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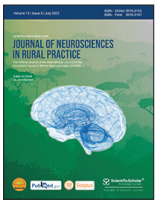
Journal of Neurosciences in Rural Practice



Brief Report

S100B and optic nerve sheath diameter correlation in head injury patients with contusions

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ABSTRACT

S100B is a biochemical marker of head injury and optic nerve sheath diameter (ONSD) is a non-invasive bedside technique to detect intracranial pressure. We aim to demonstrate whether ONSD correlates with S100B protein in head injury patients with contusions and also whether the grade of contusion correlates with S100B protein. This is a prospective study done on head injury patients aged between 18 and 75 years having isolated contusions admitted within 24 h of injury. Patients were assessed neurologically with Glasgow Coma Scale (GCS) and cranial computed tomography study on admission. Ocular sonography was done for ONSD recording, and S100B protein venous samples were collected at 24 h, 48 h, and at discharge. The outcome was evaluated with Glasgow Outcome Scale (GOS) at discharge and 3 months. Out of 42 patients, the mean age was 46.2 years and 27 were males. There were 12 patients with mild, 25 with moderate, and 5 patients with severe head injury. The mean GCS at 24 h was 12.35, the mean ONSD at 24 h was 3.9 mm, and the mean S100B at 24 h was 0.214 μg/L. There was a statistically significant correlation noted between mean S100B and contusion grade. A moderate positive correlation was noted between ONSD and S100B at 48 h in mild and moderate head injury groups. Favorable outcome (GOS 4,5) at 3 months can be predicted by GCS, contusion grade, and S100B values. Better GCS (14 and 15), focal contusion grade, and S100B values (<0.5 μg/L) predict good outcome. Although ONSD and S100B give important information in different scenarios, S100B gives better predictive information in patients with traumatic cerebral contusions.

Keywords: S100B, Head injury, Optic nerve sheath diameter, Contusion grading

Key message: S100 B and ONSD are simple biochemical and radiological investigations that can be done in every neurosurgical setup and can be useful in the management of head injury patients.

INTRODUCTION

Serum S100B level is increasingly used as a serum biomarker to diagnose or rule out a traumatic brain injury. Although the central nervous system specificity of the protein S100B is low, brain injury can be ruled out by the negative predictive value of S100B levels. A very low serum level of S100B protein can be used to predict normal findings on a computed tomography (CT) scan brain.[1] In the past two decades, many authors studied and noted that S100B was a predictor of the outcome of the head injury patient.[2]

Optic nerve sheath diameter (ONSD) measurement by orbital ultrasound is a practical, effective, and non-invasive technique to detect and monitor intracranial pressure (ICP) in head injury patients. This study can be used along with a biochemical assay of S100B in head injury patient management. Till now, no study is done using both S100B and ONSD in head injury patients.

We conducted a study to demonstrate whether ONSD correlates with S100B protein in head injury patients and also whether the grade of contusion correlates with S100B protein.

MATERIALS AND METHODS

This study was done prospectively on head injury patients admitted to the Department of Neurosurgery, NRI Academy of Sciences from September 2016 to March 2019. The inclusion criteria included head injury patients aged between 18 and 75 years, having isolated brain contusions. They should be admitted within 24 h of injury. Exclusion criteria included age <18 years, patients presenting more than 24 h after injury, patients with Glasgow Coma Scale (GCS) ≤ 4,

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Received: 25 January 2023 **Accepted:** 14 July 2023 **EPub Ahead of Print:** 07 August 2023 **Published:** 10 November 2023 **DOI:** 10.25259/JNRP_45_2023

patients taken up for surgery within 24 h of injury, and posterior fossa injuries. Polytrauma patients were excluded as their S100B values might get raised. Patients with orbital trauma and cerebrospinal fluid rhinorrhea or otorrhea were excluded as ONSD values might get affected.

