Can brain natriuretic peptide, S100b, and interleukin-6 prognosticate the neurological consequences in Egyptian patients presented with supratentorial intracerebral hemorrhage?

Hany A. Fikry Eldawoody¹, Mohammed Abdel Bari Mattar¹, Abeer Mesbah², Ashraf Zaher³, Mohammed Elsherif³

¹Department of Neurosurgery, Mansoura University Hospital, ²Department of Clinical Pathology, Faculty of Medicine, Mansoura University, ³Department of Neurology, Mansoura University Hospital, Mansoura, Dakahlia, Egypt.

E-mail: *Hany A. Fikry Eldawoody - hanyeldawoody@yahoo.com; Mohammed Abdel Bari Mattar - noramattar@yahoo.com; Abeer Mesbah - drabeerclinpath@hotmail.com; Ashraf Zaher - ashrafdr2000@yahoo.com; Mohammed Elsherif - elsherifmohammed@mans.edu.eg

ABSTRACT

Background: Biomarkers in supratentorial intracerebral hemorrhage (SICH) enhance the prognosis of the disease. This study aimed to assess the prognosticative grade of S100 calcium-binding protein B (S100B), interleukin-6 (IL-6), and the pro-brain natriuretic peptide (pro-BNP) in SICH outcome prediction.

Methods: Blood samples of 50 SICH patients were analyzed for the biomarkers. The patients were classified into two groups with and without intraventricular hemorrhage (IVH). The following scales including Glasgow Coma Score (GCS), the Barthel index (BI), intracerebral hemorrhage (ICH) score, ICH volume, National Institutes of Health Stroke Scale (NIHSS), Modified Rankin Score (mRS), and length of stay were used to evaluate the severity.

Results: The severity scores (NIHSS, GCS, BI, mRS) were significantly higher in SICH patients with IVH versus SICH patients without IVH (P = 0.002, 0.001, 0.03, and 0.03, respectively). Serum levels for a pro-BNP and S100b are significantly higher in SICH patients with IVH versus SICH patients without IVH (P = 0.027, respectively). Multivariate correlations between demographic (age), biomarkers panel (IL-6, S100b, and pro-BNP), and clinical and severity scores (ICH score, ICH volume, length of hospital stay [LOS], BI, mRS, GCS, and NIHSSS) in all studied patients showed a highly significant correlation between ICH score and pro-BNP (P = 0.04). There was a highly significant correlation between LOS and IL-6 (P = 0.003).

Conclusion: Pro-BNP, IL-6, and S100b are greatly associated with the presence of IVH that, in turn, correlated well with poor clinical outcome measures.

Keywords: Interleukin-6, Outcome, Pro-brain natriuretic peptide, S100 calcium-binding protein b, Supratentorial intracerebral hemorrhage

INTRODUCTION

A relatively common and overwhelming disease is the primary supratentorial intracerebral hemorrhage (SICH) accompanied by variable prognosis despite the great advancement in its related neurological and neurosurgical management. While immediate detection of SICH is easy by computed tomography (CT), the prospective expectation continues to be difficult to anticipate, especially at the early onset...
of the disease, particularly when there is a need to stop the medical care for unfavorable patients by their physicians. This vague misleads to a dilemma of patient prognosis, from complete recovery to long-term care in patients with persistent vegetative state, stressing the necessity for complementary outcome means which lead to the early medical choices in patients with acute SICH. Conventionally, there are many variables such as the age of the patient and the hematoma characteristics (size, location, and ventricular extension) in early-onset SICH that has been used to anticipate the prognosis. Nonetheless, those classical outcome parameters remain defective to give an actual evaluation for the prognosis in patients with SICH. While the hematoma mass effect leads to neuronal lesions that play a crucial role in the prognosis of SICH, the advances in intensive care showed improvement survivals among some patients from this primary lesion, and the deterioration was due to a secondary lesion like cerebral edema. Accordingly, neuroinflammation plays a crucial role in the pathogenesis of cerebral edema that leads to neuronal damage, and eventually, can anticipate the functional outcome. Therefore, the prognosis of SICH can be expected from biomarkers of neuronal damage and inflammation; likewise, an alternative parameter of neuropsychopathophysiology could anticipate the functional outcome. Biomarkers reflective for neuronal potentiation by astrocytic activation, like S100 calcium-binding protein B (S100b), showed a significant increase after ischemic stroke and subarachnoid hemorrhage (SAH). In addition, S100b is known to be used as a predictive biomarker in the ischemic stroke and is an indicator of the possibility of hemorrhagic transformation and prognosis. Moreover, many studies have shown that there is a correlation between S100b levels and long-term outcome in subarachnoid hemorrhage and SICH. Several studies have demonstrated that there is an increase in brain natriuretic peptide (BNP) levels after acute brain lesions, such as SAH, ischemic stroke, and traumatic brain injury. Yet, the importance of BNP in cases with SICH is unclear. However, there is an evolving proof showing that BNP could have a role in the recovery from an acute brain lesion, mostly by increasing cerebral blood flow.

