Neurotrauma

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KEYWORDS

• Neurotrauma • Traumatic brain injury • Traumatic spinal cord injury
• Neuroprotection • Neurocritical care

KEY POINTS

- Resuscitation of the patient with neurotrauma is focused on prevention of secondary injuries. Hypoxia and hypotension are associated with increased morbidity and mortality.
- Management of suspected intracranial hypertension follows a tiered approach. Hyperventilation should only be used transiently in an acute herniation syndrome as a bridge to more definitive therapy.
- The use of steroids for traumatic brain injury and traumatic spinal cord injury is not recommended.
- Care of the critically ill patient with neurologic injury by specialized neurocritical care teams has been shown to reduce hospital length of stay and in-hospital mortality.

INTRODUCTION

Injuries to the central nervous system (the brain and spinal cord) are a heterogeneous group of pathologic disorders. They can be categorized by mechanisms of injury, clinical severity, radiological appearance, or anatomic distribution. Neurologic injury from trauma not only results from the initial physical insult but also continues to occur in the ensuing hours or days. Prevention of primary neurologic injury from trauma is the focus of public health efforts such as the use of helmets and seatbelts. A major component in the management of patients with neurotrauma is the prevention of secondary injury such as ischemia and hypoxia. This article reviews common neurologic injuries associated with trauma, considerations in the critical care management of these patients, and the evidence behind current treatment therapies.

The authors have nothing to disclose.

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EPIDEMIOLOGY

Neurotrauma is a critical public health problem. Injuries remain a leading cause of death worldwide. In the United States, traumatic brain injury (TBI) contributes to nearly one-third of all injury-related deaths.[1] More than 1.3 million US emergency department visits annually are related to TBI, accounting for 4.8% of injury-related visits and 1.4% of all visits. Leading causes of TBI are falls (35.2%), motor vehicle–related injuries (17.3%), blunt impact (16.5%), and assaults (10%).[1] The incidence of blast injury in the US civilian population is low, with a report of 0.2% in a major urban trauma center. However, TBI has been associated in up to one-third of blast injuries.[2] Young children (aged <5 years), adolescents (aged 15–19 years), and the elderly (aged ≥75 years) have higher rates of TBI.[1] Although there has been a decrease in TBI-related deaths, likely reflecting preventive measures such as seat belt and helmet use, at least 3.2 million Americans live with long-term disabilities as a result of TBI.[3] The annual cost of TBI in the United States is estimated at $76.5 billion, including direct medical and rehabilitation costs and indirect societal economic costs.[4]

Traumatic spinal cord injury (SCI) is a rare but potentially severe injury that primarily affects young adults and male patients. Nearly half of all injuries occur between the ages of 16 and 30 years and 80.7% of injuries reported to the national database were in male patients. Leading causes of traumatic SCI are motor vehicle–related injuries (36.5%), falls (28.5%), and acts of violence (14.3%). Despite advances made in early recognition and treatment, less than 1% of patients experience complete neurologic recovery by hospital discharge.[5,6]

COMMON NEUROLOGIC INJURIES ASSOCIATED WITH TRAUMA

Head Injury

Blunt injury

Direct blunt impact of the head results in acceleration and deceleration of the brain within the cranial vault. These mechanical forces cause tissue compression, distortion, and shearing, resulting in parenchymal contusions, extra-axial hematomas, and diffuse axonal injury. Common patterns of brain injury seen with blunt trauma are described in **Table 1**.

Table 1
Common brain injury patterns with blunt trauma

	Pathophysiology	Typical Locations	Characteristics
Parenchymal contusions	Coup/contrecoup injury	Orbitofrontal Anterior temporal	One-third expand within 24 h after injury
Epidural hematoma	Injury to middle meningeal artery, middle meningeal vein, diploic veins, or venous sinuses	Adjacent to skull fracture	Convex (lens shaped) Does not cross skull suture lines
Subdural hematoma	Injury of bridging veins	Cerebral convexities Along tentorium or falx	Concave (crescent shaped) Crosses skull suture lines
Subarachnoid hemorrhage	Injury of pial vessels	Cerebral convexities Basal cistern Ventricles	Can be confined to few sulci and fissures or diffuse
Diffuse axonal injury	Shear injury of axons	Junction between cortex and white matter Midline white matter structures	Axonal swelling with ultimate axotomy