Patients were assessed with neurological status on admission using GCS. Head injury severity scale was used to classify the severity of the head injury into mild (GCS 14,15), moderate (GCS 9–13), and severe (GCS 3–8).[3]

S100 B protein venous samples were collected at 24 h from the time of injury, at 48 h, and discharge. Venous blood samples were processed to serum and deep frozen at −20°C until the time of assay. An electrochemiluminescence immunoassay kit (Elecsys S100; Roche Diagnostics, Mannheim, Germany) was used to analyze the S100B values. We have noted the normal S100B value in eight controls (healthy subjects). The mean normal S100B was 0.053 ± 0.035 μg/L.

A single senior radiologist performed ocular sonography in all the patients using a 7.5 MHz linear probe (PHILIPS HD 7XE) to measure ONSD. The optic nerve sheath measurement was taken at 3-mm distance from the globe in each eye separately. The average measurement of both eyes (Mean right-left ONSD) was taken for comparison. ONSD was measured for all the patients at 24 h, at 48 h, and discharge.

In the initial cranial CT study done on admission, various findings were recorded. The severity of brain injury was noted using the Rotterdam score.[4] Contusions were graded as focal or multiple. Focal contusion was defined as a contusion localized to a single site. Multiple contusion was defined as more than a single contusion located at multiple sites. The volume of the contusion was the total volume of focal (single) or multiple contusions, measured by the radiologist. The three dimensions (length, breadth, and height) of each contusion were calculated in centimeters and the volume in 3 cm was calculated by the formula l × b × h divided by 2.

Glasgow Outcome Scale (GOS) was used to assess the outcome of the patient at discharge and 3-month follow-up. GOS 4,5 were considered favorable outcomes whereas GOS 1–3 were considered unfavorable outcomes.

Descriptive statistics of patient variables have been computed. The Pearson Coefficient of Correlation was used to assess the correlation between S100B and ONSD. The difference in means between the two groups was compared by student *t*-test. $P \leq 0.05$ was considered as statistically significant. The study was approved by Institution Ethical Committee and all the patients have given consent.

RESULTS

A total of 42 patients were included in the study. The mean age was 46.2 ± 11.9 years with an age range of 25–67 years. The male-to-female ratio was 1.8:1 (27:15). There were 12 patients with mild, 25 with moderate, and 5 with severe head injury. The mean GCS at 24 h was 12.35, the mean ONSD at 24 h was 3.9 mm, and the mean S100B at 24 h was 0.214 μg/L.

The mean S100B (24 h) value was 0.066 μg/L in mild head injury patients, 0.202 μg/L in moderate head injury patients, and 0.562 μg/L in severe head injury patients. With the increase in the severity of the head injury, there was an increase in S100B and ONSD values.

The mean volume of all the focal contusions (n = 27) was 2.4 mL whereas that of multiple contusions (n = 15) was 13.4 mL. S100B at 24 h in patients with focal contusions was 0.093 ± 0.055 and in patients with multiple contusions was 0.433 ± 0.237 with a statistically significant difference ($P < 0.00001$).

Nine patients had poor GOS at the end of 3 months of follow-up, out of which one patient had mortality. The rest of the 33 patients had good GOS. S100B at 24 h, average ONSD at 24 h, average GCS, average Rotterdam score, and contusion grade were compared between good GOS and poor GOS groups [Table 1]. S100B at 24 h, average GCS, average Rotterdam score, and contusion grade had statistical significance between the two groups. There was no significant difference in average ONSD values between the two groups.

ONSD and S100B at 48 h values were correlated using Pearson correlation and there was a moderate positive correlation between them [Table 2]. This signifies that S100 B values increase with the rise in ONSD values. There was only a weak correlation between ONSD and S100B values at 24 h. S100B (48 h) values were also correlated with ONSD (48 h) in only mild head injury and only moderate head injury groups separately and there was a moderate positive correlation between them [Table 2]. As there were only 5 patients with severe head injury, the correlation was not done in that group.

