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Serum Nse Level And Incidence Of Pod In Post-Traumatic Spinal Surgery With General Anesthesia

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Introduction: Due to its high incidence and mortality, post-traumatic spinal trauma affects society. Post-traumatic spinal trauma occurs 19.54 times per 100,000 people annually. Postoperative delirium (POD) is a sudden loss of awareness, attention, cognition, and perception after surgery. POD after trauma spine surgery ranges from 0.49 to 21%. NSE is an enzymatic protein found in neurones and neuroendocrine cells. After brain or nervous system trauma, NSE is released into the bloodstream. NSE is a putative POD biomarker. Due to their increased risk of POD after spinal surgery for trauma under general anaesthesia, NSE's effect on POD is uncertain.

Objectives: This study examines the relationship between preoperative and postoperative NSE levels and POD in post-traumatic spine surgery patients undergoing general anaesthesia.

Methods: This study is an analytical observational study that examines the levels of NSE before and after surgery in patients who have undergone post-traumatic spine surgery while under general anaesthesia. Blood samples were collected prior to surgery and 24 hours post-surgery to obtain data on NSE levels. The assessment of POD was conducted once the patient regained full consciousness following the procedure.

Results: The study included 25 male participants and 10 female participants, with 4 of the males experiencing POD. The correlation analysis revealed a statistically significant difference in NSE levels before and after surgery ($p<0.001$). However, there was no significant correlation between changes in NSE levels and POD ($p=0.468$).

Conclusions: The NSE levels saw a considerable increase after post-traumatic spinal surgery with general anaesthesia, however this increase was not significantly associated with the occurrence of POD.

Keywords: neuron specific enolase, postoperative delirium, spinal surgery, general anaesthesia

INTRODUCTION

Post-traumatic spinal cord damage exerts significant socio-economic repercussions owing to its elevated morbidity and mortality rates. The epidemiology of post-traumatic spinal cord injury has been examined in multiple regions. A retrospective study conducted at a regional trauma facility in Ireland revealed a yearly incidence of post-traumatic spinal cord damage of 19.54 instances per 100,000 individuals, with falls and low-energy trauma constituting a substantial percentage of all cases [1]. A retrospective epidemiological study conducted at a level one trauma center in the Netherlands revealed that from 2007 to 2016, 1479 patients were admitted with a total of 3029 post-traumatic spinal cord injuries, primarily resulting from falls from a height, followed by road traffic accidents [2].

Post-traumatic spinal surgery is a therapeutic option for individuals with post-traumatic spinal cord injuries.

Complications, including Postoperative Delirium (POD), may arise following post-traumatic spine surgery. POD is characterized as a sudden impairment of awareness, attention, cognition, and perception that occurs post-surgery [3]. The occurrence of postoperative delirium following post-traumatic spinal surgery varies between 0.49% and 21% [4]. Additional research has identified variable incidence rates of postoperative delirium (POD) following post-traumatic spine surgery, ranging from 10% to 77% [5], [6]. The diagnosis of Postoperative Delirium (POD) is determined according to the criteria set forth in the Diagnostic and Statistical Manual of Mental Disorders (DSM) during post-operative hospitalization and before to discharge [4]. Delirium is a prevalent and significant consequence that prolongs hospital stays by 2–3 days and correlates with a 30-day death rate of 7–10% [7]. It predominantly occurs in elderly patients, individuals with pre-existing neurocognitive deficits, and those undertaking intricate or urgent treatments.

Numerous researches have examined the prevalence and risk factors of postoperative delirium following post-traumatic spinal surgery. A retrospective analysis identified preoperative cognitive dysfunction, emergency surgery, advanced age, and general anesthesia as variables related with postoperative delirium following post-traumatic spine surgery [5]. Risk factors for postoperative delirium during post-traumatic spine surgery encompass advanced age, diminished preoperative cognitive function, prolonged surgical duration, blood transfusion, depression, and general anesthesia [3], [6], [8]. A randomized controlled experiment indicated that patients administered general anesthesia exhibited an elevated risk of postoperative delirium [9]. A systematic analysis identified general anesthesia as a risk factor for postoperative delirium following elective post-traumatic spine surgery [10] Recognizing high-risk patients and executing suitable preventative measures may aid in preventing POD during post-traumatic spine surgery [3].