Elevated serum level of interleukin-6 (IL-6) is known to be associated with a variety of brain pathologies including ischemic stroke, SAH, and intracerebral hematoma. In this study, we assess the predictive value of the biomarker panel of S100b, IL-6, and pro-BNP, in the functional outcome after SICH, rather than conventional clinical and/or radiological methods.

MATERIALS AND METHODS

Participants

The present prospective study included 50 patients with SICH who were admitted to the neurosurgery/neurology departments over a 12-month period at Mansoura Emergency University Hospital, Egypt. The diagnosis was based on clinical assessment and computed tomographic (CT) head scanning immediately after the onset of the condition. All patients were assessed by taking a medical history, history of previous cerebrovascular strokes, hypertension, diabetes mellitus, and renal or hepatic disorders.

Ethical approval

A consent whether informed or written was obtained from each patient and the ethical committee also approved the study.

Clinical assessment scales

Clinical examination besides the neurological severity scales for the assessment of functional outcome at the discharge time was evaluated by Glasgow Coma Score (GCS), the Barthel index (BI), intracerebral hemorrhage score (ICHS), National Institutes of Health Stroke Scale (NIHSS), and Modified Rankin Score (mRS). GCS, BI, NIHSS, mRS, and ICHS results were tabulated. The ICHS is a validated 6-point scale to evaluate risk in patients with SICH and includes initial GCS, hematoma location, and volume, whether intraventricular hematoma is present or not, and the age. Regarding the NIHSS score, it is a measurable scale for cerebral stroke that shows the level of consciousness, neglect, language function, eye movements, visual field, facial palsy, sensory function, motor strength, and coordination. The assessment can be done quickly, and the NIHSS score can be estimated by neurologists and non-neurologists by good training. Regarding the GCS, it is a clinical scale that gives a dependable, objective method of estimating the conscious level of a patient for primary and follow-up assessment. The patient is evaluated by the scale criteria, and the estimated points give a patient score between 3 (denoting deep unconsciousness) and 15 (denoting fully conscious).

Radiology evaluation

Within the initial 24 h after hospital admission, the studied group of patients was scanned using brain computed tomography and checked for hemorrhagic volume (cm³), presence of intraventricular hemorrhage (IVH), and midline shift (MLS). On discharge from Mansoura University Hospital, we used the following functional assessment scales; BI, length of hospital stay (LOS), and mRS, by a blinded observer evaluation method as they are the best for biomarker panel data. All studied patients showed CT-proven supratentorial ICH before taking the blood samples. Regarding the CT scans evaluation, a blinded neuroradiologist used the well-known simplified ellipsoid volume equation method described by Kothari et al. The septum pellucidum MLS was evaluated.
by a blinded neuroradiologist. Any MLS more than 2 mm was considered significant.

**Laboratory assessments**

About 8 ml venous blood was withdrawn from each patient and divided as follows: 2 ml into EDTA tube for complete blood picture, 1.8 ml into the citrated tube for prothrombin time and APTT; and the remaining blood into the plain tube to get sera for routine investigations and the remaining sera were divided into three aliquots which were stored frozen at –20°C till the time of assay of specific investigations: S100 protein, IL-6, and N-terminal-pro-BNP. The routine laboratory investigations included complete blood picture, random blood sugar, liver, kidney function tests, and coagulation tests: PT and APTT. All routine laboratory chemical tests were done by fully automated chemistry analyzer Cobas c 311 (Roche Diagnostic GmbH Mannheim, Germany). A complete blood picture was done by Cell Dyn 1800, Abbott, USA. Coagulation tests were done by Siemens reagents using the Coatron Coagulometer, Germany. Quantitative determination of IL-6 was done by the enzyme-linked immunosorbent assay (ELISA) technique using RayBio Kit, Cat # ELH-IL6-001, USA.[5] The assay had a sensitivity of <3 pg/ml. Quantitative determination of S100 protein was done by the ELISA technique using DiaMetra Kit Ref: DK0074, Italy.[35] The assay had sensitivity up to 35.27 pg/ml and measuring range up to 5000 pg/ml. Assay of NT-pro-BNP was done by an electrochemiluminescence immunoassay using Elecsys 2010 (Roche Diagnostic GmbH, Mannheim, Germany). The assay had a measuring range of 3–35,000 pg/ml.[41]

