

STUDY OF SERUM S100 AND NSE CONCENTRATION IN PATIENTS WITH ACUTE CEREBRAL INFARCTION AT INTENSIVE CARE UNIT OF HUE CENTRAL HOSPITAL

Hoang Trong Hanh¹, Nguyen Cuu Loi¹, Hoang Khanh², Nguyen Dinh Toan²

(1) Hue Central Hospital, Vietnam

(2) Hue University of Medicine and Pharmacy, Vietnam

Abstract

Objective: Survey serum S100 and NSE concentration in patients with cerebral infarction during the acute phase. To understand the relationship between serum S100 and NSE concentrations with some other risk factors such as age, sex, Glasgow Coma Scale, cerebral lesion volume on computerized tomography. **Subjects and Methods:** Study of 90 hospitalized patients with cerebral infarction at ICU of Hue Central Hospital and 100 controls. Data was collected through medical records of patients with acute cerebral infarction and control. The study method was cross-sectional and descriptive. Data was analysed by medical statistics and processed by the SPSS 19.0 software. **Results:** The average age in study group was 68.3 ± 13.1 (Min 32, Max 90) and control group was 64.8 ± 12.9 (Min 33, Max 88) did not differ statistically significantly. The majority of patients with age group from 61 to 80 years old (48.9%) is retired elderly patients but it doesn't differ statistically significantly with $p > 0.05$. The average concentration of S100 and NSE in study group was higher in control group, the difference was statistically significantly ($p < 0.001$). The concentration of S100 and NSE in mortality was higher in living groups, in which S100 was different statistically significantly ($p < 0.05$). Cut-off value predicts the survival of S100 and NSE in this study is respectively 0.21 mcg/l and 20.45ng/ml. There is an inverse correlation between the S100 and NSE with Glasgow coma scale. The more comatose patients are, the more NSE and S100 increases. The correlation equation respectively: $y = -0.1975x + 10.439$ ($n = 90, r = -0.19, p > 0.05$). $Y = -0.0228x + 11.02$ ($n = 90, r = -0.29, p < 0.01$). The greater volume of lesions is, the higher the concentration of S100 and NSE is. There is an agreement correlation between the S100 and NSE with lesion volume, the correlation equations respectively: $y = 20.6x + 67.71$ ($n = 90, r = 0.397, p < 0.001$). $Y = 1.441x + 43.104$ ($n = 90, r = 0.359, p < 0.05$). **Conclusion:** The cut-off value to predict the survival of S100 and NSE in this study respectively 0.21 mcg/l and 20.45ng/ml. There is an inverse correlation between S100 and NSE with Glasgow coma scale. There is positive correlation between S100 and NSE with lesion volume. S100 and NSE can be used to predict and monitor disease progression and the volume of cerebral lesions.

Key words: Stroke, acute cerebral infarction, Glasgow coma scale, S100, NSE

1. BACKGROUND

Stroke or cerebral vascular accidents have become important issues in medical care. The rate of hypertension and stroke are increasing, and the rate of stroke increases with age. Prevalence, mortality and disability rates are still high, of which 20% of survivors needed hospital care after 3 months, 15-30% permanent disability [1], [2]. Despite advances in diagnosis and treatment, stroke not only the cause of death is the third after cancer and heart disease in developed countries, but also to the sequelae of severe neurological and require long-term care. Therefore, prevention of

risk factors is a key strategy for each community and each individual, to minimize complications occur [2], [3]. More new diagnostic method, modern, new drugs are highly effective early diagnosis, timely treatment and prevention are more effective, improve prognosis [1], [2], [3].

In recent years, there are many research techniques to monitor cerebral vascular accident and predict treatment outcomes. Clinical neurological examination is useful for nerve function has not been extensive damage but little value in the assessment of infarct volume or

- Corresponding author: Hoang Khanh, email: hoangkhanhqb@gmail.com

- Received: 27/5/2014 * Revised: 22/6/2014 * Accepted: 25/6/2014

comatose patients after cerebral infarction. The diagnostic techniques of modern neuroscience such as CT, MRI, and ultrasound to help clinicians determine the location, the volume of cerebral infarction and treatment planning. However, diagnostic imaging repeated daily is not practical. Several monitoring techniques have been developed based on measurements of various blood proteins, including NSE (Neuron-specific enolase), myelin basic protein, and S100 protein... In that protein markers of brain damage can allow regular testing with relatively low risk and therefore they are very effective in monitoring changes in disease.

