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Relationship between hypertension on admission, cerebral edema, and post-traumatic headache in mild traumatic brain injury

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ABSTRACT

Introduction: Traumatic brain injury (TBI) is a common disorder in neurosurgery. TBI is classified based on the level of consciousness of the patient using the Glasgow Coma Scale. Hypertension at initial assessment can be harmful or beneficial to the patient due to the immediate compensatory mechanism for TBI. Abnormality of the brain should be measured using a non-contrast computed tomography (CT) scan of the head. TBI is often accompanied by cerebral edema and intracranial hemorrhage. Cerebral edema and intracranial hemorrhage may increase the volume of the brain resulting in decreased perfusion of blood to the brain. Furthermore, it can generate signs, symptoms, and complications of TBI. Post-traumatic headache (PTH) is a common secondary headache developed after TBI.

Methods: This research was an analytic descriptive study using a cross-sectional design from secondary data using patient medical records. The subject of the study was patients admitted to the hospital from 2019 to 2022 with mild TBI as the diagnosis. The blood pressure value was taken from the triage data. Blood pressure with systolic pressure of more than 139 mmHg or/and diastolic pressure of more than 89 were defined as hypertension. Cerebral edema and intracranial hemorrhage were observed from head CT scan imaging. Statistical analysis was conducted to observe the relationship between hypertension on admission, cerebral edema, and intracranial hemorrhage with PTH incidence in mild TBI patients.

Results: A total of 76 mild TBI patients, consisting of 46 males and 30 females were included. Most subjects were 30 – 59 years old (47.4%). The most common cause of TBI was traffic accidents consisting of 46 subjects. Twenty-three subjects met the criteria for hypertension and 53 subjects did not meet the criteria. Cerebral edema was found in 25 subjects (32.9%), while intracranial hemorrhage was found in 8 subjects (10.5%). Incidence of PTH reached 38.2% (29 subjects). Statistical analyses showed an association between cerebral edema ($p = 0.025$) and intracranial hemorrhage ($p = 0.0002$) with the occurrence of PTH. However, hypertension ($p = 0.69$) was not related to the occurrence of PTH.

Conclusion: Cerebral edema and intracranial hemorrhage have a significant relationship with the incidence of PTH in mild TBI. While the relationship between hypertension on admission and PTH is not significant statistically.

Keywords: cerebral edema, hypertension, intracranial hemorrhage, post-traumatic headache, traumatic brain injury.
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INTRODUCTION

Traumatic Brain Injury (TBI) is a disease that is clinically grouped by level of severity based on awareness, namely: mild, moderate, and severe. Mild TBI is identical to a concussion and is usually caused by non-penetrating blunt head trauma.[1] Symptoms of TBI also have a central neurological function. A patient with mild TBI may still be alert or have a decrease of consciousness for minutes to hours. Other symptoms are headache, confusion, fatigue, tinnitus, blurred vision, behavioral change, sleep problems, and memory disorder. Moderate to severe TBI patients may have the same symptoms but are more severe and longer in duration. The symptoms are nausea and vomiting, seizure, inability to wake up, imbalance in pupil diameter, weakness or numbness of extremities, loss of balance, increased confusion, and agitation.[2] Treatment modalities vary widely based on the severity of the injury and range from daily cognitive therapy sessions to radical surgery such as bilateral decompressive craniectomy.[3]

Cerebral edema is a common phenomenon with various causes including head trauma, vascular ischemia, lesions in the intracranial, and obstructive hydrocephalus. Cerebral edema can impact from mild to fatal to a patient if untreated.[4] Cerebral edema causes the brain volume to increase due to brain tissue swelling which can decrease perfusion of blood to the brain. Signs and symptoms of cerebral edema are variable, ranging from asymptomatic to severe autonomic dysregulation, coma, and death. Usually, symptoms appear as the increased intracranial pressure (ICP) above 20 cmH_2O.[5] Treatment goals of cerebral edema are managing the underlying condition and life-threatening complications.

