Management of moderate and severe traumatic brain injury

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Traumatic brain injury (TBI) is a common disorder with high morbidity and mortality, accounting for one in every three deaths due to injury. Older adults are especially vulnerable. They have the highest rates of TBI-related hospitalization and death. There are about 2.5 to 6.5 million US citizens living with TBI-related disabilities. The cost of care is very high.

Aside from prevention, little can be done for the initial primary injury of neurotrauma. The tissue damage incurred directly from the inciting event, for example, a blow to the head or bullet penetration, is largely complete by the time medical care can be instituted. However, this event will give rise to secondary injury, which consists of a cascade of changes on a cellular and molecular level, including cellular swelling, loss of membrane gradients, influx of immune and inflammatory mediators, excitotoxic transmitter release, and changes in calcium dynamics. Clinicians can intercede with interventions to improve outcome in the mitigating secondary injury. The fundamental concepts in critical care management of moderate and severe TBI focus on alleviating intracranial pressure and avoiding hypotension and hypoxia. In addition to these important considerations, mechanical ventilation, appropriate transfusion of blood products, management of paroxysmal sympathetic hyperactivity, using nutrition as a therapy, and, of course, venous thromboembolism and seizure prevention are all essential in the management of moderate to severe TBI patients. These concepts will be reviewed using the recent 2016 Brain Trauma Foundation Guidelines to discuss best practices and identify future research priorities.

In 2010, the CDC reported that each year approximately 1.7 million people sustain a traumatic brain injury (TBI), of whom 275,000 are admitted to the hospital and 52,000 die.[1] Children, adolescents, and adults aged over 65 are most likely to suffer a TBI; most are men.[1] Older adults, aged over 75 years, have the highest rates of TBI-related hospitalization and death, predominately due to falls. Furthermore, TBI is a contributing factor to approximately one in three injury deaths, and between 2.5 and 6.5 million citizens live with TBI-related disabilities.[1]

TBI is a structural brain injury resulting from an external physical force transmitted to the head that disrupts the normal architecture and function of the brain.[1,2] Several clinical tools, or scales, exist to grade TBI severity, including radiographic (Marshall CT classification)[3] and clinical (Galveston Orientation and Amnesia Test,[4] Glasgow Coma Scale [GCS]). The GCS, originally published in 1974[5] and slightly modified 2 years later,[6] is simple, durable, and widely used by clinicians. The GCS has limitations, including provider subjectivity and the loss of the verbal component after patient intubation. That said, the best motor

ABBREVIATIONS: BTF = Brain Trauma Foundation; CPG = clinical practice guidelines; CPP = cerebral perfusion pressure; CSF = cerebrospinal fluid; DAI = diffuse axonal injury; EDH = epidural hematoma; EVD = external ventricular drain; GCS = Glasgow Coma Scale; HTS = hypertonic saline; ICP = intracranial pressure; MAP = mean arterial blood pressure; SBP = systolic blood pressure; SDHs = subdural hematomas; TBI = traumatic brain injury.

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response on GCS, once a patient has been resuscitated, is the most reliable metric of prognostication. Technological advances like head computed tomography do not add significantly to the predictive value of clinical scales.[2]

Most TBI cases (about 80%) are mild (GCS 13–15), with approximately 10% moderate (GCS 9–12), and 10% severe (GCS 3–8).[7] Approximately 1.1 million are mild TBI injuries.[7] The incidence of moderate TBI is about 15 cases per 100,000 people, and 14 cases per 100,000 people for severe TBI.[7] As expected, mortality is skewed toward more severe TBI. Overall, TBI mortality is 17 per 100,000 for out-of-hospital TBI deaths and 6 per 100,000 for in-hospital TBI deaths.[1]

TBI and spine and spinal cord injuries often occur together. Occult cervical spine injuries should be assumed in all TBI patients with altered mental status or blunt injury above the clavicle. This occurs in up to 16% of TBI victims and must be ruled out by radiographic imaging.[8,9]

The American College of Surgeons developed advanced trauma life support as the clinical practice guidelines (CPG) for the evaluation and triage of acute trauma patients, including TBI.[8] Advanced trauma life support prioritizes the identification of patients with TBI. Initial treatment goals are ABCs, including early airway protection, adequate breathing with supplemental oxygen, and circulation support to ensure adequate oxygen and blood flow delivery to the brain. Avoidance of hypoxia and hypotension are critical, as both can contribute to poor outcome. In the hospital, specialized neurological intensive care teams should help guide brain injury management.[10,11] These guidelines are summarized in Table 1.

