Open Access Indonesian Journal of Medical Reviews

Journal Homepage: https://hmpublisher.com/index.php/OAIJMR

Pathophysiological to Clinical Aspects of Head Injury: Narrative Literature Review

Rachmat Hidayat[1*]

[1]Department of Biology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

ARTICLE INFO

Keywords:
Head injury
Pathophysiology
Clinical

***Corresponding author:**
Rachmat Hidayat

E-mail address:
dr.rachmat.hidayat@gmail.com

The author has reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/OAIJMR.v2i2.174

A B S T R A C T

Head injury is a change in brain function or brain pathology, caused by external forces on the head. Changes in brain function consist of any period of loss or loss of consciousness, anterograde or retrograde amnesia, neurological deficits, or mental changes following a head injury. A study reported that the highest incidence of head injury was in the Americas, which was 1299 cases per 100,000 population, followed by Europe, which was 1012 cases per 100,000 population. The lowest incidence of head injury occurred on the African continent, which was 801 cases per 100,000 population. Based on these data, the overall incidence of head injuries in the world is 939 cases per 100,000 population with most of them being mild head injuries (55.9 million cases per year) and 5.28 million people experiencing severe head injuries.

1. Introduction

Head injury is a change in brain function or brain pathology, caused by external forces on the head. Changes in brain function consist of any period of loss or loss of consciousness, anterograde or retrograde amnesia, neurological deficits, or mental changes following a head injury.[1,2] A study reported the highest incidence of head injuries was in the Americas, namely 1299 cases per 100,000 population, followed by Europe, which was 1012 cases per 100,000 population. The lowest incidence of head injury occurred on the African continent, which was 801 cases per 100,000 population. Based on these data, the overall incidence of head injuries in the world is 939 cases per 100,000 population with most of them being mild head injuries (55.9 million cases per year) and 5.28 million people experiencing severe head injuries. At the regional level, the highest incidence of head injury in the world is in Southeast Asia, which is 18.3 million cases.[3-5] In Indonesia, there have been several reports of head injuries, during June-December 2018 there were 118 cases of head injuries were recorded at H. Adam Malik Hospital, North Sumatra with patient ages ranging from 18 years to 35 years and dominated by the male gender. man. In this study, most cases were epidural bleeding. Based on medical record data at Dr. M. Djamil General Hospital Padang there were 356 head injury cases in 2017 and 505 cases in 2018.[5]

Classification of head injury

Classification of head injuries was made based on clinical severity and was assessed using the Glasgow Coma Scale (GCS). The Glasgow coma scale consists of 3 components that allow a rapid assessment of the severity of the head injury: eye, verbal, and motor. Scores of 14-15, 9-13, and 3-8 were classified as mild head injury, moderate head injury, and severe head injury, respectively. Table 1 displays the scores on the GCS.[6,7]

Table 1 Glasgow coma scale

Response	Score					
	1	2	3	4	5	6
Eyes	Does not open eyes	Opening the eyes with pain stimulation	Opens eyes with sound	Opens eyes spontaneously	-	-
Verbals	Does not make sound	Unclear voice	Inappropriate words	Confused, disorientated	Good orientation, normal	-
Motor	No movement	Extension due to painful stimulation	Abnormal flexion to painful stimulation	Flexion/ avoids pain stimulation	Localizing pain stimulation	Following orders

Other classifications of head injuries are classified according to morphology: a) Fracture of the skull: cranium (depressive and non-depressive fractures) and the cranial base, b) Intracranial lesions: focal (epidural, subdural, and intracerebral/contusion), diffuse (concussion, ischemic injury, diffuse axon injury).[8]

The main causes of head injuries are traffic accidents, falls, and assaults. Based on the mechanism, head trauma is classified as blunt (a most common mechanism), penetrating (most fatal) and explosive. The most serious injuries result from motor vehicle collisions and falls.[9,10]

