VOLUME - 11, ISSUE - 06, JUNE - 2022 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Biochemistry

COMPARISON OF SERUM NEURON SPECIFIC ENOLASE AND RADIOLOGICAL IMAGING IN ASSESSING THE SEVERITY OF STROKE

Dr. M. P. Saravanan MD., Professor and Head, Department of Biochemistry, Stanley medical college, Chennai- 600001.

Dr. S. Vasmathie* MD., Tutor in Biochemistry, Government medical college, Ariyalur-621704. *Corresponding Author

ABSTRACT Neuron Specific Enolase (NSE) is a glycolytic enzyme. It is exclusively present in neurons and neuroendocrine cells. It is an important marker to assess functional damage to neurons. Studies have shown that NSE is more than 90% sensitive to decide the severity of stroke.

This study was conducted to compare the Serum levels of NSE and radiological imaging in assessing the severity of stroke. A hospital based descriptive study was conducted on 60 stroke patients (<72hrs from onset) and 60 controls. Glasgow Coma Scale (GCS) was assessed, and serum NSE was measured. Non contrast CT brain was taken. mRS scale was assessed after 30 days of onset of stroke. ROC curve analysis was done which showed a Sensitivity of 82.5% and Specificity of 82.5% for serum levels of NSE at a cut off value 12ng/mL. NSE showed a positive correlation with mRS; negative correlation with GCS. Hence it is advisable to measure serum NSE levels at the existing health care facilities, where CT brain is not available.

KEYWORDS : Neuron Specific Enolase, Stroke, mRS, GCS.

INTRODUCTION

Stroke is defined as abrupt onset of neurologic deficit that is attributable to a focal vascular cause. It is a medical emergency condition that can cause death if not noticed on time. (1) Annual incidence has increased from 13/1,00,000 to 145/1,00,000 population in last three decades in India (2)(3)(4).

Stroke can either be ischemic or hemorrhagic; of which around 85% were found to be ischemic. Ischemic stroke can be due to embolic occlusion of large cerebral vessels. Hemorrhages most often result from rupture of aneurysms or small vessels within brain tissue; most common cause being hypertension. Stroke is a clinical diagnosis and is supported by imaging studies. Other than radiological imaging, biochemical marker like Neuron Specific Enolase can be used (5). CT cannot be used to diagnose ischemic stroke in less than 24hours (6). MRI can be used to diagnose acute ischemic stroke within 30 minutes of onset of ischemia.

The major drawback is that MRI facilities are not available at all levels of healthcare delivery. Serum levels of NSE are elevated as early as 6 hours (7). It shows the level of cellular injury rather than relying on imaging techniques. As stroke is a leading cause of neurological disability (8), estimation of serum NSE levels can help in initiating rehabilitation at the earliest and minimize long term consequences (9).

MATERIAL & METHODS

A Hospital based descriptive study was conducted in Government Stanley Medical College Hospital, Chennai, Tamilnadu over a period of 12 months (June 2019 - May 2020). The study population was derived from inpatients suspected of stroke admitted to emergency department.

Inclusion Criteria:

1. Ischemic & Hemorrhagic Stroke patients above the age of 18years to 80years presenting less than 72hrs.

Exclusion Criteria:

1. Stroke patients presenting >72hours.
2. Neurological illness other than Stroke.
3. Recurrent stroke.
4. Hemolytic anemia.
5. Patients who sustained a cardiac arrest.
6. Carcinoma like neuro endocrine tumors, small cell carcinoma of lungs, neuroblastoma, pheochromocytoma, melanoma, seminoma, renal cell carcinoma, Merkel cell tumor, carcinoid tumors, immature teratomas and dysgerminomas.
7. Psychiatric illness like schizophrenia.
8. Age < 18years and >80years

SAMPLE COLLECTION AND PREPARATION

Informed consent was got from patient (if alert and conscious) and patient's attender. Then, necessary data and history were recorded in the pre-structured format. GCS was assessed. CT brain was done, and findings noted. Age and sex matched controls (i.e., patients admitted in hospitals without any neurological illness) were chosen.

Under aseptic precautions, 3mL of blood was collected in a red top vacutainer, allowed to clot, and centrifuged at 3000rpm for 15minutes. Serum was separated as early as possible and stored at -80°C for NSE analysis. It was later analyzed using Roche – cobas e411 (eCLIA). RFT and LFT were performed on the same day itself using Beckman Coulter AU480 Chemistry analyzer. mRSQ9 score was assessed over telephonic conversation after one month from onset of illness.

