LOMBOK HEALTH and SCIENCE JOURNAL
No. ISSN 2964-5239
https://journal.unram.ac.id/index.php/lhsj/index

Vol.2 (2024) : LHSJ February 2024 (10-23)

LITERATUR REVIEW : DIAGNOSIS AND TREATMENT OF TRAUMATIC BRAIN INJURY 2022

Mitha Yunda Pertiwi[1], Rohadi Muhammad Rosyidi[2], Bambang Priyanto[2], Surahman Hadi[2], Januarman[2]

1. Medicine Faculty, Mataram University, Indonesia
2. Neurosurgery Departement, General Hospital Of West Nusa Tenggara Province, Indonesia

Email : mitha.pertiwi15@gmail.com/rha.ns2010@gmail.com

Abstract

Traumatic brain injury (TBI) is one of the leading cause of morbidity and mortality from neurological cases worldwide. TBI can result in cognitive deficits, endocrine, psychiatric disorder and affecting the capacity to work and impair the quality of life of the patients. TBI classified as mild, moderate, and severe according to the Glasgow Coma Scale (GCS). TBI can be detected from neuroimaging. This is a review from a new guideline for diagnosis and treatment of traumatic brain injury: the neuroscience of traumatic brain injury 2022.

Keyword : Traumatic brain injury, neuroimaging, management, new guideline

Introduction

Traumatic brain injury (TBI) is one of the leading causes of morbidity and mortality from neurological cases in the world. The incidence of TBI more often in children and young adults (>640/100.00 cases in children and young adult under 24 year). Brain injury can caused two types of primary injuries: focal and diffuse. These two types can occur together or independently. Brain injury can lead to necrosis of neuronal cells and then compromised blood supply and hemorrhage at some layers of brain. The hallmark of diffuse brain damage is diffuse axonal injury (DAI) caused by the acceleration/deceleration forces imposed by the injury. The clinical manifestations of TBI can be deficits of cognitive, endocrine, psychiatric disorder and impair the quality of life of the patients. This is a review from a new guideline for diagnosis and treatment of traumatic brain injury: the neuroscience of traumatic brain injury 2022.

Clinical manifestations and Diagnosis

TBI can be caused by several mechanisms and cause many clinical manifestations like cognitive deficits, endocrine and psychiatric disorder and impair the quality of life of the patients. According to Glasgow Coma Scale (GCS), TBI classified into mild (13-15), moderate (9-12), and severe (3-8) Severe TBI is the leading cause of inpatient post injury, disability, and death. [1,2]

Neuroimaging in TBI

Neuroimaging has a important role to evaluate, diagnosis, treatment and prognosis for TBI. There are several imaging modalities such as: [3,4]

1. Head CT Scan

   Head CT is a standard imaging for patient with severe TBI. This imaging is fast and without contrast. Plain head CT is accurate to diagnosis abnormalities such as basic cranii fractures, intracranial hemorrhage, contusion, and brain herniation. But, plain CT cannot evaluate brain functional.

2. CT Angiography (CTA)

   CTA is available everywhere and practical but not a gold standard test. CTA gives anatomy information from brain blood vessels such as injuries or traumatic occlusion.

3. CT perfusion (CTP)

   CTP is an advanced neuroimaging which can gives the information about brain functional and anatomy. This imaging can evaluate perfusion parameters such as cerebral blood flow (CBF) and cerebral blood volume so we can evaluate the areas of ischemic or infarcted brain.

4. Magnetic resonance perfusion (MR Perfusion)

   MR perfusion is a non invasive technique and can detect intracranial artery blood flow and cerebral blood volume.

5. Diffusion tensor imaging (DTI)

   DTI is a promising technique that provides vital information about the connections of microstructural changes within the brain.

6. Transcranial Doppler Ultrasound (TCD USG)

   TCD USG is a non-invasive, informative, and simple technique to evaluate cerebral haemodynamic. This technique give information about etiology of cerebrovascular disorders

(rupture aneurysms, vasospasm, thrombosis), diagnosis of intracranial complication especially intracranial hypertension and cerebral ischemic.