Pathophysiology of head injuries

Head injuries can be classified into primary and secondary injuries. Primary injuries include injuries due to shifting of the brain due to direct impact, rapid acceleration-deceleration, or penetration. These injuries can lead to contusions, hematomas, or axonal injuries. The secondary injury occurs after primary injury in the form of the release of biochemical compounds such as glutamate which causes further damage to mitochondria and cell death and necrosis. A secondary head injury causes systemic hypotension, hypoxia, and increased intracranial pressure leading to brain herniation.[11-13]

The initial phase

The initial phase occurs immediately after trauma due to impaired blood flow and ischemic conditions leading to conditions of decreased adenosine triphosphate, oxygenation, glucose consumption and distribution, depolarization of calcium ion channels, increased lactate, and neuronal cell death. After neuronal cell death, glutamate exits the damaged presynaptic vesicles causing excitotoxicity. Glutamate binds to N-methyl-D-aspartate receptors, increases Ca2þ and Naþ in cells, and activates enzymes responsible for tissue damage. Excessive accumulation of calcium in neurons also stimulates *nitric oxide* and causes oxidative stress. This exacerbates cell death. [14] Necrotic areas of nerve cells and glial cells are concentrated in areas where the blood supply is impaired, which can occur due to epidural hemorrhage, subdural hemorrhage, and

intracerebral hemorrhage. Secondary contusions can occur in opposing brain tissues because of the coup and counter-coup.[13] Cognitive deficits, behavioral changes, and hemiparesis depend on the severity of the injury. In contrast to focal injury, the main mechanism of diffuse brain injury is rapid acceleration and deceleration forces that cause shear and strain injuries to cerebral brain tissue. This results in injury to axons, oligodendrocytes, and blood vessels, which leads to cerebral edema and ischemic brain damage. The degree of axonal injury and neuronal degeneration determines the severity of the head injury.[13]

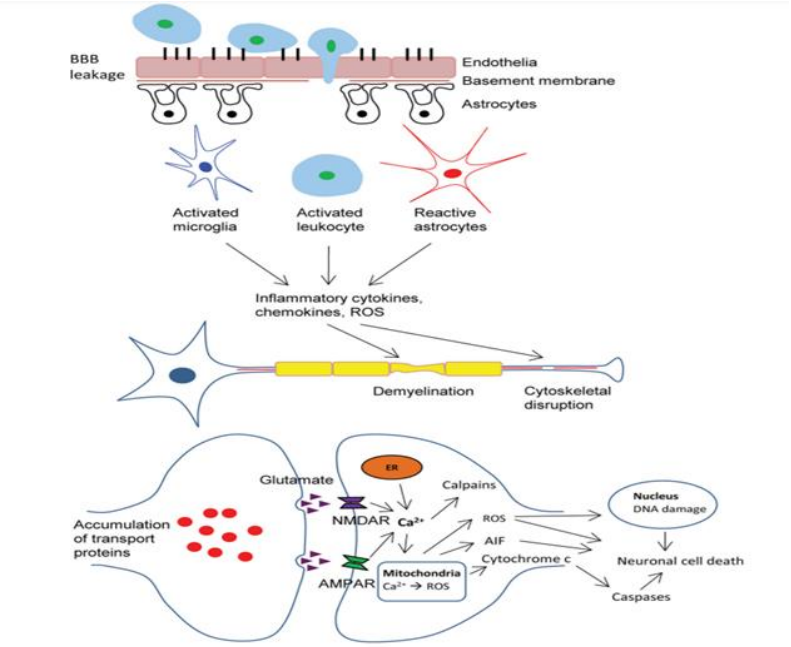

Figure 1. Schematic of the pathophysiology of head injury.

Intermediate phase

Abnormal function caused by mechanical damage and neurotrauma results in an inflammatory process. This inflammation can increase brain injury and activate microglia, which further prolongs neuroinflammation. An increase in proinflammatory cytokines and chemokines occurs approximately 1 hour after nerve injury. One of the inflammatory cytokines, IL-1b, acts on astrocytes, activates the intracellular ERK pathway, and releases matrix metalloproteinase-9. Matrix metalloproteinases will erode the extracellular matrix, impair the integrity and function of the BBB, and induce chronic neuroinflammation.[14] The brain is normally protected from immune cells and pathogens due to the presence of the *Blood-Brain Barrier* (BBB). However, damage to the BBB following head injury results in leakage of prostaglandins, nitric oxide, cytokines, and inflammatory mediators into brain tissue. After the primary injury, the inflammatory response is activated by the invasion of monocytes, neutrophils, and lymphocytes across the BBB.[15]