TABLE 1. TBI management

Vitals	Rate/Intervention
Key Guidelines for Prehospital TBI Management	
ABC	O_2sats > 90%, SBP >90%, secure airway
	Determine GCS and pupil function as soon as possible
	Triage GCS 9–13 to CSH
	GCS < 14 should not return to duty until normalized
	Sedation and analgesia as needed for transport
	Analgesics in small doses with proper monitoring
	Antibiotics for penetrating TBI is an option
Key Guidelines for TBI Management	
ICP	<25 mmHg
CPP	>60 mmHg
SBP	>90 mmHg
pO_2	>60 mmHg or
O_2 sats	>90%
	Head of bed at 30 degrees
	Antiepileptic drug for 7 days (begin w/in 24 hours)
pCO_2	34–36 mm Hg if hyperventilating for herniation
	Hypertonic resuscitation fluids (NS or higher)
HCT	>28

ABC = airway, breathing, and circulation; CPP = cerebral perfusion pressure CSH = Combat Support Hospital; GCS = Glasgow Coma Scale; HCT = Hematocrit; ICP = intracranial pressure; NS = Normal Saline; SBP = systolic blood pressure; TBI = traumatic brain injury.

MECHANISMS AND COMPLICATIONS OF INJURY

There are many different mechanisms of TBI. In general, these can be divided into two main categories: closed-head and penetrating. Closed-head injuries are more common and are associated with blunt impact to the head that does not violate the bony skull. Examples are when a patient's head is struck with a heavy object or strikes a windshield during a motor vehicle accident or the ground during a fall. Explosive blast TBI is when a patient is exposed to the forces associated with detonation. Many consider this a distinct form of closed-head injury. Penetrating head injury is when a foreign body fractures the skull and enters the brain parenchyma (e.g., a knife or gunshot wound). A penetrating TBI is almost always considered a severe injury.

The patient's age and general state of health factor in prognosis. The elderly often have less physiological reserve, making prognosis poor even following a relatively mild TBI.[12]

Mechanical forces directed over a small surface area can lead to skull fractures, which are often a harbinger of additional intracranial injuries. Depressed skull fractures often require surgical intervention for elevation of the fractured bone and debridement. Basilar skull fractures are especially problematic, as they are often associated with high forces of impact, are near cranial nerves, and may be associated with cerebrospinal fluid (CSF) leakage. Classic signs of basilar skull fractures include ecchymosis periorbital (raccoon eyes) and retroauricular (Battle sign) as well as clear rhinorrhea, suggestive of a CSF leak.[13]

Cerebrospinal fluid leaks

CSF leakage increases the risk of central nervous system infection. However, current 2016 Brain Trauma Foundation (BTF) CPG do not call for empiric antibiotics.[11] CSF leak diagnosis can be difficult. A useful bedside diagnostic test is placing a sample of fluid onto white filter paper. If there is a halo around the drop of fluid, then the sample is likely CSF, although blood mixed with tears, saline, or rhinorrhea may also produce a halo.[14] Alternatively, a sample of the fluid may be sent to the laboratory and tested for beta-2 transferrin.[15–17] Nonsurgical treatment of CSF may occasionally utilize lumbar drainage to divert CSF and promote healing.[18] In a retrospective analysis of 10,638 cases of TBI, the 1773 cases presenting with a posttraumatic CSF leak had significantly higher mortality.[19] Of those patients with CSF leak, the majority had tension pneumocephalus.