We use the S100 protein and NSE in blood to monitor, prognosis and help us diagnose cerebral infarction [9], [10], [11]. In Vietnam we have not seen the research on this issue. Therefore, to understand more about this issue, we studied S100 and NSE levels in blood during the acute cerebral infarction with two objectives:

- To survey serum S100 protein and NSE concentrations in patients with acute cerebral infarction.
- To find out the relationship between levels of S100B, NSE for age, sex, Glasgow Coma

Scale, cerebral damage volume on computerized tomography, survival prognosis in patients with acute cerebral infarction.

2. MATERIALS AND METHOD

2.1. Materials: Studying of 90 hospitalized patients with acute cerebral infarction at ICU of Hue Central Hospital and 100 controls from April 2011 to March 2014.

2.2. Method

Data was collected through medical records of patients with acute cerebral infarction and control. The study method was acrossectional and descriptive. Data was analysed by medical statistics and processed by the SPSS 19.0 software. Using t tests to compare mean values of two data sets.

- Quantification of serum S100 and NSE by immunofluorescence techniques polarization (FPIA = fluorescence Polarization Immunoassay) on biochemical autoimmune Cobas 6000 at Hue Central Hospital.

- Normal range in the blood.

S100 concentration: 0.046 to 0.105microgram/L [9]

NSE concentrations :15.7 to 17.0ng/mL [9].

3. RESULTS

3.1. The common characteristics

Table 1. The common characteristics

Gender	Study group		control group	
	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)
Male	53	58.9	59	59.0
Female	37	41.1	41	41.0
Total	90	100	100	100
p > 0.05				

The majority men in study and control group is male, which did not differ statistics significantly

The average age in study group was 68.3 ± 13.1 (Min 32, Max 90) and control group was 64.8 ± 12.9 (Min 33, Max 88) did not differ statistics significantly. The majority of patients were 61 to 80 years old (48.9%) who were retired and elderly but it doesn't differ statistics significantly with $p > 0.05$.

3.2. Survey serum S100 and NSE level

Table 2. The average concentration of S100 and NSE in study group and control group

Markers	Study group	Control group
	Mean \pm SD (n=90)	Mean \pm SD (n=100)
S100	1.489 \pm 2.663	0,062 \pm 0.029
NSE	38.36 \pm 34.46	14.79 \pm 3.49
p	p < 0.001	

The average concentration of S100 and NSE in study group was higher in control group, the difference was statistically significant ($p < 0.001$).

Table 3. The relationship between S100, NSE with gender

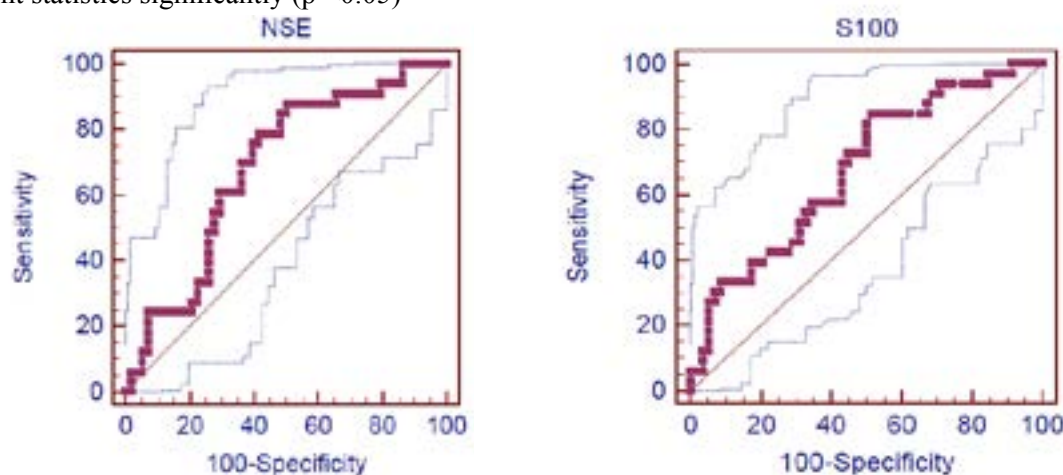
Average concentration \ Gender	Male (n=53)	Female (n=37)	P
S100	1.243±2.510	1.843±2.867	<0.05
NSE	36.27±29.04	41.35±41.25	<0.05

The relationship between S100 and NSE with gender was higher for females than for males, the difference between the two gender was statistically significant ($p < 0.05$).

