Severe Traumatic Brain Injuries: A Primer for Healthcare Providers
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Introduction:

It is estimated that 2.5 million people will be seen yearly in the emergency department with traumatic brain injuries (TBI's). Many are treated and released from the emergency department but approximately 11% of these will require hospitalization and another 2% will die as a result of their injuries.[1]

A severe TBI can significantly affect the lives of the patient as well as their families. TBI's have been demonstrated to affect not only the physical condition of a person but their cognition, behavior, emotions, and social aspects of their lives. It can have a significant impact on their ability to work following injury.[1] Depending on the severity of injury, many may require some level of care for the remainder of their lives. Those who have survived a severe TBI are much more likely to die within 5 years of their injury than would be a person of the same age in the normal population.[1] It is estimated that there are currently between 3 million and 5 million people living with the effects of a TBI within the United States.[1]

In the United States, children, adolescents, and older adults are at highest risk for TBI's. Of these groups, those older than 75 years have the highest rates of TBI-related hospitalizations and deaths.[1] The leading causes of non-fatal TBI's include motor vehicle accidents, blows to the head from blunt objects or striking the head against an object, and sports related injuries.[1] TBI's leading to death are most likely caused by motor vehicle crashes, suicides, and falls.[1]

It is crucial for healthcare providers working in many settings to understand the management of adults with TBI's. The purpose of this article is to provide healthcare providers who do not generally care for patients with severe TBI's an overview of the basic anatomy and physiology of severe TBI's as well as current recommendations for its evaluation and treatment. Treatment will focus on the management of hypotension, hypoxemia, elevated intracranial pressures (ICP), and seizure prophylaxis.

Principles of Anatomy and Physiology

Monroe-Kellie Doctrine:

In order to effectively care for a person with a severe TBI it is vital to have and understanding of several basic principles of anatomy and physiology. One key principle is the Monroe-Kellie Doctrine (MKD). The MKD states that there are three main components that fill the space within the cranial vault. These include brain tissue, blood, and cerebral spinal fluid (CSF). According to the MKD if any one of these components increases in size or volume, one or both of the other two will need to compensate be decreasing in size or volume. For example, if a person has suffered from a TBI and intracranial blood volume increases, the nervous system has the ability for the CSF to compensate by pushing CSF backward into the spinal canal. If the volume of blood is too great, it will eventually put pressure on the brain tissue itself and if not reversed the brain will herniate.

Physiologic Parameters:

Two physiologic parameters are also important to understand when treating severe TBI's. These include the intracranial pressure (ICP) and the cerebral perfusion pressure (CPP). The ICP is the pressure that is contained within the cerebral vault. As noted above, if one of the

components discussed in the MKD increases and the other two are unable to compensate adequately, the ICP will increase. A normal ICP is approximately 5-15 mmHg. A persistent ICP of > 20 mmHg has been shown to be detrimental.[2]

The CPP is the mean arterial pressure (MAP) minus the intracranial pressure (CPP = MAP-ICP). A normal CPP is > 70 mmHg.[2] This parameter could be likened to the blood pressure of the brain.

These two parameters are dependent upon each other. For example, as the ICP increases in the case of a TBI, the CPP will also need to increase in order to maintain cerebral perfusion. This will take place by increasing the MAP. If the MAP is not increased, or the ICP is unable to be lowered, the CPP will drop and the brain will not be adequately perfused.

Primary Brain Injury:

Primary brain injury occurs at the time of the initial trauma. This is actual physical damage to the skull or its contents.[3] Common mechanisms include penetrating injury, direct impact, as well as acceleration/deceleration forces.[3] These forces may result in focal contusions and acute bleeding leading to hematoma formation as well as diffuse axonal injury (DAI), which is shearing of the white matter tracts within the brain.[3] DAI may appear as multiple small, punctate hemorrhages on CT scan or MRI.

Extra-axial injury may also occur. This includes injuries outside of the brain tissue itself. Examples of extra-axial injury include epidural, subdural, subarachnoid, and intraventricular hemorrhage.[3] Each of these is related to the tearing of blood vessels within the cranial vault. Epidural bleeding occurs from tearing of the small arteries within the epidural space. These are commonly associated with skull fractures. On CT scan these are lenticula-shaped in appearance.[3] Subdural hematomas occur as a result of tearing of the bridging veins within the subdural space. On CT scan they are crescent-shaped in appearance. Subarachnoid hemorrhage is the extravasation of blood into the subarachnoid space. This is due to injury to the pia vessels which subsequently leak into the subarachnoid space.[3] Intraventricular hemorrhage results from injury to the subependymal veins or from other adjacent hemorrhages.[3] Each of these injuries lead to increased blood within the cranial vault which may lead to increased ICP's.

