Asian Journal of Research in Surgery

5(1): 31-35, 2021; Article no.AJRS.65399

Changes in Levels of S100β Protein as a Measurement of Ventriculoperitoneal Shunt Outcome in Hydrocephalus Patients

Wirandhani Kurniadi[1*], Alifianto Untung[2], Wijanarko Ferry[2], Setyono Hanis[2] and Wujoso Hari[3]

[1]Faculty of Medicine, Sebelas Maret University, Moewardi General Hospital, Surakarta, Indonesia.
[2]Department of Neurosurgery, Moewardi General Hospital, Surakarta, Indonesia.
[3]Departement of Forensic Medicine and Medicolegal, Moewardi General Hospital, Surakarta, Indonesia.

Authors' contributions

This work was carried out in collaboration among all authors. Authors WK and WF designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors SH and WH managed the analyses of the study. Author AU managed the literature searches. All authors read and approved the final manuscript.

Article Information

Editor(s):
(1) Dr. Wagih Mommtaz Ghannam, Mansoura University, Egypt.
Reviewers:
(1) Abdelhakeem A. Essa, Assiut University, Egypt.
(2) Ludmila Rocha Lemos, UNIDESC, Brazil.
Complete Peer review History: http://www.sdiarticle4.com/review-history/65399

Original Research Article

Received 10 December 2020
Accepted 13 February 2021
Published 02 March 2021

ABSTRACT

Aims: To determine the difference in S100β serum levels between pre- and post-Ventriculoperitoneal (VP) shunts in hydrocephalus patients.
Study Design: Quantitative observational analytic with cross-sectional study approach.
Place and Duration of Study: Department of neurosurgery, Dr. Moewardi Hospital Surakarta, Indonesia, between March and June 2020.
Methodology: We included 24 patients purposively (10 men, 14 women; age range: 12-60 years) with hydrocephalus. The blood sample was collected one day before the VP shunt, and the second collection was four days after the VP shunt. The S100β protein levels were analyzed using ELISA kit. We also observed changes in consciousness using the Glasgow Coma Scale (GCS).
Results: Of the 24 research subjects, it was found that the levels of S100β before and after the VP

**Corresponding author: E-mail: K.wirandhani29@gmail.com;*

shunt had a significant difference (p = 0.008). Nineteen subjects had decreased S100β levels on the fourth day of treatment after VP shunt while five subjects experienced increased levels of S100β in the blood on the fourth day of the treatment.

Conclusion: There was a significant difference in S100β protein levels before and after the VP shunt was performed in hydrocephalus patients at Dr. Moewardi Hospital, Surakarta. Based on these findings, this protein can be used as a measurement biomarker of VP shunt outcome

Keywords: Hydrocephalus, VP Shunt, S100β, GCS.

1. INTRODUCTION

Hydrocephalus occurs due to disruption in the production, flow, and absorption processes of cerebrospinal fluid [1]. The prevalence of hydrocephalus in the Netherlands and the United States is reported to be around 0.65 peril and two peril per year, respectively, while in Indonesia it reaches ten peril. A total of 40% of hydrocephalus cases are adult cases [2]. The standard procedure performed in cases of hydrocephalus is the VP Shunt. In the United States, more than 30,000 procedures to relieve hydrocephalus are performed annually [3].

Research conducted by Beems et al. [4] stated that high levels of S100β in cerebrospinal fluid can indicate possible brain damage in hydrocephalus, but it is different from serum levels, which cannot evaluate the severity of hydrocephalus [4]. In a study conducted by Brandner et al. [5], high levels of S100β in Cerebrospial Fluid (CSF) and serum indicate a high probability of needing permanent shunt in hydrocephalus patients caused by subarachnoid hemorrhage [5]. Therefore, we observed the change of S100β protein serum levels to determine the difference in S100β levels in the blood between pre- and post-VP shunts and its role as a biomarker on the VP shunt outcome in hydrocephalus patients