CT scan evaluation for Cerebral Edema

Cerebral edema is one of the main determinant factor that association with intracranial hypertension. Intracranial hypertension can caused cerebral hypoperfusion dan ischemic. This condition can cause edema became more severe and caused brain death. CT scan evaluation should be performed immediately in patients with TBI after the clinical condition stabilizes based on the ATLS recommendations. There are several parameters that need to be assessed on a CT scan to evaluate cerebral edema: high convexity sulci, basal cistern status, sylvian fissure, traumatic subarachnoid hemorrhage (SAH), and white cerebellum. On CT scan evaluation, the Marshall scale can be used to assess the correlation between result from CT scan and increased intracranial pressure. Besides Marshall scale, there is a Rotterdam scale that can be used as a parameter for evaluating CT scans in patients with TBI.[3]

Use of the World Health Organization Disability Assessment Schedule 2.0 in the Assessment of TBI

There are various types of instruments can be used to assess patients with TBI, one of them are the World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0) which was released in 2010. The WHODAS 2.0 score is derived from questionnaires administered to the patient (or the patient's caregiver). The questionnaire consists of 6 domains which are divided into 36 items. Each item was scored on a Likert scale (1 = no difficulty, 2 = mild difficulty, 3 = moderate difficulty, 4 = severe difficulty, and 5 = extreme difficulty).[4]

Table World Health Organization Disability Assesment Schedule (WHODAS) 2.0

Domain	Items
1. Cognition	1.1. Concentrating on a task form 10 min 1.2. Remembering to do important things 1.3. Analyzing and finding solutions to problems in day-to-day life

	1.4. Learning to do something new, such as getting to an unfamiliar location 1.5. Generally understanding what people say 1.6. Starting and maintaining a conversation
2. Mobility	2.1. Standing for long periods of time (e.g 30 min) 2.2. Standing up from sitting down 2.3. Moving around inside your home 2.4. Leaving your home 2.5. Walking a long distance, such as 1 km
3. Self-care	3.1. Washing your entire body 3.2. Getting dressed 3.3. Eating 3.4. Being by yourself for a gew days
4. Social	4.1. Dealing with people you do not know 4.2. Maintaining a friendship 4.3. Getting along with people who are close to you 4.4. Making new friends 4.5. Sexual activity
5. Life activities	5.1. Taking care of your household responsibilities 5.2. Doing most important household tasks well 5.3. Completing all the housework that you needed to do 5.4. Completing housework as quickly as needed 5.5. Your day-to-day work or school activities 5.6. Doing your most important work or school tasks well 5.7. Completing all the work that you needed to do 5.8. Compleitn your work as quickly as neded
6. Participation	6.1. Joining community activities 6.2. Because of barriers or hindrances that the world imposed 6.3. Living with dignity 6.4. From time spent on attending to your health condition(s)

	6.5. Feeling emotionally affected 6.6. Because your health condition(s) is/are a drain on your financial resources 6.7. With your family facing difficulties because of your health condition(s) 6.8. Doing things by yourself for relaxation or pleasure

Biomarker in TBI

Recent studies have demonstrated the important role of the immune system in TBI, particularly in post-injury autoimmunity. TBI can cause damage to the BBB resulting in the release of immune cells from the brain into the bloodstream. This causes the activation of B cells and the formation of autoantibodies against antigens originating from the central nervous system. Another mechanism leading to the formation of autoantibodies is the transport of brain antigens to cervical lymph nodes from the brain's glymphatic system. Increased autoantibodies can be a long-term biomarker in the detection and diagnosis of TBI. There are several detectable autoantibodies such as myelin basic protein (MBP), protein S100B, acetylcholine receptor (AChR), glial fibrillary acidic protein (GFAP), peroxiredoxin 6, and glutamate receptor.[5]