Blood pressure is an essential vital sign in any traumatic case. Hypotension is an

early sign of poor patient outcome because it indicates instability of the patient's hemodynamics and hemorrhage is the most common cause in trauma cases.[6] While hypertension following TBI patients may also be harmful. Recent evidence suggests that the mechanism involved in high systemic blood pressure after TBI is the catecholamine excess state. Traumatic injury to the brain often increases ICP through local mass effect and cerebral edema results in a complex interaction with the neuroendocrine response by activating the autonomic system, with further release of catecholamines. High levels of systemic catecholamine affect the rise of arterial blood pressure.[7]

Headache is the most common complication following TBI, and its prevalence is ranging from 30% to 90%. The wide range of prevalence may be because the majority of TBI cases are defined as mild TBI (concussions) in which patients may not seek immediate medical attention. Most post-traumatic headaches (PTH) affect patients recovering from mild TBI than moderate to severe TBI patients[8]. PTH is defined as a secondary headache with onset within seven days following trauma or injury, within seven days after recovering consciousness, or within seven days after recovering the ability to sense and report pain.[9] This paper discusses the relationship between hypertension on admission, cerebral edema, and post-traumatic headache in mild traumatic brain injury patients.

METHODS

This research was an analytic descriptive study using a cross-sectional design from secondary data using patient medical records. The subject of the study was TBI patients admitted to the hospital from 2019 to 2022 in Yogyakarta Islamic Hospital PDHI. Data collection using research instruments was done from medical records and head CT scan expertise by radiologists. Inclusion criteria for subjects were ages ranging from 15 – 70, mild TBI, available head CT scan, and treated completely in the hospital followed by follow-up in the outpatient clinic. Exclusion criteria were history of head surgery, history of hypertension, history of stroke, history of other persistent headache syndrome, multiple trauma cases, and presence of shock.

Data collected for this study were baseline characteristics including demographics, history of past illness, symptoms, Glasgow coma scale, blood pressure, presence of cerebral edema from head CT scan imaging, and presence of PTH obtained from follow-up in the outpatient clinic. The blood pressure value was taken from the triage data. Blood pressure with systolic pressure of more than 139 mmHg or/and diastolic pressure of more than 89 were defined as hypertension. Cerebral edema and intracranial hemorrhagic were observed from radiologist expertise of head CT scan imaging. PTH was assessed by patient complaints at the outpatient clinic following the previous hospitalization in the hospital. The patient was categorized as PTH if the patient complained of headache within seven days duration after the initial traumatic brain injury.

Statistical analysis was done to find out the relationship between hypertension on admission and PTH, also between cerebral edema and PTH. Analysis was carried out using Chi-square and Fisher exact test. SPSS 25 was used to perform analysis in this research. Ethics approval was obtained from the Ethics Committee of Ahmad Dahlan University with letter number 022302022, dated February 13th 2022. This research also had permission from the education and training division of the hospital.

RESULTS

A total of 76 mild TBI patients, 46 men and 30 women participated in this study. Based on age (mean 40.71), subjects were divided into three groups which were age 15 – 29, age 30 – 59, and age more than 60. The percentage of subjects was 34.2%, 47.4%, and 18.4%, respectively. Most subjects were admitted to the hospital with a GCS score of 15 reaching 67 subjects (88.2%). Length of stay (LOS) was 56.6% for less than 3 days, 32.9% for between 3 and 4 days, and 10.5% for more than 4 days. Of all the subjects, the most common cause of traumatic brain injury was traffic accidents reaching 46 subjects. All demographic and clinical characteristics are shown in Table 1.

Most subjects presented with headache symptoms, which reached 98.7%. Amnesia, nausea, and syncope occurred almost in one-third of total subjects accounting for 32.5%, 31.2%, and 28.6%, respectively. Blurred vision and seizure were rare symptoms that both presented in one subject. The blood pressure was collected from triage documents when the initial assessment was performed in the emergency room. Blood pressure was measured by the emergency department nurse using digital sphygmomanometer. There were 21 subjects with systolic

Table 1. Demographic and clinical characteristics of study group (N=76)