Neuron Specific Enolase (NSE) is an enzyme present in neurons and neuroendocrine cells. The function of NSE in the nervous system pertains to glycolysis, the metabolic pathway that degrades glucose to generate cellular energy, and the creation of neurotransmitters, the chemical messengers that convey impulses between neurons in the brain and nervous system. NSE is released into the bloodstream following injury to the brain or nervous system. NSE has been investigated as a possible biomarker for POD, as increased NSE levels have been observed in patients who experience POD following cardiac [11]. A study indicated that increased NSE levels correlated with POD, signifying axonal injury in the central nervous system, and were linked to the severity of POD [12]. The function of NSE in postoperative delirium following post-traumatic spinal surgery under general anesthesia remains inadequately comprehended, as these individuals exhibit an elevated risk for delirium.

OBJECTIVES

This study seeks to investigate the correlation between preoperative and postoperative NSE levels and the occurrence of POD in patients undergoing post-traumatic spine surgery under general anesthesia. Serial evaluation of NSE levels, both preoperatively and postoperatively, may serve as a possible tool for monitoring the onset of POD, as elevated NSE levels are observed in patients with POD.

METHODS

An ethical review application was filed to the Health Research Ethics Committee at Dr. Soetomo Hospital in Surabaya. Patients scheduled for elective surgery under general anesthesia who satisfied the inclusion and exclusion criteria were selected as samples. Serum NSE levels were assessed 24 hours before to surgery. Serum NSE levels were measured again 24 hours post-surgery. The CAM test was conducted 24 hours post-surgery. The independent variables of this investigation were serum NSE levels measured preoperatively and postoperatively. The study's dependent variable was the incidence of postoperative delirium, evaluated using the Confusion Assessment Method (CAM). The gathered data will be documented and organized into tables. The data processing for this study utilized SPSS 17.0 Software (SPSS Inc., Chicago, IL, USA).

All demographic characteristics (age, gender, ASA score, comorbidities, and nutritional status) will be summarized through descriptive statistics. Comparison of quantitative data via the paired t-test, with results expressed as mean and standard deviation, contingent upon normal data distribution. If the data distribution is non-normal, employ the Wilcoxon

test for comparison and utilize median, minimum, and maximum values for measurement. The link between blood NSE levels and POD incidence was analyzed using logistic regression, with serum NSE levels before and after surgery as independent variables. A p-value less than 0.05 signifies statistically significant results.

RESULTS

Table 1: Subject Characteristics

Characteristics	N (%)	Mean ± Standard Deviation	Median (*range*)	p-value*
Sex				
Men	25 (71.4%)			
Women	10 (28.6%)			
Age (years old)		44.63 ± 9.68	46 (21-59)	0.114
BMI (kg/m^2)		23.67 ± 1.90		0.298
Comorbidity				
Cardiovascular				
Yes	9 (25.7%)			
No	26 (74.3%)			
Metabolic				
Yes	2 (5.71%)			
No	33 (94.3%)			
Respiration				
Yes	7 (20.0%)			
No	28 (80.0%)			
Neurologic				
Yes	2 (5.71%)			
No	26 (94.3%)			
Gastrointestinal/ Reproduction/ Urology				
Ya	9 (25,7%)			
Tidak	26 (74,3%)			
Duration (min)		240 ± 173	210 (30-1030)	<0.001
Bleeding (mL)		585.71 ± 647.91	450 (50-3500)	<0.001
Transfusion (unit)		0.54 ± 0.85	0 (0-4)	<0.001
POD				
Yes	4 (11.4%)			
No	31 (88.6%)			
NSE difference (mg/L)		1.96 ± 4.36	0.75 (-3.69-16.45)	<0.001

NSE: neural specific enolase; POD: postoperative delirium
*normality test, p>0.05 indicates normal data distribution

Table 2: POD incidences based on subjects' characteristics.

Characteristics	POD		*p-value**
	Yes (n=4)	No (n=31)	
Sex			0.179
Men	4	21	
Women	0	10	
Age (years old)	52.25 ± 6.81	43.65 ± 9.81	0.101
BMI (kg/m^2)	23.43 ± 1.30	23.70 ± 1.98	0.788
Comorbidity			
Cardiovascular			0.238
Yes	2	7	
No	2	24	
Metabolic			0.601
Yes	0	2	
No	4	29	
Respiration			0.111
Yes	2	5	
No	2	26	
Neurologic			
Yes	0	2	0.601
No	4	29	
Gastrointestinal/ Reproduction/ Urology			0.972
Ya	1	8	
Tidak	3	23	
Duration (min)	241 ± 107	240 ± 181	0.533
Bleeding (mL)	462.50 ± 286.87	601.61 ± 682.09	0.896
Transfusion (unit)	0.50 ± 0.58	0.55 ± 0.89	0.811
NSE difference (mg/L)	4.71 ± 7.27	1.61 ± 3.89	0.468
POD: postoperative delirium; NSE: neural specific enolase *p<0.05 indicates correlation			

This study comprised a male majority, with 71.4% males and 28.6% females. Nonetheless, prior research indicates that male patients exhibit a higher propensity for postoperative delirium (POD), but this disparity was not statistically significant [13], [14]. Conversely, research by Fisher & Flowerdew and Williams-Russo et al. identified male gender as the predominant risk factor for suffering POD [15], [16].