Secondary Brain Injury:

Secondary brain injury occurs as a result of six differing molecular injury mechanisms. These mechanisms include neurotransmitter mediated excitotoxicity, electrolyte imbalances, dysfunction of the mitochondria, the inflammatory response, apoptosis, and ischemia related to vasospasm, and vascular injury.[3] Each of these mechanisms lead to neuronal death, which in turn leads to increased cerebral edema and elevated ICP's.[3]

Secondary brain injury is worsened by hypotension, hypoxia, fever, seizures, and hyperglycemia.[3] Much of the treatment of severe TBI is aimed at the prevention of secondary brain injury.

Diagnostic Workup:

Vital Signs:

Initial evaluation of any patient with a suspected TBI should include evaluation of the vital signs. The vital signs should then be repeated frequently in an attempt to identify any changes in the patient's condition.[2]

Glasgow Coma Score:

All patients suspected to have suffered any type of TBI should be immediately screened using the Glasgow Coma Score (GCS).[4] GCS's range from 15 (normal) down to 3 (severe disability) (See Table 1). A person with a GCS of 3 totally unresponsive. A score of 15 is considered normal. Scores of 13-14 indicate mild disability, 9-12 moderate disability, and 3-8 severe disability. The GCS takes into account eye opening, verbal response, and best motor response.[2] If a patient is unable to speak due to intubation or a tracheostomy the letter "T" is placed after the score. They would receive a 1T for the verbal section. A perfect score would then be considered an 11T. An intubated patient who is completely unresponsive would receive a 3T.

Table 1: Glasgow Coma Scale:[2]

Category	**Score**	**Physical Response**
Eye Opening	4	Spontaneous eye opening
	3	Eyes open to speech
	2	Eyes open to pain or noxious stimuli
	1	Eyes do not open even with stimulation
Verbal Response	5	Oriented to person, place, time
	4	Confused
	3	Inappropriate words
	2	Incomprehensible sounds
	1	No verbal response
Best Motor Response	6	Obeys commands
	5	Localizes to pain
	4	Withdraws from pain
	3	Abnormal flexion
	2	Extension (decerebrate posturing)
	1	No motor response

Evaluation of a Conscious Patient:

In the conscious patient it is important to determine if a loss of consciousness occurred, and if so, how long it lasted. It should also be determined if the patient is experiencing any traumatic amnesia.[2] In addition to determining the level of consciousness a pupillary assessment and motor examination should be completed. This should also include a cranial nerve assessment. The respiratory pattern should be continually monitored to determine any change in respiratory function.[2]

Evaluation of an Unconscious Patient:

Evaluation of the unconscious patient should include assessment of the level of consciousness using the GCS. Pupillary and motor function should also be included. In the unconscious patient it is vital to determine the need for possible intubation and airway management. This may be done by frequent assessment of the vital signs and respiratory pattern.[2]

Examination of the Head:

The skull, scalp, and face should be examined for bruising, depression, and lacerations. Any scalp laceration with a skull fracture below is considered an open fracture and places the patient at high risk for meningitis and intracranial infection. Bruising behind the ears and around the eyes may be indicative of basilar skull fractures. Indentation is indicative of a skull fracture which may place increased pressure on the brain itself.

Computed Tomography:

Once the neurological exam is completed, the patient should have an emergent non-contrast head CT scan to determine the extent of injury. Older adults and those taking antiplatelet or anticoagulants should have a CT scan even if they have a normal GCS, especially if they have any signs or symptoms of head injury or had a loss of consciousness. In high risk populations such as these, a repeat head CT should be performed within 24 hours in an attempt to determine if any additional bleeding or swelling has taken place. Of note, any patient with concern for a severe TBI should also undergo a CT of the cervical-spine to rule out neck injury.

In most cases, axial injury does not show up on the initial CT scan. As the injury progresses multiple small bleeds may be noted on CT scan. If axial injury is suspected, an MRI should be considered once the patient is stable enough to enter the MRI scanner. If an MRI is being considered it is vital to determine if the patient has any internal hardware which would be contraindicated in the MRI scanner.

Once the extent of injury is determined, frequent neurological exams should be documented. A neurological specialist should be notified immediately with any changes in the neurological exam.

Injury Management:

Once it has been determined that an injury has occurred the patient should be admitted to a critical care unit where close neurological and hemodynamic monitoring can take place. Initial management goals include the prevention of hypotension and hypoxia, as well as ensuring adequate brain perfusion through attempting to lower ICP as well as maintain an adequate CPP. All of this is done in an attempt to limit secondary brain injury.