In addition to autoantibodies, another protein that has been investigated as a biomarker of TBI is Chitinase-3-like-protein 1 (CHI3L1, otherwise known as YKL-40). YKL-40 is a biomarker associated with reactive inflammatory responses to different pathological processes such as TBI or various types of stroke. YKL-40 levels correlate with the clinical and pathological severity of TBI. However, YKL-40 still needs to be investigated further to determine its role in TBI related clinical applications, its role in lesion progression, and possible therapeutic interventions.5,6

Another biomarker that can be used is micro-ribonucleic acid (miRNA). miRNAs are released by neurons and glia into the extracellular space during TBI. miRNA levels can change within minutes and persist for several weeks after TBI. According to one study, miRNA can be used in the diagnosis or prognosis of TBI.[6,7]

Treatment

Patients with TBI who come to the ER are treated early as other traumas according to Advanced Trauma Life Support (ATLS) which consists of airway, breathing, circulation, and disability as well as patient exposure to prevent hypothermia. GCS is one of the important indicators in determining the treatment to be given to patients with TBI.[1,8,9,10]

1. Mild TBI (GCS 13-15)

Evaluation of patient with mild TBI should begin with a detailed history taking and neurological examination. The information should contain the patients's demographic characteristic, mechanism and time of injury, presence of loss consciousness (LOC), immediately after post-injury, subsequent level of alertness, amnesia (retrograde/antegrade) and the amnestic interval, headache (severity), vomiting, seizure; patient's allergies, medications (particulary about the use of anticoagulants, past medical history, last meal and event leading to injury as called AMPLE).

In the patient with mild TBI, cranial imaging studies or hospital admission is not always essential because intracranial damage is highly unlikely in these patients. Based on several guidelines, the indications of neuroimaging when there are persistent or worsening neurological signs. CT scan should be considered for diagnostic when LOC occurred more that 5 min; amnestic more than 30 min; witnessed disorientation or is currently disoriented during serial examinations); GCS score below 15 in 2 hours since injury; suspected open or depressed skull fracture; sign of basilar fracture (hemotympanum, raccoon eyes, otorrhea or rhinorrhea, battle's sign); vomits more than two times; seizure activity or convulsions; older than 65 years of age; history of using anticoagulants; and dangerous mechanism of injury (e.g motor vehicle and falls off heights higher that 3 ft or five stairs).

Patients should be admitted to the hospital with serial neuroimaging if a CT scan examination is needed but unavailable, there are abnormalities in the CT scan, GCS does not normalize in 2 hours, and there are signs of intoxication. Patients with abnormal CT or abnormal neurological examination should be consulted with the neurosurgery department, and a CT scan should be repeated if the neurological status of the patient worsens. Patients with mild TBI with normal GCS and neuroimaging can be discharged and instructed to evaluate for head injury warning rules and return for a follow-up visit.

2. Moderate TBI (GCS 9-12)

Patients with moderate TBI should be initially managed in ER based on ATLS guidelines, then the GCS score guides clinicians whether a head CT is required. Patients should be admitted to a healthcare facility with an intensive care unit for the first 12-24 hours. Patients with abnormal CT or worsened conditions should be reevaluated CT in 24 hours or worsening of neurological status requires the application of severe TBI protocols. Patients with improving neurological conditions allow safe patient discharge.

3. Severe TBI (GCS 3-8)

Moderate and severe TBI acutely managed with ATLS criteria and combined with serial neurological evaluation, a thorough systematic examination to exclude injury to other systems and, if necessary, to aid in balancing various treatment priorities (airway-breathing-circulation-disability-expose (ABCDEs) and primary survey and resuscitation). Based on ATLS, the priority of patients with TBI is to prevent secondary injury that is usualy caused by hypotension, hypoxia, hypercarbia, and increasing intracranial pressure.