Tension pneumocephalus results from air being trapped within the skull. This space-occupying lesion increases intracranial pressure (ICP), which may lead to brain compression. Treatment includes 100% oxygen and flat bed rest. The oxygen is hypothesized to exchange with the nitrogen in trapped air. The oxygen is then absorbed. Although this practice is often prescribed, there is little evidence supporting effectiveness.[20]

Epidural hematomas

An epidural hematoma (EDH) is a life-threatening potential complication of TBI typically caused by a temporal bone fracture that injures the middle meningeal artery, leading to arterial bleeding into the epidural space. Clinically, this presents with a classic lucid interval followed by rapid decline in sensorium. EDH requires urgent neurosurgical evacuation. With prompt intervention, prior to herniation or local compression, the outcome from an EDH may be good, as there is often little underlying neuronal damage compared to subdural hematomas (SDHs), which often have associated direct parenchymal injury and edema.[21]

Subdural hematomas

SDHs are life-threatening conditions that occur when bridging veins are torn. In elderly patients, whose brains have atrophied, cortical veins are stretched. Thus, what would normally be a minor head injury, like a head bump against a car door when exiting, can be sufficient to tear these veins. When this happens, there is a low-pressure bleed with blood accumulation between the dura and arachnoid layers. These hematomas develop more slowly than an EDH and are more often associated with neuronal damage. Antiplatelet and/or anticoagulation medications greatly increase the risk of SDH. As with EDH, the treatment is typically neurosurgical evacuation of the hematoma.

Diffuse axonal injury

Diffuse axonal injury (DAI) occurs from shear forces from head and brain movement. This manifests as petechial or small punctate hemorrhages. Acceleration-deceleration (e.g., motor vehicle accident), is the most common cause of DAI. Often, a computed tomography scan does not reveal this, even though the patient may be symptomatic or comatose. Magnetic resonance imaging is the preferred neuroimaging technique if DAI is suspected.[22] Advanced magnetic resonance imaging techniques such as diffuse tensor imaging and susceptibility weighted imaging are even more capable in identifying these lesions.[22]

Cortical contusions

Cortical contusions generally occur in anatomic locations where the surface of the brain makes contact with irregular surfaces of the inner table of the skull, such as the inferior frontal or temporal lobes. They are frequently hemorrhagic, due to vascular damage, and may worsen, or "blossom," with resuscitation. One can also see coup-contrecoup lesions that result when the brain impacts both side of the skull due to rebound.[22,23]

Hemorrhagic conversion of a contusion often leads to clinical worsening. Following TBI, the highest risk is within the first 9 hours. Cerebral edema peaks between 48 and 96 hours after TBI,[24] then wanes with clinical improvement and less intracranial hypertension.[25]

Morbidity and mortality

The morbidity and mortality of TBI is intimately linked with the increased ICP, hemorrhagic contusions, and cerebral edema.[26,27] Thus, prevention of these secondary brain injuries is crucial. Malignant cerebral edema is especially difficult to manage, as it is usually refractory to medical therapy and causes irreversible injury, with mortality approaching 100% when untreated.[28] Recently, several important clinical studies of surgical (decompressive hemicraniectomy, ICP monitor placement, CSF drainage) and medical (hyperosmolar therapy, sedation and coma, hypothermia) interventions have demonstrated ICP reduction, with some reduction in mortality, but no improvement in functional outcome.

INVASIVE NONOPERATIVE INTERVENTIONS

Nonoperative invasive interventions for the treatment of moderate to severe TBI begin with ICP monitors. The 2016 BTF CPG recommend ICP monitoring, as there is evidence supporting a reduction in both in-hospital and 2-week post-injury mortality.[11] The current 2016 BTF CPG criteria for ICP monitor placement is clinical judgment. If used, the ICP should be treated to stay below 22 mm Hg; higher levels have been associated with increased mortality.[11]

An external ventricular drain (EVD, or ventriculostomy), a catheter inserted into the third cerebral ventricle,[29] represents the gold standard for ICP measurement. Additionally, an EVD enables treatment of intracranial hypertension and CSF removal. The 2016 BTF CPG recommend using continuous drainage, especially for severe TBI.[11] Using antimicrobial-impregnated EVD catheters may reduce the risk of ventriculitis.[11,30]

Other ICP monitor options are intraparenchymal monitors, which are less invasive but do not offer the potential for CSF drainage and treatment of elevated ICP and are prone to drift and inaccuracy.[29]

While there is evidence that ICP management reduces in-hospital mortality,[31] other studies have reported that ICP-directed therapy did not have any impact on outcome.[32] An important conclusion is not the futility of measuring ICP but the importance of the clinical intensive care unit examination and the significant handicap the clinician faces when the patient is sedated or paralyzed.