Table 4. The relationship between S100, NSE with survival and dead group

Level \ Survive/Death	Survive (n=57)	Death (n=33)	P
S100	0.991 ±1.893	2.350±3.501	< 0.05
NSE	33.44 ± 34.07	46.86± 33.96	> 0.05

The concentration of S100 and NSE in mortality was higher in living groups, in which S100 was different statistics significantly ($p < 0.05$)

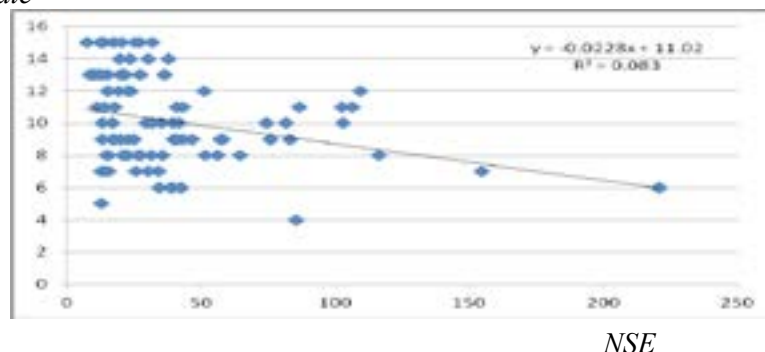
**Figure 1.** Graphical display of the ROC curve of NSE and S100 according to survival**Table 5.** Sensitivity and specificity of S100 and NSE in survival and dead group

Values	AUC	Confidence interval 95%	Cut off	Sensitivity(%)	Specificity(%)
NSE (ng/ml)	0.684	0.578-0.777	20.45	87.88	50.00
S100 (mcg/l)	0.678	0.572-0.772	0.21	84.85	48.28

The area under the curve (AUC) of S100 is 67.8% similar 68.4% of the NSE, the cut-off value to predict the survival of S100 and NSE in this study respectively 0.21 mcg/l and 20.45ng/ml.

The correlation between NSE and Glasgow coma scale

Glasgow coma scale

**Figure 2.** Regression line performance correlated between NSE concentrations and Glasgow coma scale (n=90, $r = -0.29$, $p < 0.01$)

There is an inversely correlation between the NSE with Glasgow coma scale score. The correlation equation: $y = -0.0228x + 11.02$ ($n = 90$, $r = -0.29$, $p < 0.01$).

The correlation between S100 and Glasgow coma scale

Glasgow coma scale

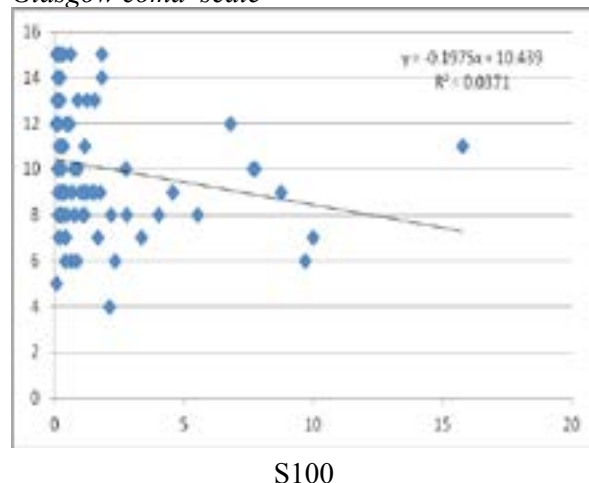


Figure 3. Regression line performance correlated between S100 concentrations and Glasgow coma scale ($n=90$, $r=-0.19$, $p>0.05$)