Characteristic	Subjects	(%)
Gender		
Male	46	60.5
Female	30	39.5
Age (Mean: 40.71)		
15 – 29	26	34.2
30 – 59	36	47.4
60 – 69	14	18.4
GCS		
<15	9	11.8
15	67	88.2
Length of stay		
< 3 days	43	56.6
3 – 4 days	25	32.9
> 5 days	8	10.5
Traffic accident		
Yes	46	60.5
No	30	39.5

Table 2. Blood pressure, cerebral edema, intracranial hemorrhage, and post-traumatic headache (N=76)

Characteristic	n	(%)
Sign and symptom		
Headache	75	98.7
Dizziness	19	24.7
Nausea	25	32.5
Vomiting	16	21.1
Amnesia	24	31.2
Head swelling	15	19.5
Syncope	22	28.6
Blurred vision	1	1.3
Head laceration wound	18	23.4
Seizure	1	1.3
Blood pressure (mmHg)		
Systolic Blood Pressure (Mean: 126.32 ± 23.27)		
< 100	4	5.3
100 – 139	51	67.1
³ 140	21	27.6
Diastolic Blood Pressure (Mean: 78.64 ± 14.30)		
< 60	1	1.3
60 – 89	57	75.0
³ 90	18	23.7
Hypertension		
Yes	23	30.3
No	53	69.7
Presence of cerebral edema		
Yes	25	32.9
No	51	67.1
Presence of intracranial hemorrhage		
Yes	8	10.5
No	68	89.5
Post traumatic headache (PTH)		
Present	29	38.2
Absent	47	61.8

Table 3. Statistical analysis of variable

Variable	Post traumatic headache		
	Present	Absent	P-value
Hypertension on admission			
Yes	8	15	0.690[a]
No	21	32	
Cerebral edema			
Yes	14	11	0.025[a]
No	15	36	
Intracranial hemorrhage			
Yes	8	0	0.0002[b]
No	21	47	
Total	21	47	

a: Chi-square test; b: Fisher exact test

blood pressure (SBP) of more than 140 mmHg, 51 subjects with SBP ranging from 100 to 139 mmHg, and only four subjects with SBP less than 100 mmHg. From diastolic blood pressure (DBP) measurement, one subject had less than 60 mmHg, 57 subjects were ranging from 60 to 89 mmHg and 18 subjects were more than 90 mmHg. From all blood pressure measurements, 23 subjects met the criteria for hypertension and 53 subjects did not meet the criteria. Cerebral edema data was collected from radiologist expertise of the head CT scan or diagnosis from a neurologist or neurosurgeon. The presence of cerebral edema was found in 25 subjects (32.9%), while 51 subjects (67.1%) did not have cerebral edema. Intracranial hemorrhage occurred in eight subjects (10.5%). Subarachnoid hemorrhage was the most common intracranial lesion found accounting for 75%. Incidence of PTH reached 38.2% (29 subjects), and other subjects did not have any complaints seven days after discharge. Table 2 gives information on blood pressure, cerebral edema, and PTH.

The analysis of the relationship between hypertension on admission and PTH showed that early hypertension is not related significantly to PTH (p = 0.690). On the other hand, statistical analysis showed a significant relationship between the presence of cerebral edema and the incidence of headache after mild traumatic brain injury (p = 0.007). Both analyses were performed using the Chi-square method. The relationship between intracranial hemorrhage and PTH incidence was performed using the Fisher exact test and showed a significant relationship statistically (Table 3).

DISCUSSION

Traumatic brain injury is still a major cause of death and disability among youth in developing countries. Based on age, adolescents between ages 15 – 19 and adults more than 65 years old are the most likely to sustain a TBI.[10] In this research, we found that mostly were in the 30 – 59 age group. This study showed that more men suffered from TBI than women. Epidemiological data also suggest that men are 40% more likely to suffer a TBI compared with women in the general adult population. However, the difference is not significant for patients aged more than 75 years old.[11] This suggests that young male adults tend to have more risk of suffering TBI due to work or having outdoor activities.