Final phase

The inflammatory process is to remove pathogens from the site of injury, regenerate damaged cells and improve nerve cell function. However, the recovery process leaves some sequelae such as seizures and epilepsy. The reduced expression of Kv.4.2 increases the excitability of the nerves thought to mediate seizures. In addition, injury-induced epilepsy is caused by activation of the trkBERK1/2-CREB/Elk-1 pathway and GAP-43 expression.[14]

Diagnosis of head injury

Anamnesis

Anamnesis is asked the mechanism of injury, symptoms and findings of physical examination

associated with head injury.[16] The mechanism of injury was associated with immediate intervention which included observation, admission to hospital or ICU, and/or neurosurgical intervention. The mechanisms of injury that most often result in severe head injuries include pedestrians being hit by vehicles, passengers being thrown from motorized vehicles, and people falling from a height of more than 1 meter. Motorcycle collisions, not wearing a helmet, and chronic alcoholism are associated with an increased risk of severe intracranial injury even with mild initial symptoms.[16,17] The presence of vomiting, especially more than two episodes, has a higher probability of developing a severe head injury. Posttraumatic seizures are also associated with a higher degree of severity.[16,17]

Physical examination

In patients with mild and moderate head injuries, physical examination findings can help predict serious injury. Focal neurologic deficits are associated with a severe head injury. Signs of skull fracture (open, depressed, or base) such as hemotympanum, otorrhea, peri-orbital ecchymosis, or skull base fracture identified by postauricular ecchymosis (*Battle sign*) are also associated with a severe head injury. A severe injury in an unconscious drunk patient may be associated with alcohol intoxication. In mild head injury, initial GCS 13, GCS worsening, and GCS <14 2 hours post-injury were all associated with more severe intracranial injury.[16]

Imaging

Radiological examination plays an important role in identifying patients with head injuries. Common imaging techniques include a CT scan of the head and an MRI. Imaging will help differentiate patients who require immediate neurosurgical intervention or who may be discharged from patients under observation. When there is a clinical indication for imaging, a non-contrast head CT scan is the first choice. MRI is superior in identifying small, focal traumatic lesions.[17] Non-contrast head CT scan is recommended as the imaging choice and can identify subdural hemorrhage, epidural hemorrhage, subarachnoid hemorrhage, intracerebral hemorrhage, cerebral contusion, skull fracture, pneumocephalus, and cerebral edema. Indications for CT scanning are divided into two criteria, namely moderate risk of intracranial injury and high risk of intracranial injury.[16]

Table 2. Indications for CT scan in head injury

Moderate risk	High risk
• Loss of consciousness after injury • Drug intoxication • Post-traumatic seizures • The mechanism of trauma is unclear • Age less than 2 years • Vomiting • Amnesia after head injury • Multiple trauma • Signs of base fracture • Severe facial injury • Suspicion of depression or fractured skull • With GCS ≤14	• Unclear decrease in consciousness • Focal neurologic deficit • Depressive fracture • Translucent skull injury

Management of head injury

Prehospital management

Care for head-injured patients should begin at the site of injury to maintain the airway and maintain adequate circulation and ventilation. Patients with moderate to severe head injuries should be immediately sent to a medical center with a neurosurgical facility. The initial goal of management was the prevention of hypoxia and hypotension because both of these doubled mortalities.[18]

- Airway management/oxygenation
  - Prevention, identification, and therapy of hypoxia (O_2 saturation < 90% and/or cyanosis).
  - Airway maneuver.
  - Ventilation with NRM.
  - Endotracheal intubation is indicated.
- Ventilation Management
  - Intubated and mechanically ventilated patient: if available, target $PaCO_2$ of 40 mmHg.
  - Prophylactic hyperventilation in the prevention of ICP is not recommended.
- Management of blood pressure
  - Hypotension: at systolic blood pressure < 90 mmHg, fluid resuscitation was performed with an initial bolus of 1 liter of normal saline or RL with a target TDS of 90 mmHg.
  - Hypertension: therapy for acute hypertension is not recommended in cases of head injury. However, IV fluids are restricted at a minimal rate if the TDS is 140 mmHg.[18]