Clinical management is more than ICP therapy alone. Knowing the ICP allows calculation of the cerebral perfusion pressure (CPP) as CPP = mean arterial blood pressure (MAP)-ICP. CPP is considered a surrogate for cerebral blood flow and represents the pressure delivering oxygen and glucose to the brain. For severe TBI, the CPP goal is 60 to 70 mm Hg.[11] Driving CPP over 70 mm Hg is not recommended, nor is the use of epinephrine and dopamine, which increase the risk of acute respiratory distress syndrome.[33]

Jugular bulb oxygen saturation is another monitoring possibility option, per the 2016 BTF CPG.[11] Venous saturations less

than 50% have been correlated with worse Glasgow Outcome Score at 3 months.[34,35] Its most practical use is to determine if and when hyperventilation therapy is beginning to cause cerebral ischemia.

Newer modalities of invasive brain monitoring include brain tissue monitors and microdialysis catheters. The evidence supporting them is incomplete, so the 2016 BTF CPG do not endorse their use.[11]

NONINVASIVE NONOPERATIVE THERAPIES

Hyperosmolar therapies and blood pressure management

Maintaining head position at 30 degrees, hyperventilation, mannitol diuresis, and hypertonic saline have become the standard of care for treating brain herniation.

Elevating the head of the bed to 30 degrees, with the head in midline position, is simple to institute. The goal is to promote venous drainage to decrease intracranial venous blood and thus decrease ICP.

The 2016 BTF CPG do not comment on the use of hypertonic saline, and no longer give mannitol, a Level III recommendation, due to the lack of clinical evidence published.[11] However, anecdotally these agents are effective at decreasing ICP and reversing herniation, and while they have not been scrutinized in a randomized controlled trial, providers who care for severe TBI patients will generally attest to their effectiveness.

Mannitol has been shown to effectively reduce ICP in patients with TBI.[36] A serum osmolality of 320 mOsm/L is generally accepted as the treatment endpoint.[37] An important cautionary note is that because mannitol is a diuretic, it should be avoided when a patient is also suffering from hypovolemic shock as during hemorrhage.

Hypertonic saline (HTS) can also increase serum osmolality but has the added benefit of doing so without compromising intravascular volume. HTS is used in concentrations of 2, 3, 7.5, and 23.4%. The solution should be made as a 50:50 mix of sodium chloride and sodium acetate so as to reduce hyperchloremic metabolic acidosis. A commonly used initial treatment goal is to achieve serum sodium levels of 145 to 155 mEq/L, which is equivalent to a serum osmolality of 300 to 320 mOsm/L in most patients.[38] Bolus doses of 30 to 60 mL of 23.4% HTS have been shown to effectively reverse herniation events in emergencies,[39] can reduce ICP, and can increase CPP.[40] When tapering off HTS, rapid drops in serum sodium are to be avoided so as not to precipitate rebound cerebral edema.

In meta-analyses comparing mannitol to HTS in patients with TBI, both mannitol and HTS are comparable on mortality and neurological outcomes, although HTS may have a more robust effect on ICP.[41,42]

Maintaining systemic blood pressure in TBI patients is important. In TBI, cerebral autoregulation is impaired. When this occurs, regional cerebral blood flow becomes directly dependent on systemic blood pressure.[43] The 2016 BTF CPG recommend maintaining a systolic BP at 100 mm Hg or greater in patients 50 to 69 years old, and 110 mm Hg or greater in patients 15 to 49 or over 70 years old,[11,44,45] which is modified from the 2007 BTF CPG.