The median age of participants in both groups, those with and without POD, was 46 years. The results indicated that age was not correlated with the occurrence of POD; nevertheless, numerous another research have demonstrated otherwise. A study by Wang et al. indicates that age correlates with the incidence of postoperative delirium (POD); patients over seventy years exhibit a fourfold increased risk compared to those under seventy years [17]. In geriatric patients, acetylcholine and cholinergic receptors are diminished due to progressive white matter degradation in the brain. In geriatrics, there is a diminished tolerance to anesthetic [18] and surgical procedures, together with a decline in physiological regulation, resulting in neuronal dysfunction during these interventions [17].

NSE

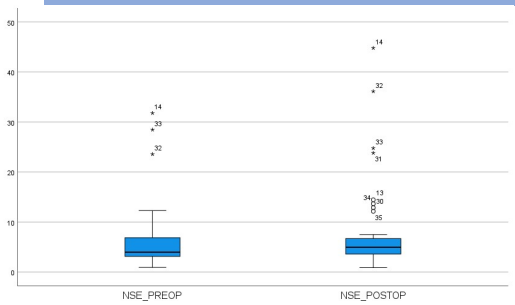

Figure 1: NSE level pre and postoperation

A study by Wang et al. [17] identified a correlation between the duration of surgery and the incidence of postoperative delirium (POD). Patients who had surgery lasting over 3 hours had a sixfold increased risk compared to those whose operation lasted less than 3 hours. Stress escalates during prolonged surgical procedures. Prolonged surgical procedures induce elevated stress levels. In this study, the duration of surgery did not influence postoperative delirium (POD) [17]. The mean BMI in this study was 23.67 kg/m². Research conducted by Wang et al. and Arshi et al. similarly indicated that BMI was not correlated with the occurrence of POD [13], [17]. A study by Chu et al. indicated that BMI correlated with the occurrence of POD. Patients exhibiting inadequate nutritional condition manifested more severe delirium symptoms and required a greater number of blood transfusions during surgical procedures [19]. Juliebø et al. discovered that patients with a BMI below 20 kg/m² exhibited thrice higher levels of POD compared to those with a higher BMI [20].

DISCUSSION

In patients undergoing post-traumatic spinal surgery under general anesthesia, postoperative serum neuron-specific enolase (NSE) levels rose to 4.97 (0.88-44.78) compared to 3.97 (0.92-31.78). Nonetheless, there was no substantial variation in NSE levels before and after surgery. In this investigation, NSE levels were consistently below 12.5, indicating a normal value [21].

Serum NSE is a glycolytic enzyme present in neurons and neuroendocrine cells. This study concentrated on long-term NSE levels, specifically serum NSE post-discharge [22]. The study identified a strong association between increased NSE levels during the perioperative period and immediately post-CPB, and diminished cognitive performance on various cognitive assessments, including the Mini-Mental State Examination (MMSE), over an extra six months.

A comparable study revealed no significant disparity between pre- and postoperative serum NSE levels in German geriatrics having heart surgery [23]. Additional research has indicated that serum NSE levels remain unchanged both preoperatively and postoperatively [24], [25], [26]. Patients exhibiting delirium do not demonstrate elevated serum NSE levels. Post-hospital discharge following heart surgery, NSE has been correlated with the degree of cognitive impairment [25], [27], [28].

The reason for the absence of an increase in serum NSE in this trial remains ambiguous. The biological half-life of blood NSE is roughly 48 hours, and measurements done 24 hours post-surgery indicated no variation in serum NSE levels. Nonetheless, investigations that assessed serum NSE at discharge revealed no significant difference [24], [26], [29]. Consequently, serum NSE may have reached a high at a certain moment before reverting to normal levels.

An elevated concentration of blood NSE levels is a definitive indicator of cerebral impairment and neural injury [30], [31]. The data imply that persistently elevated NSE levels at discharge signify more cognitive impairment [23]. Research indicates that substantial brain trauma, including stroke, post-resuscitation, or intricate neurosurgery, can elevate NSE levels [27]. This study excluded individuals with a history of stroke, hypoxia, hypotension, or those who had undergone or were scheduled for brain surgery.