Hypotension and Hypoxemia:

Both hypotension and hypoxemia have been shown to lead to increased morbidity and mortality in head injured patients. They have been demonstrated to be more detrimental in neurological injury than in the general trauma population.[5] Providers should attempt to maintain systolic blood pressure > 90 mmHg, mean arterial pressure > 60 mmHg, and Pa02 > 60 mmHg.[5] This must be balanced with the maintenance of adequate tissue perfusion as well as keeping the CPP > 70 mmHg. The goal is to maintain adequate CPP without causing an increase in ICP, cerebral hemorrhage, or swelling of the brain itself. In many cases hypertonic saline will be given in an attempt to maintain adequate fluid status as well as to prevent or decrease cerebral edema.

ICP Management:

Indications for ICP monitoring include a GCS of less than or equal to 8, evidence of structural brain damage on CT scan, need for surgery for other injuries, mechanical ventilation, or suspected or known worsening pathology.[4] An extraventricular device (EVD) is the modality of choice for monitoring ICP's. EVD's have the benefit of both providing monitoring as well as

the ability to drain CSF in order to decrease ICP.[4] The goal is to maintain an ICP of < 20-25 mmHg.

The American College of Surgeons recommends a three tiered approach to management of intracranial pressure. Tier 1 includes placing the patient in reverse trendelenberg at 30 degrees and the use of sedation and or analgesia. Recommended medications include propofol, fentanyl, or midazolam. Ventricular drainage may also be used. A repeat head CT is recommended if ICP's rise to greater than 20-25 mmHg.[4]

If ICP's continue to be > 20-25 mmHg with tier 1 management, tier 2 techniques should be initiated. These include the use of an EVD, administration of mannitol or hypertonic saline, maintenance of PaC02 of 30-35 mmHg and the consideration of neuromuscular paralysis.[4] A recent Cochrane Review found hypertonic saline to be superior to mannitol for the treatment of severe TBI's.[6]

If ICP's are not well controlled with tier 2 management, then tier 3 management would include consideration of a decompressive craniotomy and neuromuscular paralysis. The use of hypothermia (< 36^{o} C) would be considered if all other techniques have failed.[4]

Seizure Prophylaxis and Management:

Patients with a severe TBI are susceptible to both early (within 7 days of the trauma) and late (7+ days after the trauma) posttraumatic seizures.[7] Most posttraumatic seizures occur within 7 days of the initial injury and for this reason prophylaxis usually occurs for 7 days unless it is determined by the neurological specialist that the patient needs a longer period of treatment. Posttraumatic seizures (PTS) pose a significant risk to the patient during the acute phase of a severe TBI due to increased metabolic demands, increased ICP, and episodes of hypoxemia during a seizure.[8] Due to the serious consequences of PTS, seizure prophylaxis should be a key focus for the care of a patient with a severe TBI.

Current recommendations state that pharmacologic seizure prophylaxis following a severe TBI is only effective in reducing the risk for early, not late, PTS.[8] Specific risk factors for early PTS include a Glasgow score <10, one or more cortical contusions, depressed skull fractures, subdural hematoma, epidural hematoma, and intracerebral hematoma.[9] Phenytoin has been the most commonly used drug for post-TBI seizure prophylaxis in the past; however, recent studies have found that Levetiracetam is just as effective as phenytoin for post-TBI seizure prophylaxis.[10] Unlike patients receiving phenytoin, patients receiving Levetiracetam do not need frequent lab draws to determine blood levels of the drug.[11] The recommended dosage for phenytoin use in post-TBI seizure prophylaxis is a loading dose of 15-20 mg/kg administered intravenously over 30 minutes, followed by 100 mg administered intravenously every 8 hours, titrated to plasma levels for 7 days.[9] Recommended dosage for Levetiracetam use in post-TBI seizure prophylaxis is 500 mg intravenously every 12 hours for 7 days.[12] This may be changed to an oral dose once the patient is able to take oral medications safely.

Additional interventions to prevent PTS includes the drug topomirate.[11] Conversely, phenobarbital and carbamazepine are *not* advised for PTS prophylaxis due to adverse pharmacodynamic effects.[11] Lastly, vagal nerve stimulation actually had greater success preventing posttraumatic seizures than non-traumatic seizures.[11] Although not a common procedure in TBI patients, this may be considered in some cases.

Conclusion:

TBI's are commonly seen in the emergency department and critical care units. It is important for healthcare providers to understand the anatomy and physiology, initial evaluation, as well recommended treatments for these patients. The effective management of hypotension, hypoxemia, elevated intracranial pressures, and seizures is crucial in order for these patients to have the best chances of meaningful survival.

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