Penetrating injury

Penetrating TBI is less common than blunt TBI but is associated with worse prognosis, with only 9% survival reported in a statewide registry.[7] Most civilian penetrating head injury is caused by firearm injuries. As a projectile penetrates the brain, it lacerates the parenchyma. In the wake of the projectile, tissue compression and expansion in a wavelike pattern cause further tissue injury. The degree of injury depends on the kinetic energy transferred from the projectile to the surrounding tissue; therefore, higher velocity projectiles cause more injury than lower velocity projectiles.

Blast injury

Blast TBI is observed primarily in soldiers exposed to improvised explosive devices. However, any explosion can be associated with transmission of energy through the cranium and blood vessels to the brain. Malignant cerebral edema may occur rapidly (within an hour), as opposed to the more slowly developing edema seen in blunt TBI (hours to days). Cerebral vasospasm may occur in up to 50% of blast TBI. Concomitant blast injuries to the eyes and to the auditory and vestibular systems are often seen.[8]

SCI

Blunt injury

Blunt SCI occurs as a result of cord compression, distraction, or shearing by disc herniation, vertebral fracture, or subluxation. Compromise of the spinal canal also contributes to impedance of blood flow through the spinal arteries, leading to further oligemia and ischemia. Because of the mechanisms of injury, concomitant injuries to the head, chest, and abdomen are common.

Penetrating injury

Penetrating trauma can cause laceration and transection of the spinal cord. Although rare, cervical and thoracic spine is more commonly affected.

Vascular Injury

The incidence of vascular injuries associated with neurotrauma is likely underreported because vascular imaging is usually performed only when injury is suspected. When a liberal screening protocol was implemented at a level I trauma center, an incidence of 1.2% was found.[9] Blunt injuries to the extracranial carotid and vertebral arteries may present with late-onset ischemic strokes. Vertebral artery injury may be common in patients with concomitant cervical spine trauma, although no specific cervical vertebral fracture pattern has a higher association with blunt vertebral artery injury.

Secondary Injuries

Neurotrauma initiates cellular and molecular cascades that exacerbate edema and ischemia, as well as promoting cell death. Many mechanisms underlying these pathways have been studied but no neuroprotection panacea has been found. Cerebral ischemia, intracranial hypertension, systemic hypotension, hypoxia, fever, hypocapnia, and hypoglycemia have all been shown to independently worsen survival after blunt TBI.[10] Coagulopathy associated with TBI may exacerbate ischemic brain injury through microvascular thrombosis and embolism.[11] In traumatic spinal cord injuries, ischemia, inflammation, free radicals, and excitotoxicity similarly contribute to necrotic and apoptotic neuronal death.[12] A large component in the management of patients with neurotrauma is the prevention and reduction of secondary injuries.

GENERAL APPROACH AND RESUSCITATION STRATEGIES FOR THE PATIENT WITH NEUROTRAUMA

Airway, Breathing, and Circulation

Initial management of a patient with neurotrauma should be focused on the assessment and stabilization of the airway, breathing, and circulation, as with any other critically ill patient. For patients with a Glasgow Coma Scale (GCS) less than 8, endotracheal intubation should be considered for airway protection. Rapid sequence intubation with in-line stabilization of the cervical spine is the preferred method of securing the airway in patients with neurologic trauma. Pretreatment with fentanyl (3 μg/kg) may be considered for its attenuating effect on the reflex sympathetic response and associated increase of intracranial pressure (ICP) that can be seen with laryngoscopy.[13] However, evidence for pretreatment with lidocaine is mixed and limited.[14] Awake, fiberoptic intubation may be considered in patients with cervical spine injury to reduce cervical spine motion.

