

Research Article

Serum neuronal specific enolase as a biomarker in differentiating the side of brain lesion in acute hemorrhagic stroke: a hospital based study

Omkar Prasad Baidya^{1*}, Sunita Tiwari¹, Kauser Usman²

¹Department of Physiology, ²Department of Medicine, King Georges Medical University (KGMU), Lucknow, India

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***Correspondence:**

Dr. Omkar Prasad Baidya,

E-mail: omkarprasadbaidya@gmail.com

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ABSTRACT

Background: Neuronal specific Enolase (NSE) is the neuronal form of the glycolytic enzyme enolase. This study has been conducted to see the role of serum NSE in differentiating the side of brain lesion within 24 hours of acute hemorrhagic stroke onset.

Methods: The study was conducted in collaboration with the Department of Physiology and Medicine after Ethical clearance from December 2013 to April 2015. Our study group consists of 35 acute hemorrhagic stroke patients (clinically and radio logically confirmed) irrespective of age and sex, admitted in Emergency Unit, Medicine Department within 24 hours of stroke symptom onset. The patients were undergone plain CT scan brain on admission to confirm the diagnosis and the side of the lesion in brain. Serum NSE for these patients was estimated by using NSE Human ELISA Kit, in the Department of Physiology.

Results: In this study, serum NSE bears a positive significant correlation to the hematoma volume in brain ($r=0.786$, $p<0.001$) and to the National Institute of Health Stroke Scale (NIHSS) ($r=0.44$, $p=0.008$). However, there is no significance difference between the serum NSE in right hemispheric brain lesion compared to left hemispheric brain lesion ($p=0.597$).

Conclusions: Serum NSE within 24 hours of stroke onset can reflect the volume of brain lesion and severity of neurological deficit but cannot differentiate the side of brain lesion in these patients.

Keywords: NSE, CT scan, ELISA, NIHSS

INTRODUCTION

Stroke can be defined by the neurological deficit of sudden onset that is due to a vascular cause of focal origin.¹In hemorrhagic stroke, the collected and expanding hematomas in brain causes compression of the surrounding neurons leading to their damage. Beside, pressure exerted by the hematoma in the surrounding neuronal area in brain may lead to decrease in the blood supply due to compression on the blood vessels which may further lead to infarction. Hypertension or any other causes which weaken the endothelial lining of vessel may lead to the sudden rupture of the blood vessel of a focal region of brain and collection of blood in brain parenchyma. Collected hematoma then may cause mass

effect on the surrounding neurons, adjacent structures and increase the intracranial pressure which may lead to even death due to brain herniation. At present, diagnosis of acute hemorrhagic stroke is based on CT scan (Computer Tomography) as CT is highly sensitive to acute blood collection in brain.² Neuron-specific Enolase (NSE) is the neuronal form of the intracytoplasmic glycolytic enzyme enolase. This enzyme with a molecular weight of 78 kDa regulates the interconversion of Phosphoglycerate and Phosphoenolpyruvate in the glycolytic pathway in the neurons. Physiologically, NSE is not secreted actively by any cells and thus it is present in very low amount in the serum of normal healthy subjects.³ NSE is present mainly in the cytoplasm of neurons and cells of neuro-endocrine origin. It can also be found in erythrocytes and platelets

but in smaller concentrations. Elevated concentrations of NSE have been noted in neuronal injury and NSE estimation may be correlated to the degree of neuronal damage.⁴ Damaged neurons cannot use the enzyme NSE and hence serum NSE rises following acute stroke.⁵ To the best of my knowledge, literature regarding the role of serum NSE in differentiating the side of brain lesion in acute hemorrhagic stroke are lacking in Indian as well as world literature. Hence, the study had been conducted to see the significance of serum NSE as a marker of neuronal damage in acute hemorrhagic stroke in the tertiary hospital of northern India.

METHODS

The study had been conducted in collaboration with the Department of Physiology and Department of Medicine from December 2013 to April 2015. The ethical approval was obtained for this study from the Institutional Ethical Committee (IEC). This study was primarily based on data of 35 acute hemorrhagic stroke patients (clinically and radio logically confirmed) irrespective of age and sex admitted in Emergency Unit of the Medicine Department within 24 hours (<24 hours) of symptom onset of stroke. Those patients who had a history of suffering from any neurological disease like neuro-blastoma, neurodegenerative disorders like dementia, epileptic seizure, encephalopathy, chronic sequence of stroke, multiple stroke attacks, traumatic brain injury, hemolytic anemia, hepatic failure, end stage renal disease, some carcinomas like small cell lung carcinoma, Medullary Thyroid Cancer, Carcinoid Tumor, Islet cell tumours of pancreas and melanoma etc were excluded from the study.

A pre designed semi-structural proforma, for each of the acute hemorrhagic stroke patients was maintained where brief clinical information including particulars of the patient such as chief complaints, family, personal, dietary, past history etc were reported systematically. All the patients have been undergone proper general physical examination and systemic examination and the

observations have been recorded in the proforma. Informed consent from the patient/patient party was taken before including them in the study. Venous blood samples was collected under aseptic condition from all the 35 acute stroke patients on admission (within 24 hours of onset of acute stroke) in a plain vial so as to allow the blood to coagulate. Separation of the serum was done from collected coagulated samples using ultracentrifugation technique. Plain CT scan brain was done for all these acute hemorrhagic stroke patients on admission in the Emergency Department using CT scan machine Model 16 slice Brivo 385 to confirm the diagnosis and to estimate volume of hematoma in brain. Volume of hematoma was estimated from the film by using the formulae $axbxc/2$.⁶ Serum NSE for the acute hemorrhagic stroke patients was estimated by using NSE Human ELISA kit, Model-34239374 marketed by MyBiosource, Inc, USA which had been read by Microplate Reader (ELISA reader) Model No-iMark, 11915, made in Japan(Marketed by Biorad Labs) in the Department of Physiology. Data were checked for consistency and analyzed using the Statistical Package for Social Sciences (SPSS), version 16 (SPSS Inc, Chicago, IL, USA). Statistical methods like Spearman correlation coefficient and Mann Whitney Test etc were applied wherever found appropriate.