Blood pressure may be increased with intravenous fluids and/or vasoactive medications. Norepinephrine and phenylephrine are preferred, as they have the least effect on cerebral vasomotor tone. If vasopressors are being used, then continuous hemodynamic monitoring is needed with both a central venous catheter and a peripheral arterial pressure catheter.[25] However, caution should be used, as MAP augmentation has been associated with increased incidence of acute respiratory distress syndrome, particularly when a CPP goal of greater than 70 is targeted.[33]

Albumin is not recommended for resuscitation in TBI patients. Evidence from the SAFE trial shows that TBI patients who received 4% albumin had significantly higher mortality.[46] Albumin was associated with higher ICP when compared to saline.[47]

Reduction of cerebral metabolic rate with anesthetics and hypothermia

Anesthetics, such as pentobarbital[48] or propofol,[49] and hypothermia[50–55] can reduce cerebral metabolic rate of oxygen, which leads to reductions in cerebral blood flow, ICP, and tissue oxygen demand. The 2016 BTF CPG recommends high-dose barbiturates to control elevated ICP refractory to other therapies. Propofol may also be used in this context. However, no anesthetics should be used for prophylaxis against developing intracranial hypertension.[11]

Hypothermia is one the most effective TBI therapies in preclinical studies. Sadly, targeted temperature management has not been shown to be effective in improving outcome from TBI,[50–55] in spite of its apparent benefit following cardiac arrest.

SURGICAL INTERVENTIONS

Hemicraniectomy is a possible treatment of TBI with severe cerebral edema.[56] It is intended to reduce mortality and improve outcome. Neither the RESCUEICP or DECRA trials, which compared medical care to decompressive hemicraniectomy following TBI, showed significant differences between the two groups in meaningful outcome.[57,58] Nevertheless, the current 2016 BTF CPG recommend large frontotemporoparietal decompressive hemicraniectomy of not less than 12 × 15 cm or 15-cm diameter but not bifrontal craniectomy.[11] Interestingly, decompressive hemicraniectomy was shown to provide clinical benefit in severe stroke patients. The pooled analyses of the HAMLET, DECIMAL, and DESTINY trials demonstrated functional benefit when hemicraniectomy was undertaken within 48 hours of acute

ischemic stroke for malignant edema.[56,59,60] Decompressive hemicraniectomy represents a definitive treatment for intracranial hypertension and, while invasive, is reasonably safe, aside from the risks of general anesthesia, and should be considered early.

A potential contributor to better clinical outcome after hemicraniectomy is early cranioplasty or replacement of the bone flap.[61,62] A prospective clinical trial on early cranioplasty is warranted.

Laparotomy is another potential treatment of refractory ICP. By decreasing intra-abdominal pressure, there is a decrease in intrathoracic pressure, which allows for increased venous drainage from the cerebral veins, resulting in reduced intracranial blood volume and decreased ICP.[63]

TBI, HEMORRHAGIC SHOCK, AND THE TRANSFUSIONS OF BLOOD AND BLOOD PRODUCTS

Shock is a common presentation of trauma patients. The 2016 BTF CPG recommend that resuscitation of hypotensive patients due to hypovolemia is 1 to 2 L of crystalloid followed by blood transfusion. The use of crystalloid in this setting is an area of active study. It should be recognized that isolated TBI is never the cause for hypovolemic shock, regardless of the size of the hemorrhagic intracranial lesion.[8]