There is an inversely correlation between the NSE with Glasgow coma scale score. The correlation equation: $y = -0.1975x + 10.439$ ($n=90$, $r=-0.19$, $p>0.05$)

The correlation between the S100 and NSE concentration with volume of lesions

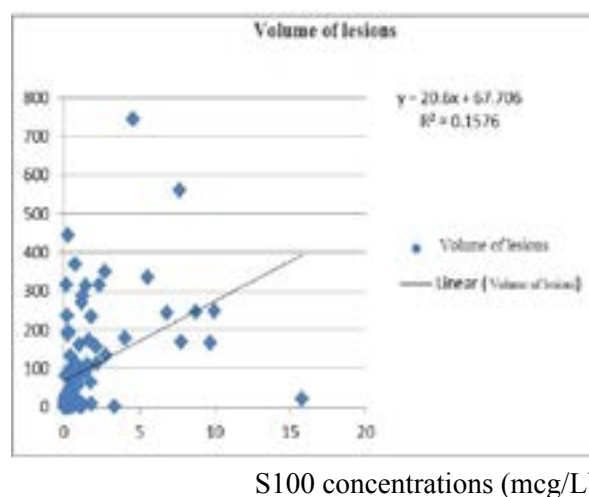


Figure 4. Regression line performance correlated between S100 concentrations and volume of lesions

The greater volume of lesions is, the higher the concentration of S100 is. There is an agreement correlation between the S100 with lesion volume. The correlation equation: $y = 20.6x + 67.71$ ($n=90$, $r=0.397$, $p < 0.01$)

volume of lesions (ml)

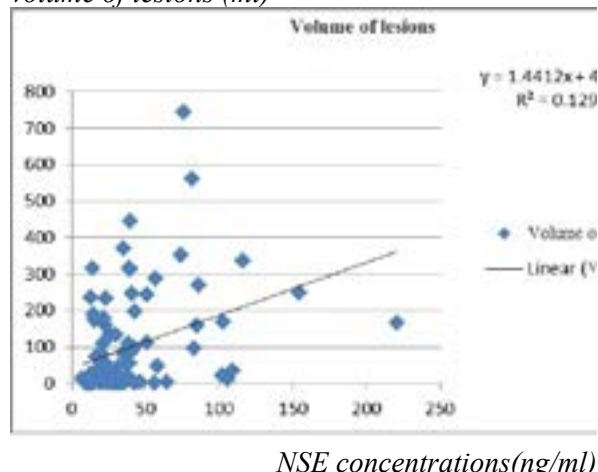


Figure 4. Regression line performance correlated between NSE concentrations and volume of lesions

There is an agreement correlation between the NSE with lesion volume. The greater volume of lesions is, the higher the concentration of S100 is. The correlation equation: $y = 1.441x + 43.104$ ($n=90$, $r=0.359$, $p < 0.05$)

4. DISSCUSION

4.1. The common characteristics

In our study, the two markers had a higher percentage in men than in women in both study group and control group, did not differ statistics significantly.

The average age in study group was 68.3 ± 13.1 (Min 32, Max 90) and control group was 64.8 ± 12.9 (Min 33, Max 88) did not differ statistics significantly.

The average age was 68.3 ± 13.1 equivalent study 44 patients of cerebral infarction of Missler et al (mean age 65.1. Min: 32; Max: 87) [7]. The majority of patients were 61 to 80 years old (48.9%), who were retired and elderly but it doesn't differ statistics significantly with $p > 0.05$.

4.2. The survey S100 and NSE concentration

The average concentration of S100 and NSE in study group was higher in control group, the difference was statistically significant ($p < 0.001$).

The relationship between S100 and NSE with gender was higher for females than for males, the difference between the two gender was not statistically significant ($p > 0.05$). The concentration of S100 and NSE in mortality was higher in living groups, in which S100 was different statistics significantly ($p < 0.05$).

The area under the curve (AUC) of S100 is 67.8% similar to 68.4% of the NSE, the cut-off

value to predict the survival of S100 and NSE in this study respectively 0.21 mcg/l and 20.45ng/ml.