**Statistical analysis**

The mean and standard deviation were used for the description of continuous variables, while percentages were used for categorical variables. The linear regression curve was used to express the correlation of CT outcomes to the biomarkers panel. The relationship between the biochemical markers panel and functional patient scores was assessed by the linear regression analysis for the BI. The mRS was evaluated as a dichotomous outcome, while the BI was evaluated as a continuous variable. Logistic regression analysis was done for mRS. Multivariate assumptions were used. The two-way interactions between covariates were used for additive effects. The tolerance and variance inflation tests were used to show the collinearity between the predictors. The SAS software version 9.3 or JMP 7.0.1 was used for the execution of those statistics.

**RESULTS**

**General characteristics**

The studied patients’ group comprised 50 patients with predominant male gender, with male-to-female ratio of 16:9 ≅ 1.7:1 patient. The mean age (in years) of the studied group was 60.7 ± 11.5. The studied SICH patients were subdivided into two groups based on the presence or absence of IVH.

**Severity scores results**

The severity scores (NIHSS, GCS, BI, and mRS) were significantly higher in SICH patients with IVH when compared with SICH patients without IVH ($P = 0.002, 0.008, 0.001$, and $0.03$, respectively), while the LOS score did not show any statistical significance [Table 1].

**Laboratory results**

Serum levels for a panel of blood biomarkers (pro-BNP and S100b) were significantly higher in SICH patients with IVH when compared with SICH patients without IVH ($P = 0.02$ and $0.027$, respectively). The IL-6 did not show any statistical significance [Table 2].

**Correlations between clinical data, laboratory results, and severity scores**

Multivariate correlations between demographic (age), biomarkers panel (IL-6, S100b, and pro-BNP), and clinical and severity scores (ICH score, ICH volume, LOS, BI, N-terminal-pro-BNP). The routine laboratory investigations included complete blood picture, random blood sugar, liver, kidney function tests, and coagulation tests: PT and APTT. All routine laboratory chemical tests were done by fully automated chemistry analyzer Cobas c 311 (Roche Diagnostic GmbH Mannheim, Germany). A complete blood picture was done by Cell Dyn 1800, Abbott, USA. Coagulation tests were done by Siemens reagents using the Coatron Coagulometer, Germany. Quantitative determination of IL-6 was done by the enzyme-linked immunosorbent assay (ELISA) technique using RayBio Kit, Cat # ELH-IL6-001, USA.[5] The assay had a sensitivity of <3 pg/ml. Quantitative determination of S100 protein was done by the ELISA technique using DiaMetra Kit Ref: DK0074, Italy.[35] The assay had sensitivity up to 35.27 pg/ml and measuring range up to 5000 pg/ml. Assay of NT-pro-BNP was done by an electrochemiluminescence immunoassay using Elecsys 2010 (Roche Diagnostic GmbH, Mannheim, Germany). The assay had a measuring range of 3–35,000 pg/ml.[41]

**Statistical analysis**

The mean and standard deviation were used for the description of continuous variables, while percentages were used for categorical variables. The linear regression curve was used to express the correlation of CT outcomes to the biomarkers panel. The relationship between the biochemical markers panel and functional patient scores was assessed by the linear regression analysis for the BI. The mRS was evaluated as a dichotomous outcome, while the BI was evaluated as a continuous variable. Logistic regression analysis was done for mRS. Multivariate assumptions were used. The two-way interactions between covariates were used for additive effects. The tolerance and variance inflation tests were used to show the collinearity between the predictors. The SAS software version 9.3 or JMP 7.0.1 was used for the execution of those statistics.

**RESULTS**

**General characteristics**

The studied patients’ group comprised 50 patients with predominant male gender, with male-to-female ratio of 16:9 ≅ 1.7:1 patient. The mean age (in years) of the studied group was 60.7 ± 11.5. The studied SICH patients were subdivided into two groups based on the presence or absence of IVH.