When treating the multitrauma patient who also has TBI, it may be difficult to maintain systolic BP according to the guidelines proposed by the 2016 BTF CPG,[11] discussed above. This is particularly true when a hypotensive resuscitation, also called permissive hypotension or hemostatic resuscitation, strategy is used, with MAP as low as 50 mm Hg being acceptable. This strategy avoids exacerbating acute blood loss and rebleeding following temporary hemostasis. Lower MAP goals continue until durable operative hemostasis can be achieved. This approach is often employed in penetrating trauma, especially to the abdomen. A prospective trial of 598 patients with penetrating injuries to the torso and a systolic blood pressure (SBP) of less than 90 concluded that delayed aggressive resuscitation, until after operative management of the injuries was completed, resulted in significantly lower mortality and lower hospital length of stay when compared to those who received immediate aggressive resuscitation.[64] Subsequently, a prospective randomized trial examining SBP goals of 100 mm Hg versus 70 mm Hg in 110 trauma patients with hemorrhagic shock (and only 50% classified as penetrating trauma) did not find any differences when comparing in-hospital mortality.[65] More recently, an out-of-hospital randomized study of mixed trauma patients with hypotension (SBP <90), the majority of which were blunt trauma, found patients in the controlled resuscitation group that received small boluses of 250 cc of crystalloid for a goal SBP of 70 mm Hg or greater had a nonsignificant decrease in mortality at 24 hours (5%), while the standard resuscitation group, who received 2 L initially and continued aggressive resuscitation to maintain an SBP of 110 mm Hg or greater had a mortality of 15% at 24 hours.[66] Patients with severe TBI were excluded from this study.[66]

Considering these and other reports, the European 2016 BTF CPG for major bleeding and coagulopathy following trauma recommend a target MAP of 80 mm Hg or greater for patients who also have severe TBI. These 2016 BTF CPG also recommend a restricted volume replacement strategy to achieve target MAP until bleeding is controlled and the administration of vasopressors, along with fluids, to maintain MAP.[67]

For the multitrauma and TBI patient, an ICP monitor should be placed to help determine whether higher MAP is needed to maintain CPP and ensure adequate brain perfusion.

Hemoglobin target

There are no current recommendations regarding appropriate hemoglobin or hematocrit concentrations in patients with severe TBI. When the 67 patients with moderate to severe TBI from the Transfusion in Critical Care Trial[68] were examined retrospectively, no benefit of a liberal transfusion strategy (goal, 10 g/dL) compared to a restrictive strategy (goal, 7 g/dL) could be demonstrated.[69] Furthermore, no significant difference was found when these same hemoglobin thresholds of 7 and 10 mg/dL were tested, along with either placebo or erythropoietin injections, in a prospective multicenter Phase III trial of TBI.[70] However, post hoc analysis revealed a higher risk of intracranial hemorrhage of all types in the higher transfusion threshold group.[71] Together, these studies suggest that higher hemoglobin levels are associated with higher medical complications while adding little clinical benefit.

Prior to this study, evidence for the hemoglobin concentrations affecting the outcome of severe TBI patients was limited to retrospective analyses and associations, which suggested that patients with lower hemoglobin fared worse.[72–78] A survey published in 2009 of the transfusion practices of trauma and neurological surgeons, and intensivists of patients with severe TBI suggested that neurosurgeons tended to use a more liberal transfusion threshold, in both the presence and absence of increased ICP, as compared to trauma surgeons and intensivists.[79] It is unclear whether the recent randomized trial will change practice trends in this group.

Coagulopathies

Coagulopathies are not uncommon in severe TBI. Known as "acute traumatic coagulopathy," it is postulated to be due to the release of tissue factor, which is in high concentrations in the brain.[80] This condition was first described in 1974[81]

and is associated with an almost 10-fold increase in death[82] and worse cognitive outcomes in survivors.[83] Consequently, coagulopathies, including thrombocytopenia and elevated international normalized ratio, should be promptly corrected in TBI patients. Although the 2016 BTF CPG do not provide practice parameters to guide management, the Neurocritical Care Society and the Society for Critical Care Medicine have published Guidelines for the Reversal of Antithrombotics in Intracranial Hemorrhage, including both spontaneous and traumatic subtypes.[84]

Platelet transfusions

There are no recommendations for platelet transfusions in TBI patients. However, there is an association between antiplatelet use and development of acute traumatic intracranial hemorrhage.[85–87] Unfortunately, evidence to date suggests that platelet transfusion does not improve clinical outcome in TBI patients with intracranial hemorrhage[88–90] or nontraumatic intracerebral hemorrhage.[91] There is also an association between coumadin use and intracranial hemorrhage following TBI.[92,93] Progression of hemorrhagic contusions has been associated with antiplatelet and anticoagulation; however, only the presence of subarachnoid blood, subdural blood, or skull fracture, and not medication, are independent predictors of outcome.[94]

Tranexamic acid has been studied in TBI patients with promising results. Although definitive improvement in outcome has not yet been demonstrated, there is evidence that tranexamic acid reduces intracerebral hemorrhage progression.[67,84,95–100] Further study is warranted.