Medical treatment of TBIs

The principle of TBI management is to prevent cerebral edema and decrease intracranial pressure, prevent hypoxia and ischemic, protect neural tissue, manage coagulant disturbance and prevent hemorrhage progressivity, and prevent other systemic complications like pulmonary disturbance, infection, nutrition, thromboembolic, musculoskeletal, and neurologic. The steps for medical treatment for TBI is :

1. Intravenous Fluid : In patients with TBI, it is important to give adequate hydration. Patient with TBI should not be given hypotonic fluids such as 5% dextrose or 0.45% sodium chloride because they can exacerbate cerebral edema. The initial choice of fluids that can be given are isotonic crystalloid fluids and blood products intravenously. If the blood pressure target (MAP value) is not achieved, a vasopressor such as phenylephrine or norepinephrine can be given.
2. Anticoagulant correction: A history of chronic anticoagulant use should be asked in patients with TBI and an international normalized ratio (INR) examination should be tested immediately. Reverse anticoagulation is not indicated in TBI unless there is active bleeding

or pathologic signs on a CT scan. If reverse anticoagulation with warfarin is needed, fresh frozen plasma, prothrombin complex concentrate, and/or vitamin K can be given.

3. Tranexamic acid : Administration of tranexamic acid should consider the benefits of giving greater than the risks of thrombosis and embolism such as myocardial infarction, stroke, pulmonary embolism, and deep vein thrombosis.
4. Transfusion :Red blood cell (RBC) transfusion is recommended if the Hb level is <7 g/dL.
5. Body positioning : The recommended body position is head elevation between 30-45°. Body position effectively lowers ICP.
6. Hyperosmolar agents such as manitol and hyperosmolar saline are routinely administered to patients with increased ICP and cerebral disc herniation. Administration of hyperosmolar agents is effective in reducing ICP and cerebral edema through several mechanisms such as inducing temporary hyperosmolarity in the extracellular space, creating an osmotic pressure difference in the BBB, and removing water from brain tissue into the intravascular hypertonic compartment.
7. Hyperventilation for TBI still being debated.Hyperventilation will cause hypocapnia which will increase the pH of the CSF, which will cause cerebral vasoconstriction, decreased cerebral blood volume, and decrease ICP. However, if hyperventilation is given with prophylactic purposes, especially in the first 24-48 hours, it can cause a decrease in cerebral perfusion which will lead to brain ischemia and worsening of neurological damage.
8. Temperature management: The purpose of temperature management is to maintain a normothermic temperature. Severe TBI can trigger a temperature-sensitive cascade that can trigger secondary brain trauma such as cerebral ischemia and hypoxia, inflammatory reactions, metabolic disturbances, and BBB damage.
9. Sedation and analgesia: Patients with TBI need to be given optimal sedation and adequate analgesia because agitation and pain can increase ICP. Propofol is an option for sedation to control ICP. If propofol is not effective, then fentanyl and remifentanil can be added because they have a synergistic effect with propofol.
10. Seizure management: Seizures have the potential to exacerbate intracranial hypertension by increasing cerebral metabolism and CBF. The TBI guidelines recommend the use of prophylactic antiepileptics for 1 week after TBI to prevent seizures. After 1 week,

antiepileptics can be discontinued. The anti-epileptic agents of choice are phenytoin, fosphenytoin, levetiracetam, and valproic acid.

11. Calcium channel blockers (CCB): The use of CCBs (nimodipine, ziconotide) is still being debated, but CCB administration is thought to decrease the damage progressivity in TBI.

Pharmacological Treatment

Until now there is no recommended therapy for TBI by Food and Drug Administration (FDA) for TBI. But, immediately after injury, inhibiting the mechanisms underlying the symptoms are effective in improving those symptoms. In general, pharmacological therapy aims to relieve symptoms, but efficacy is limited.[1,9]

The FDA recommends neuroprotective therapy to prevent secondary injury as a complication of TBI. Neuroprotective interventions usually aim to modulate cascades of injury such as cellular stress, oxidative stress, immunotoxicity, and inflammation. Some of the options for neuroprotective therapy are[1,8]:

Table. Pharmacological Intervention Of TBI

Potential TBI treatment	Mode of action	Outcome	Limitations
N-acetylcysteine	Replenishes glutathione synthesis	In animal studies : • Promoted cortical sparing • Reduce apoptosis • Lessened inflammation and oxidative stress • Improve cognition and psychomotor performance	Less substantial improvements in clinical trials
Mitoquinone	Mitochondria-targeted anti-oxidant	In a mouse model :	• Pre-clinical trials are scarce

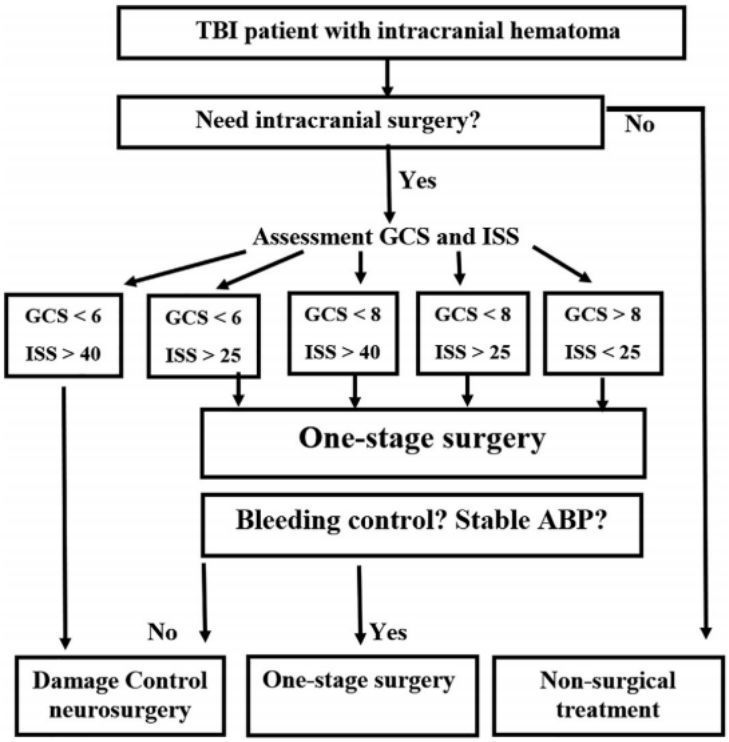
		• Improved neurological deficits • Reduced brain edema • Reduced neuronal death in the cortex • Imrpved the activity of the anti-oxidant enzymes such as SOD and GPx	• Has not been tested for the treatment of TBI in a clinical trial
Edarovone	Anti-oxidant	In a mouse model : • Enhanced meurological function • Reduced neuronal apoptosis • Reduced inflammation and oxidative stress	• Short half-life • Pre-clinical trials are scarce • Has not been tested for the treatment of TBI in clinical trial
Lipoic acid	Endogenous anti-oxidant; suppresses lipid peroxidation	In a rat model : • Reduced neuronal cell death • Reinforced the activity of the anti-oxidant enzymes SOD and GPx	• Short half-life • Pre-clinical and clinical trials are scarce
Memantine	Uncompetitive NMDA receptor antagonist	In a rat model :	• Pre-clinical and clinical trials are scarce

		• Improve motor and sensory functional outcomes • Decreased neuronal apoptosis, astrogliosis, and microgliosis • Decrease the volume of the cerebral infarction 72 hours after TBI • Enhanced neuronal survival • Alleviated neuronal nitrosative stress in the peri-lesioned cortex	
Diclofenac	Cyclooxygenase-2 inhibitor	In a rat model : • Reduced apoptosis • Reduced the lesion area	• Pre-clinical trials are scarce • Has not been tested for the treatment of TBI in a clinical trial
Hyperbaric oxygen therapy	Increases oxygen concentration in the body	Exhibits potential in the clinical setting	Surrounded by controversy with respect to its safety, feasibility, and mixed result

LOMBOK HEALTH and SCIENCE JOURNAL
No. ISSN 2964-5239
https://journal.unram.ac.id/index.php/lhsj/index
Vol.2 (2024) : LHSJ February 2024 (10-23)