2. MATERIALS AND METHODS

2.1 Patient Population

Research subjects were patients diagnosed with hydrocephalus based on computed tomography (CT) scan examination and were scheduled for VP shunt procedure. Between March and June 2020, 24 patients with hydrocephalus were chosen purposively based on inclusion and exclusion criteria. We included the patients who agreed to be part of this study with an age range of 1-60 years. Patients who underwent another invasive procedure during the observation time experienced a deterioration of conditions or death, and malfunction of the VP shunt during observation time were excluded from the study. Patients who had systemic comorbidities and the history of neurology or neurodegenerative disease were also excluded from the study. We also observed changes in the patient's consciousness level using the Glasgow Coma Scale (GCS).

2.2 Sample Collection and Processing

Blood serum were collected while patients were hospitalized. Patients who underwent VP shunt procedure were usually hospitalized for 5 days, therefore, blood serums were collected twice, a day before and four days after the procedure, from each patient**.** Measurements used the Biorad Model 680 Microplate Reader instrument (Bio-rad Laboratories Inc, CA, USA) with Microplate Manager software ver 5.2.1 (Bio-rad Laboratories Inc., CA, USA). The reagent kit used was Human S100B ELISA (BioVendor-Laboratorni Medicina a.s, Brno, Czech Republic).

2.3 Statistical Analysis

Distributions of data were analyzed using Shapiro-Wilk test. Data of this study were not normally distributed. Therefore, Statistical analysis was performed using the Wilcoxon signed-rank test, and the statistical significance was accepted with $p < 0.05$. Analyses were performed using Statistical Product and Service Solution Software for Windows version 22.

3. RESULTS AND DISCUSSION

3.1 Patient Characteristics

Univariate analysis was carried out to see the data characteristics of the research subjects. Table 1 shows that this study had 24 subjects consisting of 10 (41.7%) males and 14 (58.3%) females. The median age of the research subjects was 50 years, with the youngest of 12 years and the oldest of 60 years.

The consciousness level of the research subjects was assessed before and after the procedure of VP shunt using the GCS measurement. The preoperative median GCS score was 15 with the lowest GCS score of 5 and the highest of 15 while the postoperative GCS median score was 15 with the lowest score of 13 and the highest of 15.

Blood serum samples were analyzed using the Biorad Model 680 Microplate Reader instrument (Bio-rad Laboratories Inc, CA, USA) with Microplate Manager ver 5.2.1 software (Bio-rad Laboratories Inc., CA, USA). The median of S100β levels before the procedure was 28.7 pg/mL with the lowest level of 17.35 pg/mL and the highest level of 305 pg/mL. After the patient underwent a VP shunt procedure, the blood serum sample was collected again on the fourth day of treatment. The median value of S100β levels after VP shunt action was 19.6 pg/mL with the lowest level of 16.74 pg/mL and the highest of 181.77 pg/mL.

3.2 Bivariate Analysis

To find out the difference in S100β levels, an analysis was performed using the Wilcoxon Signed-Rank test. The difference was significant if the p-value was < 0.05. Table 2 shows the results of the Wilcoxon test analysis for the levels of S100β. The level of S100β before the procedure had a median value was 28.7 pg/mL with the lowest level of 17.35 pg/mL and the highest level of 305 pg/mL. The median value of S100β levels after VP shunt action was 19.6 pg/mL with the lowest level value of 16.74 pg/mL and the highest of 181.77 pg/mL. It was found that the S100β levels before and after the VP shunt action had a significant difference (P = 0.008). In nineteen subjects, it was found that S100β levels decreased on the fourth day after the VP shunt procedure while five study subjects experienced increased levels of S100β on the fourth day after the procedure.