There is an inversely correlation between the S100 and NSE with Glasgow coma scale score, The more comatose patients are, the more S100 and NSE increases due to greater brain damage. The correlation equation respectively: $y = -0.1975x + 10.439$ ($n = 90, r = -0.19, p > 0.05$). $y = -0.0228x + 11.02$ ($n = 90, r = -0.29, p < 0.01$). There is an inversely correlation with the survival rates.

The greater volume of lesions is, the higher the concentration of NSE is. There is an agreement correlation between the NSE with lesion volume, the correlation equations: $y = 20.6x + 67.71$ ($n = 90, r = 0.397, p < 0.001$) which is similar to the results of international authors [5], [9], as Cunningham et al studied 83 patients with cerebral infarction and showed that NSE concentrations correlated with lesion volume ($r = 0.36, p = 0.001$) [4], Missler et al studied 44 patients with cerebral infarction and showed that NSE concentrations correlated with cerebral lesion volume ($r = 0.37, p < 0.05$) [7], Wu et al studied 38 patients with cerebral infarction, which showed concentrations NSE correlated with

lesion volume ($r = 0.81, p < 0.01$) [11]. For S100, similarly the larger lesion volume is, the higher the concentration of S100 is. There is positive correlation between S100 with lesion volume, the correlation equation: $y = 20.6x + 67.71$ ($n=90, r=0.397, p < 0.001$) similar to the results of international authors [5],[9], as Missler et al studied 44 patients with cerebral infarction showed S100 concentrations correlated with lesion volume ($r = 0.75, p < 0.001$) [7]. Edward C.Jauch et al studied 359 patients and showed S100 concentration correlated with the volume of cerebral lesions on CT scan ($r = 0.239, p < 0.0001$) [6].

5. CONCLUSION

The cut-off value to predict the survival of S100 and NSE in this study respectively 0.21 mcg/l and 20.45ng/ml. There is an inversely correlation between S100 and NSE with Glasgow coma scale. There is positive correlation between S100 and NSE with lesion volume. S100 and NSE can be used to predict and monitor disease progression and the volume of brain lesions. In the future, research with larger numbers is need to get more accurate results.

REFERENCES

1. Dang Nguyen Van (2003), Practice neurological diseases and common syndromes, Medical Publishing House, Ha Noi, p. 569-636.
2. Khanh Hoang (2010). Cerebral vascular accident, Lecture Postgraduate Neurology, University Publishing Hue.
3. Luong Ho Huu (1998). Cerebral vascular accident, Medical Publishing House, Ha Noi.
4. Cunningham RT et al (1991). Serum neurone specific enolase (NSE) levels as an indicator of neuronal damage in patients with cerebral infarction. *Eur J Clin Invest.* 21:497-500.
5. Daniel T.Laskowitz et al (2009). Clinical usefulness of a biomarker-based diagnostic test for acute stroke. "The biomarker rapid assessment in ischemic injury (brain) study. *Stroke.* vol.40, pp 77-85. American heart Association, Inc.
6. Edward C.Jauch et al (2006), Association of serial biochemical markers with acute ischemic stroke. *Stroke*, vol.37, pp 2508-2513. American heart Association, Inc.
7. Martens P et al (1998). Serum S-100 and Neuron-Specific Enolase for prediction of Regaining Consciousness after Global Cerebral Ischemia. *Stroke.* 29(11): 2363-2366.
8. Missler Ulrich et al (1997). S100 protein and neuron-specific enolase concentration in blood as indications of infarction volume and prognosis in acute ischemic stroke. *Stroke a Journal of cerebral circulation.* Volume 28. No10. pp 1956-1960.
9. Nishant Anand, Latha G. Stead (2005). Neuron-Specific Enolase as a Marker for Acute Ischemic Stroke: *Cerebrovasc Dis*; Vol. 20, No. 4 pp 213-219
10. Roche Diagnostics (2009). S100, NSE pp1-4
11. Schaarschmidt H, Prange HW, Reiber H (1994). Neurone specific enolase concentrations in blood as a prognostic parameter in cerebrovascular diseases. *Stroke.* 25:558-565.
12. YC Wu, YB Zhao, (2004), Correlation between serum level of neuron-specific enolase and long-term functional outcome after acute cerebral infarction: prospective study, *Hong Kong Med J*, volume 10, No 4, pp 251- 254.