In patients with TBI, hypoxia, defined as Pa_{O_2} less than 60 mm Hg or O_2 saturation less than 90%, is significantly associated with increased morbidity and mortality.[15] Hyperoxygenation with Pa_{O_2} greater than 470 mm Hg is also discouraged.[16] Target Pa_{CO_2} is 35 to 45 mm Hg with target end-tidal CO_2 of 30 to 40 mm Hg.[17] Hyperventilation should be avoided except in the acutely herniating patient as a bridge to more definitive therapies.

Hypotension is similarly associated with a 2-fold increase in mortality compared with matched controls in TBI.[15] In studies of the Traumatic Coma Data Bank (TCDB), a single observation of systolic blood pressure less than 90 mm Hg was one of 5 most powerful predictors of outcome, along with age, admission GCS motor score, pupillary function, and intracranial hypertension.[18] However, systolic pressure greater than 90 mm Hg may be desirable during resuscitation of patients with neurotrauma, but no studies have been performed thus far to determine a resuscitation target. Instead, 90 mm Hg should be considered a threshold to avoid.

Fluid Resuscitation

Fluid resuscitation in a patient with TBI needs special emphasis on the osmolality of the choice of fluid. Hypo-osmotic fluids can increase cerebral edema and ICP in the context of an injured blood-brain barrier. In 2004, 2 large randomized multicenter trials examined the use of albumin and hypertonic saline (HTS) in the resuscitation of patients with TBI. From the Saline versus Albumin Fluid Evaluation (SAFE) study, a post hoc study of 460 patients with TBI revealed that resuscitation with albumin was associated with higher mortality but similar functional outcome in survivors compared with saline.[19] Cooper and colleagues[20] examined the use of HTS in prehospital resuscitation of 229 hypotensive patients with TBI and found no significant difference in survival or neurologic outcome. A similar study by Bulger and colleagues[21] comparing HTS, HTS with dextran, and normal saline in out-of-hospital resuscitation of patients with TBI without hypovolemic shock was terminated for futility.

Resuscitation of the patient with neurogenic shock from SCI may require the use of vasopressors after achieving euvolemia to counteract the loss of sympathetically mediated vascular tone.

ICP

ICP is a function of the volume and compliance of each component of the intracranial compartment: brain tissue, blood, and cerebrospinal fluid (CSF). This concept was described by Alexander Monro and George Kellie, stating that to maintain a state of

volume equilibrium in a fixed compartment, any increase in volume of one component must be compensated by a decrease in volume of another. Normal compensation to an increase in intracranial volume (eg, mass, hemorrhage, cerebral edema) is a decrease in cerebral blood volume and egress of CSF into the spinal space. Once these compensatory mechanisms are maximized, the addition of further volume leads to a sharp increase in ICP. Cerebral ischemia can be caused by increased ICP from reduction of cerebral perfusion pressure (CPP), or direct mass effect on cerebral arteries. Intractable intracranial hypertension can lead to compression of the brainstem and herniation syndrome, most classically described by the Cushing triad of widening pulse pressure, irregular respirations, and bradycardia. Inability to attenuate or reverse this process ultimately leads to cardiopulmonary arrest or brain death.

Initial management of suspected intracranial hypertension includes elevating the head of bed, maintaining the neck in neutral position, and avoiding neck constriction such as with poorly fitted cervical collars or circumferential tape or ties used to secure the endotracheal tube. Adequate treatment of pain, agitation, fever, and seizures can also reduce increases of ICP.

Comatose patients with GCS less than or equal to 8 are at highest risk for intracranial hypertension, thus ICP monitoring is recommended by the Brain Trauma Foundation (BTF) for patients with severe TBI. The preferred method for ICP monitoring is an external ventricular drain, because of its ability to provide a more reliable measure of global ICP and immediate effect on increased ICP from CSF drainage. ICP increase greater than 20 mm Hg is treated by the algorithm shown in **Table 2**, using a tiered approach of therapies. When using osmotic agents such as mannitol, clinicians should avoid intravascular volume depletion and hypotension with concurrent replacement of urinary losses with isotonic fluids. Hyperventilation is an effective emergent treatment of intracranial hypertension because CSF alkalosis is a potent vasoconstrictor of cerebral blood flow (CBF). However, it should be used transiently in an acute herniation syndrome as a bridge to more definitive therapy. Sustained and vigorous hyperventilation may result in cerebral ischemia and worse outcome.[22]