DISCUSSION

As the volume of the contusions increases, the damaged neuroglial cellular mass increases leading to an increase in S100B levels. We have noted a statistically significant difference between the S100B levels in focal contusion and multiple contusion groups in our study. Similar findings were recorded in earlier studies.[2,5]

There was a significant positive correlation between the increase in ICP and the rise in serum S100B levels. It was noted by some authors in earlier studies.[6-8] In all these studies, ICP was recorded either by intraparenchymal pressure monitoring device or intraventricular catheter (invasive). In our study, ocular sonography to record ONSD,

Table 1: Comparison of various factors between Good GOS (favorable outcome) and Poor GOS (unfavorable outcome) groups at 3 months.

n=42	Favorable outcome (*n*=33)	Unfavorable outcome (*n*=9)	Statistical test	*P*-value
S100 B at 24 h	0.124±0.092	0.544±0.241	*t*=−8.201 (student t test)	**<0.00001**
Average ONSD at 24 h	3.79±0.51	3.85±0.032	*t*=−0.35	0.72
Average GCS	12.4±1.95	9.67±1.58	*t*=3.85 (student t test)	**0.0004**
Average Rotterdam score	2.78±0.78	3.88±1.05	*t*=−3.47 (student t test)	**0.0012**
Focal contusion (*n*=27)	100% (27)	0% (0)	Fisher's exact test	**0.000011**
Multiple contusion (*n*=15)	40% (6)	60% (9)		

GOS: Glasgow Outcome Scale, ONSD: Optic nerve sheath diameter, GCS: Glasgow Coma Scale

Table 2: Pearson's correlation between variables.

Cohort	Variable 1	Variable 2	r	Strength of correlation
All the patients (*n*=42)	S100B 24 h	ONSD 24 h	0.1889	Weak positive
All the patients (*n*=42)	S100B 48 h	ONSD 48 h	0.5027	**Moderate positive**
Only mild head injury patients (*n*=12)	S100B 48 h	ONSD 48 h	0.5666	**Moderate positive**
Only moderate head injury patients (*n*=25)	S100B 48 h	ONSD 48 h	0.5174	**Moderate positive**

ONSD: Optic nerve sheath diameter

a non-invasive method to detect ICP, was performed as described in our earlier study[9] and compared the values with S100B. We have noted a moderate positive correlation between ONSD and S100B values at 48 h.

As per our knowledge, this is the first study to compare ONSD recordings and S100B values in head injury patients. Although recently, a study comparing them in preeclampsia patients was published.[10] In that study, they have not identified a meaningful correlation between S100B and ONSD.

Although invasive ICP monitoring is the standard method, ONSD measurement for ICP monitoring is practical, reliable, and more affordable and is available in many centers. ONSD can be done easily in the intensive care unit, on the bedside, and can be repeated multiple times as and when required without any known complications. It can be of great value if combined with S100B values to monitor the patients, particularly in semi-comatose patients. Further studies are to be done to evaluate the usage and limitations of combined ONSD and S100B measurements.

As noted in the study by Wolf *et al*., cerebral edema produces the highest levels of S100B compared to other intracranial hemorrhagic lesions followed by contusions, subarachnoid hemorrhage, subdural hemorrhage, and extradural hemorrhage.[11] The cellular volume of the brain that is traumatized might be high in cerebral edema followed by cerebral contusions compared to other hematomas. More neuroglial tissue injury results in higher S100B values. The same pathology of cerebral edema or contusions may also result in an increase in ICP which will be reflected in ONSD measurements. Hence, serum S100B values and ONSD measurements may act synergistically and effectively help in patient management.

Limitations of the study

Follow-up of the patients is of less duration. Direct ICP measurement was not done in our study to compare with S100B. Number of patients in the study was small.

CONCLUSION

Better GCS (14 and 15), focal contusion grade, and S100B values (<0.5 μg/L) predict a good outcome. Although ONSD and S100B give important information in different scenarios, S100B gives better predictive information in patients with traumatic cerebral contusions.

Acknowledgment

We acknowledge Mrs. Naga Saritha Kolli, Lecturer in Statistics at NRI Medical College, Chinakakani, for her assistance with the statistical analysis of the study.

Declaration of patient consent

Institutional Review Board (IRB) permission was obtained for the study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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How to cite this article: Thotakura AK, Velivela KC, Marabathina NR, Riyaz AA, Vuddandi SP, Danaboyina AR. S100B and optic nerve sheath diameter correlation in head injury patients with contusions. J Neurosci Rural Pract 2023;14:599-602.