Neurosurgical Treatment

Damage control technique (DCS) in neurosurgery can be applied to cases of cerebral compression with multiple traumas such as the abdominal cavity, thorax, pelvis and long bones. The DCS consists of early prevention of increased ICP, prevention of secondary brain injury caused by hypoxia, arterial hypotension, and hyperthermia. DCS neurosurgery is divided into 2 stages, the first stage is to reduce/eliminates brain compression, while the second stage is to reduce blood loss, control cerebral edema, circulation, and respiratory disorders. In surgery management, there is an algorithm for operating stages in TBI patients with multiple traumas.[1,6]



Picture. Surgery algorithm

Nutrition Supplementation

The role of nutritional supplementation is currently being studied. Many studies state that nutritional supplementation provides benefits to patients' output. These is some nutritional sources that have been studied in TBI patients such as omega-3 fatty acid, creatine, vitamin (especially D, E and B3), zinc, and magnesium.[1,2]

LOMBOK HEALTH and SCIENCE JOURNAL
No. ISSN 2964-5239
https://journal.unram.ac.id/index.php/lhsj/index
Vol.2 (2024) : LHSJ February 2024 (10-23)

Cognitive Rehabilitation

TBI can trigger gradual cognitive deterioration over time, which can lead to long-term cognitive impairment. Cognitive rehabilitation is an essential program for the clinical improvement of TBI patients, especially in increasing functional output and quality of life. The goal of cognitive rehabilitation is to trigger functional adaptation through environmental stimulation tailored to the patient's needs. Cognitive rehabilitation is based on the principle of neuroplasticity, which is the brain's ability to change so it can interact with the outside environment. In planning interventions, it should be noted that individual variations can affect the rehabilitation process such as the extent of injury, age, level of awareness, level of education, family support, and motivation. Rehabilitation consists of several phases, that is the initial phase is the identification and analysis of neuropsychological disorders through family and patient history, assessment of abnormalities, and clinical observation. The next step is to start rehabilitation. Rehabilitation is divided into 2 types, namely conventional and innovative methods such as PC-based methods, virtual reality, robotics, and telemedicine.[1,4]

Reference

1. Rajendram, R, Preedy, VR, Martin, CR. Diagnosis and Treatment od Traumatic Brain Injury: *The Neuroscience of Traumatic Brain Injury*. Elsevier. 2022
2. Acute mild traumatic brain injury assessment and management in the austere setting-a review. Ownbey MR, Pekari TB. *Mil Med.* 2021;187:47-51
3. Traumatic brain injury: classification, models, and markers. Najem D, Rennie K, Ribecco-Lutkiewicz M, et al. *Biochem Cell Biol Biochim Biol Cell.* 2018;96: 391-406
4. Moderate and severe traumatic brain injury. Robinson CP. *Contin Minneap Minn.* 2021;27:1278–1300
5. Neurobiology of traumatic brain injury. Bagri K, Kumar P, Deshmukh R. *Brain Inj*. 2021;35:1113–1120
6. Perceived change in physical, cognitive, and emotional symptoms after mild traumatic brain injury in patients with pre-injury anxiety or depression. Karr JE, Iverson GL, Huang S-J, Silverberg ND, Yang C-C. *J Neurotrauma.* 2020;37:1183-1189
7. A review of seizures and epilepsy following traumatic brain injury. Fordington S, Manford M. *J Neurol.* 2020;267:3105–3111
8. Traumatic brain injury: an age-dependent view of post-traumatic neuroinflammation and its treatment. Delage C, Taib T, Mamma C, Lerouet D, Besson VC. *Pharmaceutics.* 2021;13
9. Dynamics of choline-containing phospholipids in traumatic brain injury and associated comorbidities. Javaid S, Farooq T, Rehman Z, et al. *Int J Mol Sci.* 2021;22
10. Traumatic brain injury: an overview of epidemiology, pathophysiology, and medical management. Capizzi A, Woo J, Verduzco-Gutierrez M. *Med Clin North Am.* 2020;104:213–238.