Clinical herniation can occur at ICP less than 20 mm Hg, depending on the location of an intracranial mass lesion. Pupillary abnormalities occurring with ICP values as low

Table 2
ICP management by a tiered approach

Tier 0	Head of bed >30° Optimize physiologic parameters Normothermia goal Adequate sedation and analgesia
Tier 1	CSF drainage via ventriculostomy Mannitol 0.5–1 g/kg bolus
Tier 2	Hypertonic saline bolus Propofol bolus and infusion
Tier 3	Decompressive craniectomy Pharmacologic coma Hypothermia Decompressive laparotomy or thoracotomy

Data from Brain Trauma Foundation, American Association of Neurological Surgeons, Congress of Neurological Surgeons, et al. Guidelines for the management of severe traumatic brain injury. Methods. J Neurotrauma 2007;24(Suppl 1):S3–6; and Stevens RD, Huff JS, Duckworth J, et al. Emergency neurological life support: intracranial hypertension and herniation. Neurocrit Care 2012;17(Suppl 1):S60–5.

as 18 mm Hg have been reported.[23] Therefore, management of intracranial hypertension should be correlated with the clinical examination and neuroimaging for each patient.

Cerebral Perfusion

Resuscitation of the injured brain is directed at restoring and maintaining adequate cerebral metabolism by ensuring sufficient delivery of oxygen and glucose to the brain tissue. In the uninjured brain, an autoregulatory mechanism maintains constant CBF across a wide range of CPP through modulation of cerebral vascular diameters (**Fig. 1**). However, autoregulation can be disrupted in brain injury, thus changes in CPP can significantly affect CBF. The use of CPP as a surrogate parameter for CBF therefore assumes that autoregulation is impaired.

Systemic hypotension is highly associated with increased morbidity and mortality in TBI.[24,25] Low CPP is also associated with poor physiologic indices as well as poor clinical outcome.[26] Studies suggest that there is a critical threshold for CPP between 50 and 60 mm Hg. Robertson and colleagues[27] conducted a randomized controlled trial of therapy targeting CPP greater than 70 mm Hg compared with therapy targeting ICP less than or equal to 20 mm Hg while maintaining CPP greater than 50 mm Hg. They found no difference in outcome, but the aggressive CPP target group had a 5-fold incidence of acute respiratory distress syndrome and more frequent use of vasopressor agents. BTF guidelines recommend maintaining CPP between 50 and 70 mm Hg with the goal of avoiding cerebral hypotension rather than aggressive increase of CPP. Optimization of CPP in the normotensive patient with neurotrauma should begin with attempts to lower ICP, because the ICP response to CPP increase is not predictable when autoregulation is compromised.[28]

EVIDENCE FOR CURRENT THERAPIES WITH NEUROTRAUMA

ICP Monitoring

Intracranial hypertension has been correlated with poor outcome in patients with severe TBI. Comatose patients with GCS less than or equal to 8 are at highest risk.[18,29] In