Medical Interventions

Head elevation

Elevation in head injuries generally has a rapid effect on lowering intracranial pressure. Intracranial pressure (ICP) is reduced by displacement of cerebrospinal fluid from the intracranial compartment and promoting venous outflow. Although the mean carotid pressure is reduced during head elevation, ICP is reduced and cerebral blood flow is not affected.[14]

Hyperventilation

Hyperventilation lowers ICP by reducing the intraarterial partial pressure of carbon dioxide ($PaCO_2$) and causing vasoconstriction. However, this action ultimately causes a decrease in cerebral blood volume. Prophylactic hyperventilation is not recommended, because vasoconstriction reduces blood flow to the brain. The use of hyperventilation in the setting of severe head injury is usually only used for a short time during acute neurologic deterioration. Hyperventilate to $PaCO_2$ 25 mm Hg to lower ICP.[19-21]

Seizure prophylaxis

Current head injury guidelines state that 1 week of prophylactic antiepileptic use is acceptable to help prevent early seizures. Currently, the recommended drug is phenytoin. However, there has been no proven benefit in the long-term prevention of seizures after the head injury, so prophylaxis was discontinued after 7 days.[22-24]

Hyperosmolar therapy

Hyperosmolar therapy in head injuries can be given as a bolus or infusion. Administration of mannitol is recommended in euvolemic severe head injury patients.[22] Mannitol is used to reduce the increase in ICP. The most common preparation is a 20% solution (20 g of mannitol per 100 ml of solution). Strong indications for administering mannitol in euvolemic patients are pupillary dilation, hemiparesis, and decreased consciousness.[22]

Medications that cause coma status

The patient is brought into a coma by infusion of a benzodiazepine or barbiturate. The administration is carried out with a continuous electrocephalogram. This therapy serves to reduce the metabolic needs of the brain. This administration is only recommended in cases of severe refractory increase in ICP after medical therapy and maximal reduction in ICP.[22,23]

Therapeutic hypothermia

This therapy can reduce oxidative injury due to the effect of decreasing the metabolic demands of the brain but at risk of changes in blood sugar, platelet count, and coagulation factors. This therapy is performed on severe head injuries.[24,23]

Surgical Intervention

Surgical intervention is generally required when there is a mass effect of either an epidural

hemorrhage, subdural hemorrhage, intracerebral hemorrhage, or contusion with significant blood volume. The principal management of epidural hemorrhage is craniotomy of the traumatized area, with the evacuation of the hematoma and cauterization of the torn vessel, often the middle meningeal artery. Acute subdural hemorrhage is usually associated with more severe brain injury. [24,25]

2. Conclusion

Head injury is a change in brain function or brain pathology, caused by external forces on the head. Changes in brain function consist of any period of loss or loss of consciousness, anterograde or retrograde amnesia, neurological deficits, or mental changes following a head injury.