Statistical Analysis

- The collected data were analyzed with IBM.SPSS statistics software 23.0 Version.
- To describe about the data; descriptive statistics frequency analysis, percentage analysis was used for categorical variables and the mean & S.D were used for continuous variables.
- To find the significant difference between the bivariate samples in independent groups; the Unpaired sample t-test was used.
- For the multivariate analysis, one-way ANOVA was used.
- To assess the relationship between the variables; Pearson's Correlation was used.
- To find the efficacy of the variables; the ROC [Receiver Operating Curve] with Sensitivity, Specificity was used.
- In all the above statistical tools the probability value .05 is considered as significant level.

RESULTS

The difference between gender and mean age of controls and cases were statistically insignificant. GCS score was lower in cases when compared to controls. Statistically highly significant elevation in mean serum NSE level was seen in cases when compared to controls with p value 0.0005. ROC curve analysis of NSE shows sensitivity of 82.5%, specificity of 82.5% and cutoff 12ng/mL.

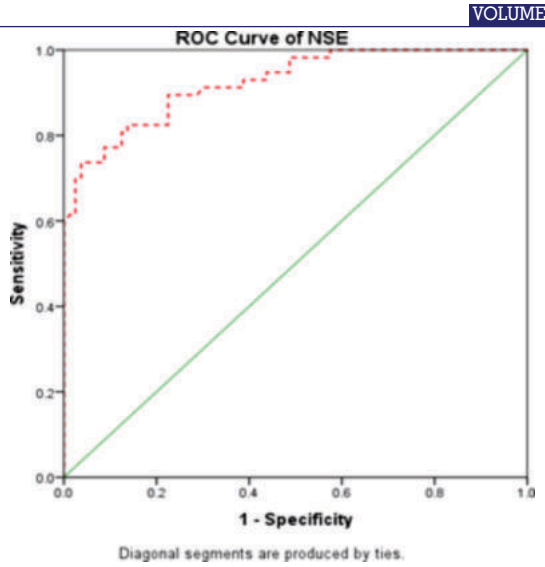

Fig 1. ROC curve of NSE

Comparison of NSE with site of lesion showed statistically significance with p value of 0. 039. On comparison of NSE with duration shows no significant difference. Also, comparison of NSE values between ischemic and hemorrhagic stroke was not significant.

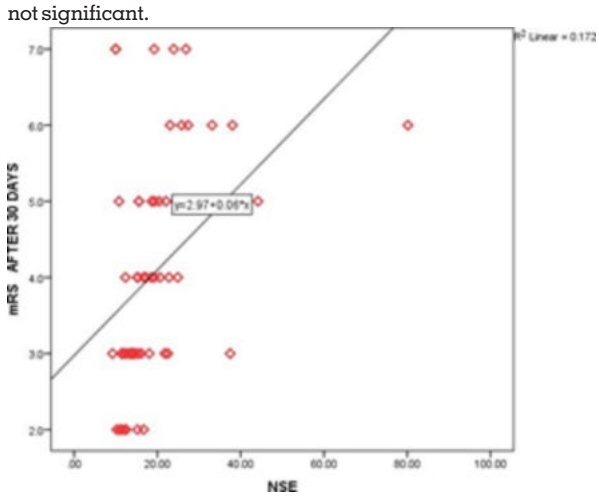

Fig 2. Correlation Between mRS After 30 Days And NSE

The above figure shows Correlation between mRS after 30 days and NSE by Pearson's Correlation were r-value=0.414, p=0.001<0.01 which shows highly statistically significant positive linear relationship between mRS after 30 days and NSE. GCS score and mRS were found to have a negative correlation (r-value = -0.427) and was highly significant (p=0.001).

DISCUSSION

In our study, we aimed at comparing the role of NSE with radiological imaging and find out if NSE could be a better marker for severity of the disease, because non contrast CT brain cannot pick up ischemic lesions earlier (<24hours) and accessibility to the facility is not easy and is time consuming. This time gap can be bridged by using an early bed side blood test like NSE.

The serum levels of NSE have a Sensitivity of 82.5% and a Specificity of 82.5% (AUC=0.924) for a cut off value 12ng/mL when measured within 72 hours of the onset of Stroke. When the cut off value was lowered to 11ng/mL, Specificity improved to 91.8% but at the risk of Sensitivity.

GCS was found to be in negative correlation (r-value= -0.328) with NSE and statistically significant (p=0.013), showing that lower the GCS; higher the NSE levels, which in turn shows poor outcome. mRS after 30days and NSE values showed positive correlation. Hence, poor outcome with increased levels of NSE.