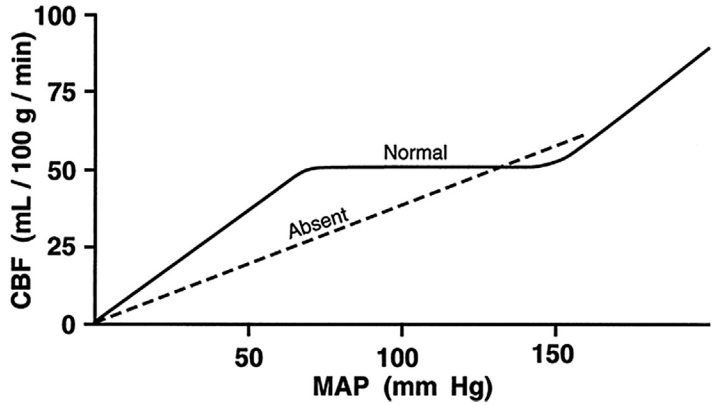

Fig. 1. Cerebral autoregulation. In the normal brain with intact cerebral autoregulation, compensatory mechanisms maintain constant CBF over a range of mean arterial pressures (MAP). In the injured brain with impaired or absent cerebral autoregulation, CBF depends directly on MAP, thus optimization of MAP and associated CPP is critically important. (*Adapted from* Drummond JC, Patel PM. Neurosurgical anesthesia. In: Miller RD, editor. Anesthesia. 5th edition. Philadelphia: Churchill Livingstone; 2000. p. 1901.)

a prospective series of patients with severe TBI, Narayan and colleagues[29] found that comatose patients with abnormal computed tomography (CT) scans have an incidence of intracranial hypertension of 55% to 63% compared with those with normal CT scan at admission (13%). However, the risk of intracranial hypertension was similar for patients with normal CT scans if they had 2 of 3 risk factors: age greater than 40 years, unilateral or bilateral motor posturing, or systolic blood pressure less than 90 mm Hg. In the largest prospective observational study that analyzed ICP in increments of 5 mm Hg, ICP greater than 20 mm Hg had the most predictive value.[18]

ICP monitoring can be the first indicator of worsening intracranial disorder.[30] Without ICP monitoring, CPP cannot be used as a therapeutic target for resuscitation and intervention. A pressure transduction device for ICP monitoring can be placed in the epidural, subdural, subarachnoid, parenchymal, or ventricular location. The ventricular fluid–coupled ICP monitor is the established reference standard for measuring ICP. Parenchymal transducer devices have similar accuracy to ventricular ICP devices but have the potential for drift because of the inability to recalibrate.[31] The 2 most common complications associated with invasive ICP monitoring are infection and intracranial hemorrhage. Although it has been standard of care per recommendations by the BTF guidelines, ICP monitoring has not been shown to improve outcome. In 2012, a multicenter randomized trial of 324 patients with severe TBI found that therapy targeted to maintain ICP less than 20 mm Hg was not superior to therapy based on clinical examination.[32] It would be incorrect to extrapolate results from this study to indicate that ICP monitoring is optional; the results from this randomized controlled trial indicate that more research is needed to better understand the complexities of cerebral hemodynamics. ICP remains a robust predictor of outcome but management of intracranial hypertension should be a clinical decision.

Surgical Decompression

Surgical management of TBI includes evacuation of intracranial mass lesions, repair of depressed skull fractures, as well as decompressive craniectomy for refractory intracranial hypertension. **Table 3** summarizes recommendations for surgical intervention.

The use of decompressive craniectomy for treatment of refractory intracranial hypertension was studied in the multicenter DECRA (Decompressive Craniectomy in Diffuse Traumatic Brain Injury) trial.[33] Bifrontotemporoparietal decompression was performed in randomized patients with severe TBI who failed ICP management with first-tier interventions. Although decompressive craniectomy decreased ICP compared with standard care, the craniectomy group had worse functional outcomes. There have been many discussions and criticisms regarding the DECRA trial.[34–36] However, decompressive craniectomy is an area of ongoing study with the current multicenter RESCUEicp (Randomised Evaluation of Surgery with Craniectomy for Uncontrollable Elevation of Intra-Cranial Pressure) trial.[37]

The timing of surgical management of unstable spinal fractures/subluxations was studied in the Surgical Timing in Acute Spinal Cord Injury Study (STASCIS).[38] Early decompression performed within 24 hours of injury had higher odds of improving neurologic outcome by a 2-grade improvement on the American Spinal Injury Association (ASIA) impairment scale (**Table 4**).