**Severity scores results**

The severity scores (NIHSS, GCS, BI, and mRS) were significantly higher in SICH patients with IVH when compared with SICH patients without IVH ($P = 0.002, 0.008, 0.001$, and $0.03$, respectively), while the LOS score did not show any statistical significance [Table 1].

**Laboratory results**

Serum levels for a panel of blood biomarkers (pro-BNP and S100b) were significantly higher in SICH patients with IVH when compared with SICH patients without IVH ($P = 0.02$ and $0.027$, respectively). The IL-6 did not show any statistical significance [Table 2].

**Correlations between clinical data, laboratory results, and severity scores**

Multivariate correlations between demographic (age), biomarkers panel (IL-6, S100b, and pro-BNP), and clinical and severity scores (ICH score, ICH volume, LOS, BI,
Eldawoody, et al.: Can brain natriuretic peptide, S100b, and interleukin-6 prognosticate the neurological consequences in Egyptian patients presented with supratentorial intracerebral hemorrhage?

mRS, GCS, and NIHSSS) in all studied patients showed a highly significant correlation between ICH score and pro-BNP (P = 0.04). Moreover, there was a highly significant correlation between LOS and IL-6 (P = 0.003) [Table 3].

**DISCUSSION**

Many studies have shown that there is a correlation between the biochemical marker panels and the prognosis in various acute onset brain lesion pathogenesis, such as ischemic stroke,[14,48] traumatic brain injury,[6] and SAH.[9,47] Moreover, it showed a promising advantage in the diagnostic and prognostic accuracy that expressed a higher value with a panel of the biochemical markers than a single one.[52] Therefore, the use of laboratory biomarkers panels with the classical clinical and radiological methods gave additional prognostic information that helps in decision-making, especially in hypoxic encephalopathy after cardiac arrest,[12,46] and as an alternative parameter in many studies, for instance in SAH,[9] and ischemic infarction.[43,48] Therefore, this study showed that S100b and pro-BNP are highly statistically correlated with prognostic clinical scales in discharged SICH patients and this adds supplementary prognostic value in addition to the classical methods. During the acute neuronal injury, the microglia and Schwann cells release S100b in the cerebrospinal fluid and then into the blood with breakage in the blood–brain barrier (BBB). Accordingly, serum S100b is an indicator of both neuronal injury and BBB dysfunction.[2,27] In addition, S100b is stable and not affected by hemolysis allowing dependable laboratory results. Finally, the short half-life of S100b allows the applicable results to represent the current pathophysiological situation and gives valuable time for intervention in emergency neurological situations.[6] The BNP is considered as a neurohormone elaborated initially as a pro-hormone then enzymatically induced BNP and the aminoterminal part. It is produced mainly from the cardiac ventricles in reaction to high wall tension.[38] Serum BNP is increased with heart failure,[39] also BNP levels showed a marked increase in acute onset brain insult.[40] BNP has many effects such as vasodilation, inhibition of the sympathetic nervous system, and modifications of the electrolytes and fluid balance by its action of diuretic and natriuretic properties.[14,16,41] Many studies have shown that there are elevations of BNP after SAH,[18,36,56] ischemic stroke,[24,40] and traumatic brain injury.[51] The elevation of BNP after acute onset brain insults is correlated with an augmentation in cerebral blood flow, although it is still vague whether this is an adjusting reaction[12,21,42] or a harmful response from cerebral ischemia.[49,50] Few studies have discussed the role of biomarkers in patients with ICH. Many published data have shown the relationships in certain serological markers to differentiate between ischemic and hemorrhagic cerebral stroke,[43,42] and also the expectation of hematoma progression, like matrix metalloproteinases.[11] The well-known serum biomarkers used to evaluate neurological prognosis after ICH are IL-11 and S100b.[15,22] Weglewski et al. stated that there is a time course for S100b serum level to increase then decrease after ICH.[54] Moreover, in patients with ICH, the initial worsening, and long-term prognosis for up to 3 months, was associated with S100b serum levels on admission. Delgado et al. stated that elevated serum level of S100b after spontaneous ICH is closely correlated to the initial ICH volume. Nevertheless, initial ICH volume is the best predictor for early deterioration and worse neurological outcome using multivariate analysis.[10] Dziedzic et al. stated that acute ICH triggers elevated levels of serum IL-6 and IL10 which correlate with initial ICH volume and shift of midline structures which, in turn, correlates well with the final functional neurological outcome.[11] In this study, we could not find a statistically significant correlation between serum level of IL-6 and any of the utilized clinical evaluation scales at hospital discharge which is contrary to the results of Dziedzic et al., although we could acknowledge a statistically significant correlation between the IL-6 and the LOS that could be explained by other early hospital-related infectious complications rather than direct relation.