Traumatic brain injury is classified based on the level of consciousness which is measured using the Glasgow coma scale (GCS). There are three group

classifications, which are mild (GCS 13 – 15), moderate (GCS 9 – 12) and severe (3 – 8). Epidemiologically, mild TBI is the most common type of TBI with incidence estimated at 200 – 300/100,000 persons per year for hospitalized patients and probably twice as high if non-hospitalized patients are included.[12] In this research, mild TBI with GCS 15 was 89.7%. This finding is consistent with research conducted by Chojak *et al*[13] which stated that most mild TBI patients were admitted with a GCS score equal to 15 (64%). Regarding the length of stay, most were discharged from the hospital in less than three days. However, this is irrelevant to the previous study that showed most mild TBI had a length of stay of more than seven days.[13] Our study showed that the most common cause of mild TBI was traffic accidents accounting for 61.8%. This data is in accordance with another study which described that 82% of TBI was caused by traffic accidents.[14]

Hypertension is a common condition in TBI. Previous research has shown that the prevalence of hypertension in mild TBI is 38.8%.[15] In experimental animals, it has been shown that pre-existing hypertension increases mortality post-TBI. Although the blood pressure cut-off for hypertension used was similar (SBP ³ 140 mmHg or DBP ³ 90), our study showed a slightly higher prevalence accounting for 27.9%. Hypertension after TBI may indicate cerebral pressure autoregulation (CPA) to optimize cerebral blood flow (CBF) and cerebral perfusion pressure (CPP).[16] This condition can change both blood pressure and cerebral metabolic requirements. The important mechanism is the regulation of cerebrovascular resistance through vasoconstriction and dilatation which are adjusted using various mediators. Cerebral pressure reactivity is one of the important systems in cerebral autoregulation and enables the response of vascular smooth muscle to changes in blood pressure. In normal conditions, compensatory vasoconstriction which causes hypertension will lead to an increase in cerebrovascular resistance to maintain normal CBF.[17] The catecholamine excess is suggested as the mechanism of increased blood pressure in TBI. Local mass effect and cerebral edema often occur in TBI which increase ICP as a result of complex interaction with the neuroendocrine response by activating the autonomic system with further release of catecholamines. Increased catecholamine level results in increased arterial blood pressure.[7] Hypertension induced by catecholamine may have an impact on secondary brain injury due to increased intracapillary hydrostatic pressure which leads to vasogenic cerebral edema and intracranial hypertension.[18]

This study showed that there is no association between hypertension on admission and incidence of PTH. Previous research conducted by Izzy *et al* provided information that mild TBI has a high risk of developing hypertension (HR = 5.9; 95%CI = 3.9 – 9.1).[19] On the other hand, the risk of PTH in mild TBI is higher than the moderate and severe TBI. Although the pathophysiology of PTH is still unclear, however, there are several theories describing the underlying cause of PTH, including impaired descending modulation, neurometabolic changes, and trigeminal sensory system activation.[20]

Cerebral edema is one of the abnormal brain conditions which is often found in TBI. Previous studies have shown that the incidence of cerebral edema in TBI was 1.8%. On the contrary, present research showed a higher incidence of cerebral edema among TBI as much as 33.8%. This difference may be caused by the considerable inequality of the total subjects of both studies. Cerebral edema causes mass effects which can lead to herniation, increased intracranial pressure (ICP), decreased cerebral perfusion pressure (CPP), and decreased cerebral oxygenation.[21] Fluid accumulation in the brain may arise due to dysfunction of the cell membrane (cytotoxic edema), blood-brain barrier (BBB) disruption (vasogenic edema), outflow of cerebrospinal fluid (CSF) from intraventricular space to the interstitial space (interstitial edema), and due to water being pulled from the plasma by the brain cells due to osmotic derangements (osmotic edema). In TBI, the initial mechanism is vasogenic edema which is followed by cytotoxic.[4]