Table 3 shows the results of the Wilcoxon test analysis of the GCS level of the research subjects measured before and after VP shunt action. The median pre-operative GCS score was 15 with the lowest GCS level of 5 and the highest of 15, while the postoperative GCS median value was 15 with the lowest GCS score of 13 and the highest of 15. This shows insignificant differences between the scores of GCS before and after the procedure (P = 0.06). However, GCS values did not change in twenty patients who underwent VP Shunt insertion. GCS scores increased in four subjects, and none of the study subjects experienced a decrease in GCS.

Table 1. Patient demographics

Characteristics		Description (n = 24)
Sex	Male	10 (41.7%)
	Female	14 (58.3%)
Age		50 (12-60)
Preoperative GCS		15 (5 - 15)
Postoperative GCS		15 (13 -15)
Preoperative S100β Levels		28.7 (17.35 - 305)
Postoperative S100β Levels		19.6 (16.74 – 181.77)

(Primary Data, 2020)

Table 2. Difference in S100β levels

	Median (Minimum-Maximum)	P-Value
Pre-VP Shunt Level	28.7 (17.35 - 305)	0,008
Post-VP Shunt Level	19.6 (16.74 – 181.77)	

Wilcoxon test, S100β levels on 19 subjects decreased, 0 subjects remained, and 5 subjects increased

Table 3. Difference in GCS levels

	Median (Minimum-Maximum)	P-Value
Pre-VP Shunt GCS	15 (5 - 15)	0,06
Post-VP Shunt GCS	15 (13 -15)	

Wilcoxon test, no subjects with decreased GCS, 20 subjects remained, and 4 subjects increased

3.3 Discussion

This cross-sectional study showed insignificant differences between the GCS values before and after the procedure (p = 0.068). Likewise, studies conducted on traumatic brain injury patients showed a good correlation between S100β levels and the patient's GCS [6]. However, none of the patients experienced a loss of consciousness after VP shunt insertion. In accordance with the research conducted by Beems et al. [4], all patients who underwent surgery achieved maximum postoperative GCS levels and did not experience permanent neurological dysfunction [4].

S100β protein is present in several tissues, more abundant in cerebrospinal fluid [7]. However, the measurement of S100β protein in serum can represent measurements in cerebrospinal fluid [8]. Measurement of S100β protein uses the gold standard ELISA examination which takes 4-6 hours for examination [9]. In this study, S100β levels were examined using the Biorad Model 680 Microplate Reader instrument (Bio-rad Laboratories Inc., CA, USA) with Microplate Manager ver 5.2.1 software (Bio-rad Laboratories Inc., CA, USA). The reagent kit used was Human S100β ELISA (BioVendor-Laboratorni medicina a.s, Brno, Czech Republic). S100β protein levels significantly increased in hydrocephalus patients compared to healthy groups [10]. The presence of S100β protein in the blood indicates a functional or morphological disorder in the blood-brain barrier which is usually found in cases of astrogliosis and children with hydrocephalus [11].

Previous research conducted by Brandner et al. [5] stated that high serum levels of S100β indicate a high probability of using permanent shunts in hydrocephalus patients, but this study was only conducted in patients with subarachnoid hemorrhage [5]. Our study found that the levels of S100β before and after the VP shunt procedure had a significant difference (p = 0.008). Following the research by Budi and Parenrengi (2013), there was a significant relationship between high CSF and serum S100β levels with lower ventricular size changes after CSF drainage [8]. Five study subjects experienced an increase in serum levels of S100β after VP shunt placement. This may be caused by the fluctuation of serum S100β levels in hydrocephalus patients during the observation. In successful subjects without external ventricular drainage (EVD), levels of S100β reached normal on day 7 while subjects who failed had a significant increase in S100β levels on days 4-7, while in the dependent group, VP shunt continued to have high S100β levels for 10 days [5].