Hyperosmolar Therapies

Hyperosmolar therapy is a key component in the medical management of intracranial hypertension. Both mannitol and HTS are effective in decreasing ICP and improving CPP by their capacity to decrease brain water.[39–41] They also seem to increase CBF in regions of hypoperfusion.[42]

Table 3
Recommendations for surgical management of TBI

	Indications for Surgery
Epidural hematoma	EDH >30 cm^3 GCS <9 with anisocoria
Subdural hematoma	SDH clot thickness >10 mm or midline shift >5 mm, regardless of GCS GCS decline by $\geq$2 Asymmetric or fixed and dilated pupils ICP >20 mm Hg
Parenchymal lesions	Progressive neurologic deterioration, refractory intracranial hypertension, or signs of mass effect on CT referable to the lesion GCS 6–8 with frontal or temporal contusions >20 cm^3, midline shift $\geq$5 mm, or cisternal compression on CT Any lesion >50 cm^3
Posterior fossa lesions	Mass effect on CT, neurologic dysfunction or deterioration referable to the lesion
Depressed skull fractures	Open (compound) fractures greater than thickness of cranium Open (compound) fractures with dural penetration, significant intracranial hematoma, depression >1 cm, frontal sinus involvement, gross cosmetic deformity, wound infection, pneumocephalus, or gross wound contamination

Abbreviations: EDH, epidural hematoma; SDH, subdural hematoma.
Data from Bullock MR, Chesnut R, Ghajar J, et al. Guidelines for the surgical management of traumatic brain injury. Neurosurgery 2006;58(Suppl):S2-1–3.

Mannitol has been an osmotic agent in clinical practice for 5 decades, replacing the use of urea and glycerol. Administered as a 20% solution, immediate rheological effects include increased deformability of erythrocytes and decreased blood viscosity, thereby increasing CBF in hypoperfused regions.[43–45] In brain regions with intact autoregulation, compensatory vasoconstriction decreases cerebral blood volume with associated decrease in ICP.[44,46,47] The osmotic effect is delayed while a gradient is established between plasma and cells. Rebound increase in ICP is possible because mannitol is not impermeable to the blood-brain barrier.[48,49] The associated osmotic diuretic effect of mannitol may compromise intravascular volume. There is also a risk of renal failure with cumulative doses of mannitol.[50]

Table 4
ASIA impairment scale

ASIA A	Complete injury	No sensory or motor function preserved in sacral segments S4–S5
ASIA B	Incomplete sensory injury	Sensory but not motor function preserved below neurologic level and includes sacral segments (motor complete)
ASIA C	Incomplete motor injury	Motor function preserved below neurologic level and more than half of key muscles below neurologic level have muscle grade <3 (motor useless)
ASIA D	Incomplete motor injury	Motor function preserved below neurologic level and more than half of key muscles below neurologic level have muscle grade $\geq$3 (motor useful)
ASIA E	Normal function	—

Worksheet for dermatomes and grading of muscle function and ASIA scale is available at www.asia-spinalinjury.org.

The use of HTS for intracranial hypertension was discovered from studies on small-volume resuscitation in patients with polytrauma with hemorrhagic shock in which the TBI subgroup had the greatest benefit in survival.[51] HTS can be given in concentrations ranging from 2% to 23.4% solutions. It has similar rheological effects that improve CBF[52–54] and osmotic effects that decrease brain water content.[41,55] Because sodium chloride is impermeable to the intact blood-brain barrier, the theoretic risk of rebound increase in ICP is less than that of mannitol. Although HTS also has a diuretic effect through stimulation of atrial natriuretic peptide release, the risk of hypovolemia is less. The most common adverse effect with the use of HTS containing chloride is hyperchloremic metabolic acidemia.

There are few clinical studies that directly compare hyperosmolar therapies in brain injury in a randomized fashion. A retrospective review of patients with TBI treated with mannitol and 23.4% HTS showed a longer duration of ICP reduction with 23.4% HTS despite a smaller osmotic load administered.[56] HTS effectively lowered ICP in who that were refractory to mannitol.[57,58] Compared as isovolume interventions, 7% HTS was superior to mannitol in ICP reduction.[59] However, compared as equimolar interventions, both mannitol and 7.45% HTS were effective in decreasing ICP, although mannitol was also observed to improve CPP.[60]