Vascular, neuronal, and axonal injury may occur as the result of mechanical and shearing forces in TBI. Immediate disruption of the BBB during and after primary traumatic impact causes contusion edema of the brain that develops surrounding the damaged necrotic area. Substance P, calcitonin G-related peptide, matrix metalloproteinase (MMPs), and vascular endothelial growth factor (VEGF) are important substances in producing vasogenic edema by promoting vascular permeability. The transitory elevated BBB permeability is held up to four to six hours post-injury. Late vasogenic edema can develop in five days when BBB permeability reaches the second peak which is potentially due to microglia activation by inflammatory cascades.[4] Cytotoxic edema in TBI occurs due to neuronal ischemia and metabolic disturbances from one hour to seven days after the injury. The fluid and proteins extravasated into brain interstitial fluid. Increased ICP leads to occlusion of small vessels which perpetuates further ischemic damage.[22] The cytotoxic edema is worsened by hypoxia and hypotension. Furthermore, the presence of vasogenic edema exacerbates the cytotoxic edema.[4]

In this study, cerebral edema has a significant relationship with the incidence of PTH ($p = 0.007$). We have not found any similar previous study that analyzes the relationship between cerebral edema and PTH. A study by Schwedt *et al* showed the presence of structural differences in cortical thickness and cerebral volumes in PTH compared to healthy controls. However, there was doubt in the research due to the obscurity of cerebral volume explanation, whether swelling or shrinking.[20] Although the etiology of PTH remains unclear, cerebral edema can last longer than we expected due to aggravated by both vasogenic or cytotoxic mechanisms that cause PTH. This finding suggests treating cerebral edema in mild TBI accurately to prevent PTH from occurring.

The prognosis of cerebral edema is highly variable and depends on the involvement of the brain, the severity, and the etiology of the edema. If the patient is comatose upon discovery, the prognosis may be poor. If the edema is widespread and severe enough to cause significantly elevated intracranial pressure without initiation of treatment, the patient may die or develop

persistent and irreversible brain injury. An example is seen in prolonged cardiac arrest causing diffuse anoxic brain injury. The basis for prognosis in milder forms is usually the diagnosis and underlying cause (for example, tumor, stroke, traumatic brain injury, infection, and others) and early recognition and treatment. Cerebral edema as a consequence of reversible diagnoses, such as diabetic ketoacidosis, uncontrolled hypertension, or mild head trauma can be reasonably good.[24]

Another important abnormality in mild TBI is intracranial hemorrhagic. Hemorrhage in the brain has some features depending on the location of the bleeding source, including epidural hematoma (EDH), subdural hematoma (SDH), intracerebral hematoma (ICH), intraventricular hemorrhage (IVH), cerebral contusion and subarachnoid hemorrhage (SAH).[25] Intracranial hemorrhage in TBI can have a greater impact force on the brain. It also can cause loss of consciousness, post-traumatic seizure, and PTH. A previous study in Bandung conducted by Halimi *et al* stated that PTH incidence was higher in TBI with SDH and ICH (100%), followed by EDH (70.6%) and depressed skull fracture (33.3%).[26] Hemorrhage under the durameter has the highest incidence of PTH in TBI.

The present study showed a significant relationship between intracranial hemorrhage and incidence of PTH. The previous study conducted by Halimi *et al* in 2015, showed different result in which traumatic intracranial hemorrhage and PTH is not related.[26] Hong *et al* researched the association of PTH with minimal traumatic intracranial hemorrhage and showed significant results.[27] The mechanism of PTH after TBI with intracranial hemorrhage is not clearly understood. Due to a lack of disease pathophysiology understanding, the treatment choice for PTH is still unclear. PTH may last up to three to 12 months after trauma. The quality of life is usually interrupted by PTH so they tend to be neglected because the clinical focus is to achieve a good outcome (to minimize morbidity and mortality).[27]

This present study had some limitations. The sample size is not as large as expected. Also, PTH measurement was only carried out by collecting patient complaints when patients were admitted to the outpatient clinic after hospital discharge due to mild TBI. Pain level, duration, and characteristics were not compared among groups.

CONCLUSION

Cerebral edema and intracranial hemorrhage have a significant association with the incidence of PTH in mild TBI. While the association between hypertension on admission and PTH is not significant statistically.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest in this research.

AUTHOR CONTRIBUTION

Both authors contributed to concept, design, literature research, and discussion making. The first author executes data collection and analysis, statistical analysis, and manuscript writing.

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