MECHANICAL VENTILATION

Prompt airway management with supplemental oxygen is important for severe TBI. Hyperventilation is a recommended treatment for elevated ICP with $PaCO_2$ goal of 34 to 36 mm Hg.[11] Prophylactic hyperventilation for patients without elevated ICP is not recommended. Evidence shows that hyperventilation for a goal $PaCO_2$ of less than 25 mm Hg has worse outcomes.[101]

PAROXYSMAL SYMPATHETIC HYPERACTIVITY

Paroxysmal sympathetic hyperactivity or diencephalic seizures are frequent following severe TBI. Paroxysmal sympathetic hyperactivity is episodes of severe dysautonomia with mydriasis, flushing, diaphoresis, tachycardia, hypertension, hyperthermia, tachypnea, and ICP elevations. This dysautonomia is responsive to dopamine agonists and opioids.[102] Other strategies may include gamma-aminobutyric acid agonists, adrenergic antagonists, gabapentin, dantrolene, propofol, and/or acetaminophen.[103]

POSTTRAUMATIC SEIZURES

TBI is a common cause of seizures.[104] Posttraumatic seizures may be classified as immediate seizures (occurring less than 24 hours after injury), early seizures (occurring 24 hours to 7 days after injury), and late seizures (occurring more than 7 days after injury). Late seizures often lead to lifelong epilepsy.[104] Antiepileptic medication reduces immediate and early seizures but not late seizures. Thus, the 2016 BTF CPG recommend that phenytoin be prescribed for the first 7 days after injury to reduce the incidence of early PTS.[11] Other options are levetiracetam and carbamazepine, although there is not good evidence supporting their use. Valproate and phenobarbital are not recommended.

VENOUS THROMBOEMBOLISM

Because of the coagulopathy associated with TBI, along with subsequent prolonged immobility, venous thromboembolism is common.[105] TBI has been shown to be independently associated with the formation of deep vein thrombosis, and a three- to fourfold increased risk of deep vein thrombosis formation is consistent across all prophylaxis groups among patients with TBI.[106] Consequently, the 2016 BTF CPG recommend the use of low-molecular-weight heparin or low-dose unfractionated heparin in combination with mechanical prophylaxis for the prevention of venous thromboembolism, with the caveat that it may exacerbate any intracranial hemorrhage.[11]

NUTRITION

Hypermetabolism, catabolism, and nitrogen loss all accompany severe TBI.[107,108] The 2016 BTF CPG recommend feeding patients with at least a basal caloric replacement by the fifth day (seventh at the latest) to reduce mortality.[11]

CONCLUSIONS

TBI is a common trauma-related condition. Reducing the impact of secondary brain injury mechanisms is critical to improved outcome. The 2016 BTF CPG for managing moderate to severe TBI is an evidence-based approach to clinical practice. Unfortunately, there are still significant gaps in TBI treatment. Particularly, there is an incomplete understanding of the role of transfusion and lack of effective pharmacological agents. Therefore, the focus of therapy is to maintain ventilation, optimize blood flow, control ICP, maintain CPP, and support general physiology. Despite success in decreasing ICP, many of these interventions have not translated to robust functional outcomes. Future research areas are focused on improving diagnostics, treatment strategies, and improving other aspects of intensive

care unit care with the goal of improving functional and neurological outcome of TBI victims.

CONFLICT OF INTEREST

PA and ND have disclosed no conflicts of interest. GSFL is a member of the NFL Health Foundation Board, the NFLPA Mackey-White Health Committee, and has given a lecture under the sponsorship of Medtronic, Inc.

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