RESULTS

The present study is based on the primary data of 35 acute hemorrhagic stroke patients. In 35 acute hemorrhagic stroke patients, serum NSE bears a positive significant correlation to the volume of hemorrhage in brain (Spearman Correlation Coefficient $r=0.786$, $p<0.001$) (Table 1). Serum NSE also bears positive significant correlation to the NIHSS ($r=0.44$, $p=0.008$) (table 2). Beside, serum NSE also shows negative but insignificant correlation to the Glasgow Coma Scale in these patients ($r=-0.329$, $p=0.054$) (Table 3). However, there is no significance difference between the serum NSE in left sided brain lesion compared to the right sided brain lesion ($p= 0.597$) (Table 5).

Table-1: Correlation of serum NSE to the volume of hemorrhage in acute hemorrhagic stroke patients.

Cases	Parameters	Median±Standard deviation(SD)	Correlation coefficients (R)	P value
Acute hemorrhagic stroke patients (n=35)	Volume of hemorrhage(cc)	96.64 ± 87.69 cc	Spearman correlation (vol.=nonparametric) $r=0.786$	P< 0.001
	Serum NSE (ng/ml)	20 ± 12.75 ng/ml		

Table 2: Correlation of serum NSE to NIHSS in acute hemorrhagic stroke patients.

Cases	Parameters	Median±SD	Correlation coefficients (r)	P value
Acute hemorrhagic stroke patients (n=35)	Serum NSE (ng/ml)	20±12.75 ng/ml	(Spearman Correlation Coefficient) r= 0.440	P=0.008
	NIHSS	16.65±8.16		

Table 3: Correlation of serum NSE to Glasgow coma scale in acute hemorrhagic stroke patients.

Cases	Parameters	Median±SD	Correlation coefficients (r)	P value
Acute hemorrhagic stroke patients (n=35)	Serum NSE (ng/ml)	20±12.75 ng/ml	Spearman correlation r= -0.329	P=0.054
	Glasgow-Coma Scale(GCS)	10±3.79		

Table 4: Distribution of acute hemorrhagic stroke patients based on the side of lesion.

Side of lesion	Acute ischemic stroke patients (n=35)	Percentage (%)
Left-hemispheric brain lesion	18	51.43
Right-hemispheric brain lesion	17	48.57

Table 5: Comparison between the serum NSE level in left sided and right sided lesion in acute hemorrhagic stroke patients.

Cases	Parameters	Median±SD	Mann-Whitney Test	p value
Acute hemorrhagic stroke patients (n=35)	Left sided stroke	20±12.14	Mann Whitney U value =137.00 Wilcoxon= 308	P= 0.597
	Right sided stroke	19.65±13.57		

DISCUSSION

In this study, serum NSE bears a positive significant correlation to volume of hemorrhage in acute hemorrhagic stroke patients ($r=0.786$, $p<0.001$). This positive significant correlation suggests that serum NSE can reflect the volume of hematoma in acute hemorrhagic stroke patients. Another study also reported significant correlation of serum NSE level to the volume of hemorrhage in acute hemorrhagic stroke patients, within 24-48 hours of onset ($r=+0.894$; $p<0.001$).⁷ However, no studies has been reported which can correlate the volume of hematoma to the serum NSE within 24 hours of acute hemorrhagic stroke onset. In this study, the serum NSE bears a negative but insignificant correlation to the Glasgow coma scale in acute hemorrhagic stroke patients ($r= -0.329$). But, to the best of our knowledge no studies has been reported which focus on the correlation of the serum NSE to the Glasgow coma scale on admission within 24 hours of acute hemorrhagic stroke onset. In the present study, serum NSE also bears positive significant correlation to the NIHSS scale ($r= 0.440$, spearman's rho, $p=0.008$) which suggest that serum NSE can reflect the severity of neurological deficit in acute hemorrhagic

stroke patients. In another study, NSE serum concentrations has been correlated with NIHSS at 24 h for ICH ($r=0.407$, $P=0.0001$).⁸ However, no studies have been reported which focus on the correlation of the NSE to the NIHSS within 24 hours of acute hemorrhagic stroke onset. This significant correlation means that serum NSE can reflect the severity of stroke and neurological deficit in acute hemorrhagic stroke patients. However, in this study, it has been observed that there is no significant difference between the serum NSE in left vs right sided stroke in acute hemorrhagic stroke patients which means that serum NSE cannot differentiate the side of lesion in brain. No such previous studies have been reported which focuses on the role of serum NSE in differentiating the side of lesion in acute hemorrhagic stroke patients.

CONCLUSION

Serum NSE within 24 hours of stroke onset can reflect the volume of brain lesion and severity of neurological deficit but cannot differentiate the side of brain lesion in these patients.

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Conflict of interest: None declared

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