| Item   | Age | ICHS | NIHSSS | GCS | ICHV | LOS | BI  | mRS | Pro-BNP | S100-B | IL-6 |
|--------|-----|------|--------|-----|------|-----|-----|-----|---------|--------|------|
| Age    | 0.7 | 0.6  | 0.9    | 0.2 | 0.2  | 0.2 | 0.7 | 0.45| 0.4     | 0.4    | 0.9  |
| ICHS   | 0.7 | 0.00**| 0.00**| 0.01**| 0.02 | 0.7 | 0.7 | 0.45| 0.4     | 0.4    | 0.9  |
| NIHSSS | 0.7 | 0.00**| 0.00**| 0.00**| 0.2  | 0.00**| 0.001**| 0.01**| 0.2     | 0.4    | 0.4  |
| GCS    | 0.9 | 0.00**| 0.00**| 0.008*| 0.008| 0.3  | 0.00**| 0.008*| 0.09    | 0.5    | 0.4  |
| ICHV   | 0.2 | 0.001**| 0.00**| 0.008*| 0.008*| 0.6  | 0.001**| 0.02* | 0.6     | 0.5    | 0.5  |
| LOS    | 0.2 | 0.1  | 0.3    | 0.3  | 0.6  | 0.4  | 0.4  | 0.2  | 0.9     | 0.7    | 0.003**|
| BI     | 0.7 | 0.00**| 0.00**| 0.00**| 0.001**| 0.4  | 0.00**| 0.1  | 0.4     | 0.3    |      |
| mRS    | 0.5 | 0.01* | 0.008*| 0.008*| 0.008*| 0.2  | 0.00**| 0.4  | 0.4     | 0.1    |      |

*Significant (test is considered significant when P<0.05), **Highly significant (P<0.005), LOS: Length of hospital stay score, BI: Barthel index, mRS: Modified Rankin Score, GCS: Glasgow Coma Score, NIHSSS: National Institutes of Health Stroke Scale Score, IL-6*: Interleukin-6, BNP: Brain natriuretic peptide, ICHS: Intracerebral hemorrhage score, ICHV: Intracerebral hemorrhage volume
Eldawoody, et al.: Can brain natriuretic peptide, S100b, and interleukin-6 prognosticate the neurological consequences in Egyptian patients presented with supratentorial intracerebral hemorrhage?

In the current study, we have been faced with several restrictions during data gathering that could be explained by, relatively small number of patients included in this study, so the interpretation of the study results should be dealt with caution. To be implemented in clinical practice, it should be validated by further future wider scale studies. Nevertheless, the study endpoint clinical scales were assessed at the time of SICH patient hospital discharge which could be modified after a good period of successful rehabilitation program which, in turn, could change the functional neurological outcome but at a more prolonged period of clinical follow-up. We believe that adding a follow-up biomarker level after several days of initial hospital admission could influence the global prognostic value achieved if combined with the initial measurement at the first 24 h and then correlated to the classical clinical-radiological prognosticator previously discussed. Even though the biomarker pro-BNP in this study correlates with ICHS which, in turn, correlates with the functional neurological outcome, IL-6 correlates with LOS in this study, the presence of IVH correlates with higher morbidity and mortality among the clinical severity scores [BI, NIHSS, GCS, and mRS; Table 1] that, in turn, correlate well with both S100b and pro-BNP in our study [Table 2]. From the previously discussed data, one can elucidate the probable valueability of initial biomarker assessment expecting the future functional outcome of our SICH patients. There is a lot of controversy regarding the withdrawal of care that could be influenced by regional laws and religious issues. For instance, Egyptian law does not allow for the withdrawal of care in terminally ill patients although it is an acceptable bylaw in other countries.[22] Based on our current data and supported by other references, worse neurological and functional outcome could be expected from laboratory biomarkers at an early stage of hospital admission, especially when combined with clinical-radiological prognosticators that could influence the decision of care withdrawal, particularly in SICH patient with IVH, a decision prohibited by law in our region although allowed elsewhere.[22]