Steroids

Steroids were introduced in the early 1960s as treatment of brain edema from experimental evidence that showed restoration of altered vascular permeability, reduction of CSF production, and attenuation of free radical production.[61,62] For many years, steroids became common in the treatment of head injury. However, several studies have called into question the benefit of glucocorticoid therapy in TBI. In 2004, the multicenter international CRASH (Corticosteroid Randomization After Significant Head Injury) trial changed the landscape of steroid therapy in TBI. This study of 10,008 patients from 239 hospitals in 49 countries was stopped early because interim analysis showed an increased risk of death in the steroid group, even when patients were adjusted for extracranial injuries.[63] When the CRASH trial results are included in a meta-analysis, the absolute risk of death with corticosteroids in TBI is 2%.

The use of steroids in SCI is controversial. The National Acute Spinal Cord Injury Studies (NASCIS)[64,65] suggested that high-dose methylprednisolone given within 8 hours of injury for a duration of 24 hours improved neurologic recovery. Criticisms of these studies included that these conclusions were reached by post hoc analyses. A multicenter study by Otani and colleagues was also flawed by the lack of blinding.[66] Current guidelines by the American Association of Neurologic Surgeons (AANS) and the Congress of Neurologic Surgeons (CNS) do not recommend the use of steroids in SCI.[67]

Induced Hypertension

Cardiovascular instability can be seen in patients with acute SCI above the level of T4 caused by the loss of sympathetic tone. This autonomic instability is most common during the first week after injury.[68] Hemodynamic augmentation with volume resuscitation and vasopressors to maintain a mean arterial pressure goal greater than or equal to 85 mm Hg is commonly used in practice per recommendations by the AANS/CNS guidelines.[67] However, complications including arrhythmias, electrocardiogram/troponin changes, and acidosis have been reported with vasopressor use in SCI.[69] Further studies are necessary to determine whether blood pressure augmentation has an impact on outcomes following SCI and the most appropriate threshold and duration of therapy.

Pharmacologic Coma

Barbiturates have been shown to reduce ICP in patients with refractory intracranial hypertension.[70] Their ICP reducing and cerebral protective effects have been attributed to alterations in vascular resistance, suppression of cerebral metabolism, and inhibition of neuronal excitotoxicity.[71,72] High-dose barbiturates have risks and can cause numerous complications including hypotension, gastroparesis, and immunosuppression.[73,74] A Cochrane Review in 2012 did not find any evidence that barbiturates improved outcome in patients with severe TBI. Instead, barbiturate therapy resulted in a decrease in blood pressure in 1 in 4 treated patients.[75]

Hypothermia

Prophylactic hypothermia, used irrespective of ICP, has been studied as a potential neuroprotectant. Despite promising data from small single-center studies, a Cochrane Review in 2009 found no benefit in mortality or outcome.[76] A follow-up multicenter study was terminated for futility in adults with severe TBI.[77] A meta-analysis of 13 trials with a total of 1339 randomized patients found nonsignificant improvements in mortality and neurologic outcome, but the benefits were greatest when cooling was maintained for more than 48 hours and in patients who were not receiving barbiturates for ICP management.[78]

In contrast, therapeutic hypothermia has been shown to be effective in reducing intracranial hypertension. The beneficial effect on ICP is seen in patients with severe TBI,[79] malignant stroke,[80] and even acute hepatic failure.[81] Fever is a strong independent predictor of worse clinical outcome across a variety of brain injuries.[82–84] Targeted temperature management reduces cerebral metabolic rate[85] and posttraumatic release of excitatory neurotransmitters,[86] and attenuates the opening of the blood-brain barrier.[87] Failure of this beneficial effect to translate to improved neurologic outcomes may be caused by rebound ICP increases associated with rewarming.[80]

Hypothermia has also been promising in SCI in preclinical studies.[88] It is currently an experimental clinical therapy. A multicenter trial is being planned to evaluate its effects.

