tool to predict vascular occlusion in acute ischemic stroke. Circulation, 18–22.

Swerdel, J. N., Janevic, T. M., Kostis, W. J., Faiz, A., Cosgrove, N. M., & Kostis, J. B. (2016). Association Between Dehydration and Short-Term Risk of Ischemic Stroke in Patients with Atrial Fibrillation. Translational Stroke Research. https://doi.org/10.1007/s12975-016-0471-9

Westendorp, W. F., Nederkoorn, P. J., Vermeij, J., Dijkgraaf, M. G., & Beek, D. Van De. (2011). Post-stroke infection : A systematic review and meta-analysis. BMC Neurology, 11(1), 110. https://doi.org/10.1186/1471-2377-11-110

Xing, Y. (2016). Low Density Lipoprotein Cholesterol and the Outcome of Acute Ischemic Stroke : Results of a Large Hospital-Based Study. 195–201. https://doi.org/10.1159/000450604

Zanzmera, P., Srivastava Prof., P., Garg, A., Bhatia, R., Singh, M., Tripathi, M., & Prasad, K. (2012). Prediction of stroke outcome in relation to Alberta Stroke Program early CT score (ASPECTS) at admission in acute ischemic stroke: A prospective study from tertiary care hospital in north India. Neurology Asia, 17(2), 101–107.