CONCLUSION

Pro-BNP, IL-6, and S100b are greatly associated with the presence of IVH that correlated well with poor clinical outcome measures by NIHSSS, GCS, BI, and mRS. Moreover, these contribute to the prognostic biomarkers data over the severity scales that integrate both the clinical and radiographic characteristics. Nevertheless, those laboratory biomarkers added more prognostic value when conjoined with clinical severity scores, especially ICH score and pro-BNP. Further investigation of serial serum biomarkers measurements could be of value over a prolonged period, especially with the addition of cognitive function evaluation.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Abilleira S, Montaner J, Molina CA, Monasterio J, Castillo J, Alvarez-Sabin J. Matrix metalloproteinase-9 concentration after spontaneous intracerebral hemorrhage. J Neurosurg 2003;99:65-70.
2. Abraha HD, Butterworth RJ, Bath PM, Wassif WS, Garthwaite J, Sherwood RA. Serum S-100 protein, relationship to clinical outcome in acute stroke. Ann Clin Biochem 1997;34:366-70.
3. Akdemir G, Luer MS, Dujovny M, Misra M. Intraventricular atrial natriuretic peptide for acute intracranial hypertension. Neurrol Res 1997;19:515-20.
4. Allard L, Lescuyer P, Burgess J, Leung KY, Ward M, Walter N, et al. ApoC-1 and ApoC-III as potential plasmatic markers to distinguish between ischemic and hemorrhagic stroke. Proteomics 2004;4:2242-51.
5. Bauer J, Herrmann F. Interleukin-6 in clinical medicine. Ann Hematol 1991;62:203-10.
6. Biberthaler P, Mussack T, Wiedemann E, Kanz KG, Mutschler W, Linsenmaier U, et al. Rapid identification of high-risk patients after minor head trauma (MHT) by assessment of S-100B: Ascertainment of a cut-off level. Eur J Med Res 2002;7:164-70.
7. Broderick J, Connolly S, Feldmann E, Hanley D, Kase C, Krieger D, et al. Guidelines for the management of
spontaneous intracerebral hemorrhage in adults: 2007 update: A guideline from the American heart association/American stroke association stroke council, high blood pressure research council, and the quality of care and outcomes in research interdisciplinary working group. Stroke 2007;38:2001-23.

8. Büttner T, Weyers S, Postert T, Sprengelmeyer R, Kuhn W. S-100 protein: Serum marker of focal brain damage after ischemic territorial MCA infarction. Stroke 1997;28:1961-5.

9. Chaudhry SR, Stoffel-Wagner B, Kinfe TM, Güresir E, Vatter H, Dietrich D, et al. Elevated systemic IL-6 levels in patients with aneurysmal subarachnoid hemorrhage is an unsppecific marker for Post-SAH Complications. Int J Mol Sci 2017;18:2580.

10. Delgado P, Sabin JA, Santamarina E, Molina CA, Quintana M, Rosell A, et al. Plasma S100B level after acute spontaneous intracerebral hemorrhage. Stroke 2006;37:2837-39.

11. Dzedzic T, Bartus S, Klimkowicz A, Motyl M, Slowik A, Szczudlik A. Intracerebral hemorrhage triggers interleukin-6 and interleukin-10 release in blood. Stroke 2002;33:2334-5.

12. Ekemtizoglou KA, Xanthos T, Papadimitriou L. Biochemical markers (NSE, S-100, IL-8) as predictors of neurological outcome in patients after cardiac arrest and return of spontaneous circulation. Resuscitation 2007;75:219-28.

13. Elting JW, Sulter GA, Kaste M, Lees KR, Diener HC, Hommel M, et al. AMPA antagonist ZK200775 in patients with acute ischemic stroke: Possible glial cell toxicity detected by monitoring of S-100B serum levels. Stroke 2002;33:2813-8.

14. Epstein M, Loutzenhiser R, Friedland E, Aceto RM, Camargo MJ, Atlas SA. Relationship of increased plasma atrial natriuretic factor and renal sodium handling during immersion-induced central hypervolemia in normal humans. J Clin Invest 1987;79:738-45.

15. Epstein M, Loutzenhiser R, Friedland E, Aceto RM, Camargo MJ, Atlas SA. Relationship of increased plasma atrial natriuretic factor and renal sodium handling during immersion-induced central hypervolemia in normal humans. J Clin Invest 1987;79:738-45.

16. Floras JS. Sympathoinhibitory effects of atrial natriuretic factor and renal sodium handling during immersion-induced central hypervolemia in normal humans. J Clin Invest 1987;79:738-45.