S100β as a biomarker has been widely studied in cases of traumatic brain injury, and there are significant results that this biomarker will increase in these cases. This study tries to see if there was a change in S100β biomarker levels in cases of hydrocephalus. Research on hydrocephalus cases is still rarely done, especially in Indonesia. The S100β biomarker itself has not become a routine examination for brain injury and hydrocephalus in Indonesia. Some studies only state that elevated levels of S100β indicate brain damage in hydrocephalus. In this study, we looked for changes in S100β levels in patients with hydrocephalus who underwent a VP shunt. It is hoped that the results of this study can become the basis for future research and allow this serum biomarker to become an invasive measuring tool to determine the effectiveness of the VP shunt procedure in cases of hydrocephalus.

Many factors can affect the level of Future research needs to be carried out with more attention to the possibility of other variables that may influence S100β levels. This study assessed changes in serum levels of S100β in one measurement frequency so that it could not show the highest and lowest levels and the process of decreasing the levels of these biomarkers in the serum during observation.

4. CONCLUSION

In this study, we found a significant difference in S100β protein levels before and after the VP shunt was performed in hydrocephalus patients at Dr. Moewardi Hospital, Surakarta. This study also compared the values of patient consciousness before and after VP shunt. The patient's GCS score did not have a significant difference between before and after the shunting procedure. Based on these findings, this protein can be used as a measurement biomarker of VP shunt outcome.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not

intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT AND ETHICAL APPROVAL

As per university standard guidelines, participant consent and ethical approval have been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Pal SS, Dubey S. A study of VP shunt in management of hydrocephalus. Int Surg J. 2017;4:1697-701.
2. Satyanegara, Arifin Z, Hasan RY, Abubakar S, Yuliatri N, Prabowo H, et al. Ilmu bedah saraf satyanegara edisi V. Gramedia Pustaka; 2014.
3. Khan F, Rehman A, Shamim MS, Bari ME. Factors affecting ventriculoperitoneal shunt survival in adult patients. Surg Neurol Int. 2015;6:25.
4. Beems T, Simon KS, van Geel WJA, de Reus HPM, Vos PE, Verbeek MM. Serum- and CSF-concentrations of brain specific proteins in hydrocephalus. Acta Neurochir. 2003;145:37–43.
5. Brandner S, Xu Y, Schmidt C, Emtmann I, Buchfelder M, Kleindienst A. Shunt-dependent hydrocephalus following subara chnoid hemorrhage correlates with Increased S100B levels in cerebrospinal fluid and serum. Acta Neurochirurgica Supplementum. 2012;114.
6. Yoon SM, Choi YJ, Kim HJ, Shim JJ, Bae HG, Yun IG. Prognostic value of serum s100 protein by elecsys s100 immuno assay in patients with spontaneous subarachnoid and intracerebral hemorr hages. J Korean Neurosurg Soc. 2008;44 (5):308-313.
7. Gazzolo D, Pluchinotta F, Lapergola G, Franchini S. The Calcium-binding S100B protein: An important diagnostic and prognostic neurobiomarker in pediatric laboratory medicine. Methods in Molecular Biology. 2019;1929.
8. Nadjiullah Budi, Muhammad Arifin Parenrengi, Korelasi Kadar. S100 β cairan serebrospinal dan serum dengan perubahan cerebral mantle dan ukuran ventrikel pasca operasi drainase pada hidrosefalus kongenital. Indonesian Journal of Neurosurgery 2013 1(1).2-6. ISSN: 2338-9524
9. Thelin EP, Nelson DW, Bellander B. A review of the clinical utility of serum S100B protein levels in the assessment of traumatic brain injury. Acta Neurochirp; 2016.
10. Ahmet Guzelcicek, Ataman Gönel, Ismail Koyuncu, Gulyara Cigdem, Dogan Kose, Mehmet Karadag et al. Investigating the Levels of Brain-Specific Proteins in Hydrocephalus Patients, Combinatorial Chemistry & High Throughput Screening. 2020;23:1
11. Tarnaris A, Watkins LD, Kitchen ND. Biomarkers in chronic adult hydrocephalus. Biomed Central; 2006.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/65399