3. References

1. Kusuma et al. Neutrophil to lymphocyte Ratio and platelet to lymphocyte ratio as an inflammatory Biomarker in Predicting the Severity of Secondary Brain Injury: A Review Article. Macedonian Journal of Medical Science. 2020; 8(F):272-82.
2. Ristanto R, Indra R, Poeranto S, Setyorini I. The accuracy of the revised trauma score as a predictor of mortality in patients with head injuries. Jurnal Kesehatan Hesti Wira Sakti. 2016; 4(2):76-90.
3. Yuksen et al. Clinical factors predictive for intracranial hemorrhage in mild head injury. Hindawi Neurology Research International. 2017; 20: 1-5.
4. Riskesdas Team 2018. National RISKESDAS Report 2018. Jakarta; 2019.
5. Dewan MC, Rattani A, Gupta S, Baticulon RE, Hung YC, et al. Estimating the global incidence of traumatic brain injury. J Neurosurg. 2018.
6. Hazeldine J, Lord JM, Belli A. Traumatic brain injury and peripheral immune suppression: primary and prospectus. Frontiers in Jurnal Sinaps. 2018; 1(2):20-8.
7. Siahaya N, Laura B, S Huwae, Ony W. The prevalence of head injury cases based on the classification of severity in inpatients at Dr. M. Haulussy General Hospital Ambon in 2018: Mollusca Medica. 2020; 12:1-7.
8. Watanitanon A, Lyons VH, Lele AV, Krishnamoorthy V, Chandee T, et al. Clinical epidemiology of adults with moderate traumatic brain injury. Journal of critical care medicine. 2018; 46;781-7.
9. Baum J, Entezami P, Shah K, Medhkour A. Predictors of outcome in traumatic brain injury. World Neurosurg. 2016; 90:525-9.
10. Gyoneva S, Ransohoff RM. Inflammatory reaction after traumatic brain injury: Therapeutic potential of targeting cell-cell communication by chemokines. Trends Pharmacol Sci. 2015; 36(7):471–80.
11. Tangkudung G, Sampoerna JM, Khosama H. Relationship between leukocyte count and impaired executive function in mild to moderate head injury. Neurona. 2016; 33: 164-70
12. Morgan E, Bankole O, Kanu O, Ojo O, Poluyi E. Comparison of the Predictive Strength of Total White Blood Cell Count within 24 hours on Outcome of Traumatic Brain Injury with Glasgow Coma Score and Pupillary Reactivity. J Clin Case Rep Trials. 2018; l(1): 2-13.
13. Kaslong M, Subrata I, Tangkudung G, Khosama I. Neutrophil lymphocyte ratio and the outcome of traumatic brain injury. Jurnal Sinaps. 2018; 1(2):20-8.
14. Chen W, Yang J, Li Bingbing, Peng G, Li Tianfei. Neutrophil to lymphocyte ratio as a novel predictor of outcome in patients with severe traumatic brain injury. J Head Trauma Rehabil. 2017;1-7.
15. Sabouri et al. Neutrophil to lymphocyte ratio as a novel predictor of outcome in patients with severe traumatic brain injury. World Neurosurgery. 2020; 4:185.

16. Yeatts SD, Palesch YY, Temkin N. Biostatistical issues in TBI Clinical Trials [Internet]. 2nd ed. Handbook of Neuroemergency Clinical Trials: 2nd ed. Elsevier Inc. 2018; 2:167–85.
17. Callahan BP, Rabb CH. Traumatic Brain Injury [Internet]. Abernathy's Surgical Secrets. Elsevier Inc.; 2009: 99–104
18. Chen J, Qu X, Li Z, Zhang D, Hou L. Peak neutrophil-to-lymphocyte ratio correlates with clinical outcome in patients with severe traumatic brain injury. Neurocrit Care. 2019; 30(2): 334-9.
19. Muhammad Zaki, Syaiful S, Hesti L. comparison of lymphocyte neutrophil ratio in head injury patients with blood and without intracranial bleeding in Dr. M. Djamil General Hospital. Biomedical Journal of Indonesia. 2021; 7(1).
20. Najem et al. Traumatic brain injury: classification, models, and markers. Biochem. Cell Biol. 2018; 96: 391-406.
21. Shaikh F, Waseem M. Head Trauma. https://www.ncbi.nlm.nih.gov/books/NBK430854/. Accessed October 2021.
22. Advance Trauma Life Support, Student Course Manual. 10th ed. Chicago: American College of Surgeons; 2018.
23. Ng SY, Lee AYW. Traumatic Brain Injuries: Pathophysiology and potential therapeutic targets. Front Cell Neurosci. 2019; 13:528.
24. Galgano M, Toshkezi G, Qiu X, Russel T, Chin L. Traumatic brain injury: current treatment strategies and future endeavors. Cell Transplantation 2017; 26(7):1118-30.
25. Crupi R, Cordaro M, Cuzzcrea S, Impellizzeri D. Management of traumatic brain injury: from present to future. Antioxidants. 2020; 9:297.