17. Foerch C, Wunderlich MT, Dvorak F, Humpich M, Kahles T, Uklić T. Novel diagnostic test for acute stroke. Stroke 2007;38:2491-5.

18. Fukui S, Nakashiro H, Otani N, Osi-gawa H, Toyooka T, Tsuchiya N, et al. Focal brain edema and natriuretic peptides in patients with subarachnoid hemorrhage. Acta Neurochir Suppl 2003;86:489-91.

19. Garibi J, Bilbao G, Pomposo I, Hostalot C. Prognostic factors in a series of 185 consecutive spontaneous supratentorial intracerebral haematomas. Br J Neurosurg 2002;16:355-61.

20. Hemphill JC 3rd, Bonovich DC, Besmertis L, Manley GT, Johnston SC. The ICH score: A simple, reliable grading scale for intracerebral hemorrhage. Stroke 2001;32:897-1.

21. Iida H, Iida M, Takenaka M, Oda A, Uchida M, Fujiwara H, et al. The effects of alpha-human atrial natriuretic peptide and milrinone on pial vessels during blood-brain barrier disruption in rabbits. Anesth Analg 2001;93:177-82.

22. James ML, Blessing R, Phillips-Bute BG, Bennett E, Laskowitz DT. S100B and brain natriuretic peptide predict functional neurological outcome after intracerebral hemorrhage. Biomarkers 2009;14:388-94.

23. James ML, Blessing R, Bennett E, Laskowitz DT. Apolipoprotein E modifies neurological outcome by affecting cerebral edema but not hematoma size after intracerebral hemorrhage in humans. J Stroke Cerebrovasc Dis 2009;18:144-9.

24. James ML, Warner DS, Laskowitz DT. Preclinical models of intracerebral hemorrhage: A translational perspective. Neurocrit Care 2008;9:139-52.

25. Jönsson H, Johnson P, Birch-Iensen M, Alling C, Westaby S, Blomquist S. S100B as a predictor of size and outcome of stroke after cardiac surgery. Ann Thorac Surg 2001;71:1433-7.

26. Juvela S. Risk factors for impaired outcome after spontaneous intracerebral hemorrhage. Arch Neurol 1995;52:1193-200.

27. Kanner AA, Marchi N, Fazio V, Mayberg MR, Koltz MT, Simion V, et al. Serum S100beta: A noninvasive marker of blood-brain barrier function and brain lesions. Cancer 2003;97:2806-13.

28. Koenig MA, Puttgen HA, Prabhakaran V, Reich D, Stevens RD. B-type natriuretic peptide as a marker for failure in patients with acute stroke. Intensive Care Med 2007;33:1587-93.

29. Kokocinska D, Wieczorek P, Partyka R, Jarzab J, Jalowiecki P, Sikora J. The diagnostic utility of S-100B protein and TPA in patients with ischemic stroke. Neuro Endocrinol Lett 2007;28:693-8.

30. Kothari RU, Brott T, Broderick JP, Barsan WG, Sauerbeck LR, Zuccarello M, et al. The ABCs of measuring intracerebral hemorrhage volumes. Stroke 1996;27:1304-5.

31. Laragh JH. Atrial natriuretic hormone, the renin-angiotensin axis, and blood pressure-electrolyte homeostasis. N Engl J Med 1985;313:1330-40.

32. Laskowitz DT, Blessing R, Floyd J, White WD, Lynch JR. Panel of biomarkers predicts stroke. Ann N Y Acad Sci 2005;1053:30.

33. Lyden P, Raman R, Liu L, Grotta J, Broderick J, Olson S, et al. NIHSS training and certification using a new digital video disk is reliable. Stroke 2005;36:2446-9.

34. Lynch JR, Blessing R, White WD, Grocott HP, Newman MF, Laskowitz DT. Novel diagnostic test for acute stroke. Stroke 2004;35:57-63.

35. Mårtenson ED, Hansson LO, Nilsson B, von Schoultz E, Brahe EM, Ringborg U, et al. Serum S-100b protein as a prognostic marker in malignant cutaneous melanoma. J Clin Oncol 2001;19:824-31.

36. McGirt MJ, Blessing R, Nimjee SM, Friedman AH, Alexander MJ, Laskowitz DT, et al. Correlation of serum brain natriuretic peptide with hyponatremia and delayed ischemic neurological deficits after subarachnoid hemorrhage. Neurosurgery 2004;54:1369-74.