Seizure Prophylaxis

Seizures occur in 10% to 30% of patients with TBI, with the incidence close to 50% in penetrating brain injury. Posttraumatic seizures (PTS) are classified as early, occurring within 7 days of injury, or late, occurring after 7 days following injury. In the acute post-injury period, seizures may worsen outcome by increasing cerebral metabolism and ICP, resulting in excess neurotransmitter release and potential cerebral ischemia. **Table 5** presents risk factors for development of PTS.

Temkin and colleagues[89] conducted a large randomized controlled trial of 404 patients with TBI evaluating the effect of phenytoin on early and late PTS. Treatment with phenytoin had a significant reduction in the incidence of early but not late PTS. Other antiepileptic drugs have also been studied in the prophylaxis of PTS. Compared with phenytoin, valproate is as effective for prophylaxis of PTS, but there was a trend toward higher mortality in patients treated with valproate.[90] An equal rate of early PTS was found when levetiracetam was compared with phenytoin.[91]

From these studies, BTF recommends the use of antiepileptic medications for 1 week following injury to decrease the incidence of early PTS. However, the available evidence does not show that prevention of PTS improves outcome.

Table 5
Risk factors for PTS

Risk Factors for Early PTS	Risk Factors for Late PTS
GCS ≤10	Early PTS
Immediate seizures	Cortical contusion
Cortical contusion	Loss of consciousness
Depressed skull fracture	Posttraumatic amnesia lasting >24 h
Penetrating head injury	Acute intracerebral hematoma
No or brief loss of consciousness	Age >65 y
Posttraumatic amnesia lasting >30 min	
Subdural, epidural, or intracerebral hematoma	
Age ≤65 y	

Data from Torbic H, Forni A, Anger KE, et al. Use of antiepileptics for seizure prophylaxis after traumatic brain injury. Am J Heal Pharm 2013;70(9):759–66.

Infection Prophylaxis

Infections contribute to morbidity, mortality, and increased hospital length of stay of any critically ill patient, including patients with neurotrauma. Patients with severe TBI are at risk for infections associated with ICP monitoring as with any other invasive monitoring. The incidence of infection with ICP monitors is reported to be as high as 22%, but this depends on the method of detection.[92] In a cohort of 584 patients with severe TBI, Holloway and colleagues[93] found the risk of external ventricular drain (EVD) infection increased over the first 10 days but there was no difference in the infection rate with routine catheter exchange. There is limited and conflicting evidence for prophylactic antibiotics throughout the duration of use of an EVD.[94] In a multicenter trial, Zabramski and colleagues[95] found that catheters impregnated with minocycline and rifampin reduced CSF infection rates and catheter colonization. There is no consensus on the use of prophylactic antibiotics with ICP monitoring, but periprocedural antibiotics are commonly used.[96]

Because basilar skull fractures and CSF leakage have been associated with the risk of meningitis, antibiotics are often given prophylactically. However, a Cochrane Review in 2011 did not support this practice.[97] The common use of prophylactic antibiotics for compound skull fractures has also been based on limited evidence.[98]

FUTURE OF NEUROCRITICAL CARE

Care of the critically ill patient with neurologic injury has grown into a specialty of neurocritical care. Practitioners have multidisciplinary backgrounds and are content experts in both critical care and neurologic disorders. Implementation of a specialized neurocritical care team has been shown to reduce hospital length of stay and in-hospital mortality of neurocritically ill patients.[99] Research in neurocritical care includes neuroprotection; however, to date, no single medication has proved beneficial in the outcome of the patient with neurologic injury. Research in advanced magnetic resonance imaging may improve prognostic accuracy. Real-time bedside monitoring of cerebral physiology may provide more relevant physiologic end points for resuscitation of the critically ill patient with neurologic injury.

SUMMARY

Neurotrauma continues to be a significant cause of morbidity and mortality. Prevention of primary neurologic injury is a critical public health concern. Early and thorough

assessment of the patient with neurotrauma with high index of suspicion of traumatic spinal cord injuries and traumatic vascular injuries requires a multidisciplinary approach involving prehospital providers, emergency physicians, neurosurgeons, and neurointensivists. Critical care management of the patient with neurotrauma is focused on the prevention of secondary injuries. Much research is still needed for potential neuroprotection therapies.

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