Serum levels of NSE was found to vary from 10-14ng/mL for slight disability, 11-17ng/mL for moderate and moderately severe disability (but levels as high as 37ng/mL have also been reported), 20-24ng/mL for severe disability, >29ng/mL for non-survivors. The NSE levels for disability scale of 3 and 4 were overlapping and hence analyzing a greater number of stroke patients would help us in deciding a cut off value for each category, because only 4 out of 57 patients did not survive.

No significant change was seen between Infarctive and Hemorrhagic lesions (p=0.729), this explains only the extent of cellular injury and not the cause for the cellular injury. A significant change in NSE levels were seen when compared with site of lesion in the brain (p=0.039). This could be attributed to the differentiation of white and grey matter in the brain parenchyma.

When risk factors were analyzed, only 3 out of the 60 cases were without any comorbidities. 20% of the cases did not have any comorbid illness but were either smokers or alcoholics. 33% of the cases were hypertensive,11% were diabetic, 5% were known cases of ischemic heart disease and 23% had more than one comorbid illness.

CONCLUSION

The significant elevation of mean serum NSE levels makes it a good predictor of neurological outcome in stroke patients at the earliest, while it takes more than 24 hours for a CT scan to pick up definitive ischemia. Hence it is advisable to measure serum NSE levels at the existing health care facilities, where CT scan facilities are not available. Also, NSE stays as a cost-effective tool compared to imaging techniques of brain like CT and MRI.

LIMITATION

1. Our study was not a Multi centric study. Hence the data available is minimal.
2. Serum Neuron Specific Enolase values could have been done serially, so that NSE levels at the time of discharge can also be studied.
3. Majority of our patients were beyond 50years. Age wise segregation and comparison would give a better understanding.

Future Scope

1. POCT device must be worked up and implemented. It can be used at the level of Primary Health Centre for earlier referral of patients and prevention of complications. It can be used as a supportive tool in NPCDCS programme for prevention and control of Stroke.
2. Genetic markers should be identified, so that it can be used as a screening tool to predict the occurrence of Stroke.
3. To study the MRI-Diffusion Weighted Imaging sequences parallel with the NSE levels, so that cellular changes can be correlated.

In Compliance With Ethical Standards.

Conflicts Of Interest – There are no conflicts of interest.

REFERENCES

1. *Kasper D, Fauci A, Hauser S, Longo D, Jameson J, Loscalzo J. Harrison's Manual of Medicine. 2016. 46–48 p.*
2. *Abraham J, Rao PSS, Inbaraj SG, Shetty G, Jose CJ. An Epidemiological Study of Hemiplegia due to Stroke in South India. Stroke. 1970;1(6):477–81.*
3. *Dalal PM, Malik S, Bhattacharjee M, Trivedi ND, Vairale J, Bhat P, et al. Population-based stroke survey in Mumbai, India: Incidence and 28-day case*

fatality. Neuroepidemiology. 2008;31(4):254–61.

4. *Mishra NK, Khadilkar S V. Stroke program for India. Ann Indian Acad Neurol. 2010;13(1):28–32.*
5. *Haupt WF, Chopan G, Sobesky J, Liu WC, Dohmen C. Prognostic value of somatosensory evoked potentials, neuron-specific enolase, and S100 for short-term outcome in ischemic stroke. J Neurophysiol. 2016; 115(3):1273–8.*
6. *Manwani B, Rath S, Lee NS, Staff I, Stretz C, Modak J, et al. Early Magnetic Resonance Imaging Decreases Hospital Length of Stay in Patients with Ischemic Stroke. J Stroke Cerebrovasc Dis [Internet]. 2019;28(2):425–9. Available from: https://doi.org/10.1016/j .jstrokecere brovasdis.2018.10.015*
7. *Smith R, Chepisheva M, Cronin T, Seemungal BM. Diagnostic approaches techniques in concussion/mild traumatic brain injury: Where are we? [Internet]. Neurosensory Disorders in Mild Traumatic Brain Injury. Elsevier Inc.; 2019. 247–277 p. Available from: http://dx.doi.org/10.1016/ B978-0-12-812344-7.00016-9.*
8. *WARREN MD. Social and preventive medicine. Br J Clin Pract. 1961; 15:217–27.*
9. *Coleman ER, Moudgal R, Lang K, Hyacinth HI, Awosika OO, Kissela BM, et al. Early Rehabilitation After Stroke: A Narrative Review. Curr Atheroscler Rep. 2017;19(12).*