37. Mizukoshi G, Katsura K, Katayama Y, Matsumoto T, Hommel M, et al. The diagnostic utility of S-100B protein and TPA in patients with ischemic stroke. Neuro Endocrinol Lett 2007;28:693-8.

38. Mukoyama M, Nakao K, Hosoda K, Suga S, Ogawa Y, et al. Increased human brain natriuretic peptide in congestive heart failure. N Engl J Med 1990;323:757-8.
40. Nakagawa K, Yamaguchi T, Seida M, Yamada S, Imae S, Tanaka Y, et al. Plasma concentrations of brain natriuretic peptide in patients with acute ischemic stroke. Cerebrovasc Dis 2005;19:157-64.

41. Nir A, Lindinger A, Rauh M, Bar-Oz B, Laer S, Schwachtgen L, et al. NT-pro-B-type natriuretic peptide in infants and children: Reference values based on combined data from four studies. Pediatr Cardiol 2009;30:3-8.

42. Nogami M, Shiga J, Takatsu A, Endo N, Ishiyama I. Immunohistochemistry of atrial natriuretic peptide in brain infarction. Histochem J 2001;33:87-90.

43. Pettigrew LC, Kasner SE, Gorman M, Atkinson RP, Funakoshi Y, Ishibashi H, et al. Effect of arundic acid on serum S-100beta in ischemic stroke. J Neurol Sci 2006;251:57-61.

44. Reynolds MA, Kirchick HJ, Dahlen JR, Anderberg JM, McPherson PH, Nakamura KK, et al. Early biomarkers of stroke. Clin Chem 2003;49:1733-9.

45. Sanchez-Peña P, Pereira AR, Sourour NA, Biondi A, Lejean L, Colonne C, et al. S100B as an additional prognostic marker in subarachnoid aneurysmal hemorrhage. Crit Care Med 2008;36:2267-73.

46. Sodeck GH, Domanovits H, Sterz F, Schillinger M, Losert H, Havel C, et al. Can brain natriuretic peptide predict outcome after cardiac arrest? An observational study. Resuscitation 2007;74:439-45.

47. Stranjalis G, Korfias S, Psachoulia C, Kouyialis A, Sakas DE, Mendelow AD. The prognostic value of serum S-100B protein in spontaneous subarachnoid haemorrhage. Acta Neurochir (Wien) 2007;149:231-8.

48. Suzuki S, Tanaka K, Suzuki N. Ambivalent aspects of interleukin-6 in cerebral ischemia: Inflammatory versus neurotrophic aspects. J Cereb Blood Flow Metab 2009;29:464-79.

49. Sviri GE, Feinsod M, Soustiel JE. Brain natriuretic peptide and cerebral vasospasm in subarachnoid hemorrhage. Clinical and TCD correlations. Stroke 2000;31:118-22.

50. Sviri GE, Shik V, Raz B, Soustiel JE. Role of brain natriuretic peptide in cerebral vasospasm. Acta Neurochir (Wien) 2003;145:851-60.

51. Sviri GE, Soustiel JE, Zaaroor M. Alteration in brain natriuretic peptide (BNP) plasma concentration following severe traumatic brain injury. Acta Neurochir (Wien) 2006;148:529-33.

52. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974;2:81-4.

53. Valli N, Gobinet A, Bordenave L. Review of 10 years of the clinical use of brain natriuretic peptide in cardiology. J Lab Clin Med 1999;134:437-44.

54. Weglewski A, Ryglewicz D, Mular A, Juryńczyk J. Changes of protein S100B serum concentration during ischemic and hemorrhagic stroke in relation to the volume of stroke lesion. Neurol Neurochir Pol 2005;39:310-7.

55. Woiciechowsky C, Schöning B, Cobanov J, Lanksch WR, Volk HD, Döcke WD. Early IL-6 plasma concentrations correlate with severity of brain injury and pneumonia in brain-injured patients. J Trauma 2002;52:339-45.

56. Yarlagadda S, Rajendran P, Miss JC, Banki NM, Kopelnik A, Wu AH, et al. Cardiovascular predictors of in-patient mortality after subarachnoid hemorrhage. Neurocrit Care 2006;5:102-7.

How to cite this article: Eldawoody HA, Mattar MA, Mesbah A, Zaher A, Elsherif M. Can brain natriuretic peptide, S100b, and interleukin-6 prognosticate the neurological consequences in Egyptian patients presented with supratentorial intracerebral hemorrhage? Surg Neurol Int 2020;11:460.