Elevated NSE levels indicate neuronal inflammation and damage, as per the blood-inflammatory process [28], [32], [33].

NSE expression in neurons may result from central nervous system (CNS) inflammation, leading to compromised blood-brain barrier (BBB) integrity and neurotoxicity. Consequently, neurons sustain structural damage and can leak NSE into the bloodstream [34]. In addition to neuronal injury, NSE is produced during neuroinflammation. Furthermore, serum NSE more distinctly reflects BBB integrity [12].

A separate investigation identified an elevation in serum NSE 48 hours post-surgery. The elevation in serum NSE 48 hours post COX-2 inhibitor delivery was not statistically significant. [35] COX-2 inhibitors may provide anti-inflammatory effects via COX-2-independent mechanisms. Celecoxib inhibits inflammation, particularly the infiltration of inflammatory cells into the central nervous system, as a result of COX-2 deficiency [36]. This substantiates neuroinflammation and the mechanism of serum NSE.

This study revealed a difference in NSE levels before and after surgery with POD in patients undergoing spinal surgery under general anesthesia; however, the difference was not statistically significant. This was also observed in prior research. The limited number of studies investigating this matter renders the association between NSE and POD unclear. A 2018 study indicated that there were no variations in blood NSE levels between POD and non-POD patients [37]. Moreover, serum NSE levels were not significantly different between individuals with POD and those after non-cardiac surgery. Furthermore, no correlation was observed between serum NSE and postoperative cognitive deterioration [24], [26], [29]. These investigations indicate that NSE is released solely in instances of significant brain injury, such as stroke, or following recuperation or surgical interventions associated with nervous system problems [38].

The mechanism underlying the neuroinflammatory system is referred to as the pathophysiology of POD [39]. Perioperative hypoxia, microembolism, or hypotension may induce transitory neuronal injury in the brain, resulting in postoperative delirium [40], [41]. Serum NSE levels are closely associated with POD, indicative of axonal injury in the central nervous system. The diagnostic threshold value of NSE for POD is 201.2 ng/mL, indicating that NSE can also signify the beginning and severity of POD. Furthermore, a link exists between the occurrence of POD and nerve injury resulting from inflammation [12].

Research indicates that localized anesthetic may mitigate cognitive and immunological dysfunctions in elderly individuals with hip fractures, as evidenced by NSE [42]. The impact of anesthetic on NSE remains uncertain. Consequently, the selection of anesthetic for older patients undergoing elective surgery significantly influences inflammatory responses, NSE levels, and the occurrence of delirium.

One of the control variables influencing serum NSE in this investigation is the administration of general anesthesia. This study shown that preoperative administration of ketamine safeguards neurons and astrocytes, resulting in a notable reduction in serum NSE both prior to and during surgery with ketamine [43]. The protective action of ketamine against glial cells, namely N-Methyl-D-Aspartate (NMDA) antagonists, may induce this effect [44], [45], [46].

Serum NSE levels were elevated in ICU patients with delirium, according to a 2011 study [47]. Furthermore, a correlation was observed between POD and patients undergoing liver transplantation [48]. Serum NSE was significantly elevated in another trial conducted on the first to third postoperative day in individuals with malignant tumors. The findings indicated that serum NSE levels in delirious patients upon ICU admission were markedly elevated, persisting for over four days [47]. Postoperative NSE levels were elevated in patients with POD on the third day and were substantially correlated with POD, irrespective of age, as per serum NSE analysis [12]. The biological half-life of serum NSE is approximately 48 hours [12]. Consequently, NSE may necessitate a reduced timeframe to assess the occurrence and intensity of delirium.

This research possesses limitations. This study exclusively monitored patients on the initial day following their surgical procedures. The measurement of NSE in blood and cerebral fluid may yield disparate readings. In certain trials, there was no significant association between NSE levels in blood and cerebrospinal fluid [49]. Measuring NSE in cerebrospinal fluid in patients poses challenges due to ethical considerations. This study possesses numerous advantages. This study encompassed non-geriatric patients, CAM assessments, administration of general anesthesia, and elective surgeries at

Dr. Soetomo Hospital Surabaya. This study's findings have enhanced understanding of NSE's role in the incidence of POD.

CONCLUSION

No significant correlation was observed between NSE fluctuations and the occurrence of POD in individuals undergoing post-traumatic spinal surgery with general anesthesia. The threshold values for elevated post-operative NSE levels associated with the occurrence of post-operative delirium in patients having post-traumatic spinal surgery under general anesthesia have not been established.

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