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Management of Head Trauma*

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Traumatic brain injury (TBI) is a major cause of disability and death in most Western nations and consumes an estimated $100 billion annually in the United States alone. In the last 2 decades, the management of TBI has evolved dramatically, as a result of a more thorough understanding of the physiologic events leading to secondary neuronal injury as well as advances in the care of critically ill patients. However, it is likely that many patients with TBI are not treated according to current treatment principles. This article presents an overview of the current management of patients with TBI.

Key words: critical care; CT scanning; epidural hematoma; head injury; hypertonic saline solution; ICU; intracranial pressure; mannitol; subdural hematoma; trauma

Abbreviations: CBF = cerebral blood flow; CPP = cerebral perfusion pressure; CSF = cerebrospinal fluid; GCS = Glasgow Coma Scale; ICP = intracranial pressure; TBI = traumatic brain injury

The management of traumatic brain injury (TBI) has evolved dramatically in the last 2 decades. This is the result of a more thorough understanding of the physiologic events leading to secondary neuronal injury after TBI, as well as advances in the care of critically ill patients. Despite enormous progress in the understanding of TBI, current opinion suggests that the majority of patients are not treated according to current treatment guidelines.1,2 This article presents an overview of the current management of patients with TBI.

Epidemiology

TBI is a leading cause of death and disability in children and adults in their most productive years. It is estimated that there are nearly 1.6 million head injuries every year in the United States, with > 250,000 of these patients being admitted to the hospital.3,4 Overall, each year there are approximately 60,000 deaths from TBI and an estimated 70,000 to 90,000 patients are left with permanent neurologic disabilities.3,5,6 The financial burden of TBI in terms of both lost productivity and the cost of medical care is estimated to be approximately $100 billion annually in the United States alone.3,5,6 Motor vehicle accidents are the most common cause of closed head injuries and are especially common in teenagers and young adults.7 Falls are responsible for the next largest group of injuries and are more common at the extremes of age. Alcohol as been shown to be a contributing factor in approximately 40% of all severe head injuries.7

Pathophysiology

Primary Brain Injury

The pathophysiology of primary brain injury can be divided into focal and diffuse lesions. Focal brain injury is typically associated with blows to the head that typically produce cerebral contusions and hematomas. Focal injuries impact morbidity and mortality based on their location, size, and overall progression. Diffuse axonal injury is caused by inertial forces that are commonly produced by motor vehicle accidents. In clinical practice, diffuse axonal injury and focal brain lesions frequently coexist. The common types of primary head injuries are discussed below:
Skull Fractures: Skull fractures may be seen in the cranial vault or skull base, may be linear or stellate, and may be depressed or nondepressed. The presence of a skull fracture implies that a large amount of force was transmitted to the patient’s head. A linear vault fracture increases the likelihood of the presence of an intracranial hematoma. Basilar fractures may manifest as hemotympanum, postauricular ecchymosis (Battle sign), periorbital ecchymosis, and possible cranial nerve palsies.

Epidural Hematomas: Epidural hematomas are relatively uncommon, being present in < 1% of all head-injured patients and in < 10% of those who are comatose. Epidural hematomas are located outside the dura but within the skull, and are typically biconvex or lenticular in shape (Fig 1). They are most often located in the temporal or temporoparietal region, and often result from laceration of the middle meningeal artery caused by a fracture. In many cases, but not always, there is loss of consciousness followed by a period of lucency, followed by neurologic deterioration. With prompt evacuation, patients usually have a relatively favorable outcome.

Subdural Hematomas: Subdural hematomas are more common than epidural hematomas, occurring in approximately 30% of severe head injuries. They result most frequently from tearing of a bridging vein between the cerebral cortex and a draining venous sinus. With subdural hematomas, the force of impact is often transmitted to the brain itself. In approximately 80% of subdural hematomas, it is the underlying brain injury that determines the patient’s course and outcome. A subdural hematoma will appear on a CT scan as a crescent-shaped blood collection between the brain and the dura (Fig 2). There is frequently an adjacent parenchymal contusion, and if large may cause a midline shift.

Intracerebral Hematomas: Intracranial hemorrhage occurs commonly in association with moderate and severe head injuries and usually produces mass lesions. The majority of lesions occur in the frontal and temporal lobes. During sudden rotations of the head, the intraparenchymal blood may be transmitted to the ventricular system, especially into the frontal horns of the lateral ventricles. This is of particular concern in those with a subdural hematoma, in whom the risk of intraventricular hemorrhage is increased. In severe cases, this may result in an acute rise in intracranial pressure and death if not promptly treated by surgery and, in some cases, can cause herniation of the brain through a weakened point on the dura or the falx cerebri.

Figure 1. CT scan demonstrating a right temporal epidural hematoma (arrow).

Figure 2. CT scan demonstrating a large right subdural hematoma with midline shift (arrow).
head, these regions impact on the rough surface of the underlying skull base, causing so called “gliding contusions.” Blood within the parenchyma of the brain will be seen as a hyperdense areas on the CT scan (Fig 3). Many intraparenchymal hematomas may be delayed, appearing on the CT scan ≥ 24 h after the initial insult. Therefore, clinical deterioration or progressive uncontrolled intracranial hypertension should prompt repeat CT scanning.

**Diffuse Axonal Injury:** Diffuse axonal injury is caused by shearing forces affecting axons that traverse large areas of the brainstem, leading to dysfunction of the reticular activating system. It is believed that axons are not torn at the moment of injury but rather undergo sequential, focal changes that lead to swelling and disconnection over multiple hours after injury. As a consequence of this disconnection, the downstream disconnected fibers degenerate leading to diffuse deafferentation of target sites. Evidence suggests that the traumatic axon injury results from damage to the axolemma, allowing for calcium influx, triggering local intra-axonal cytoskeletal and mitochondrial damage. In addition, an increase in intra-axonal caspase-3 suggests that apoptosis may play a role in the demise of the axonal appendage. Diffuse axonal injury may cause immediate and prolonged unconsciousness. Affected patients have a high morality, and if they survive, a high morbidity, often improving only to a persistent vegetative state. Diffuse axonal injury may be identified by diffusion-weighted MRI.

**Secondary Brain Injury**

The primary brain injury is the result of direct mechanical damage that occurs at the time of trauma. Secondary brain injury occurs after the initial trauma and is defined as the damage to neurons due to the systemic physiologic responses to the initial injury. A number of biochemical substances have been postulated to play a role in the propagation of neural injury following TBI. The release of these substances initiates a deleterious cascade of continued cell membrane breakdown and ionic shifts that further harms the injured brain. These substances include the excitatory amino acids glutamate and aspartate, cytokines, and free radicals.

The importance of hypotension and hypoxia as major causes of secondary brain injury have become recognized. Seminal studies published in 1978 and 1982 by Miller and colleagues established that hypotension and hypoxia occurring during the early posttraumatic period were primary determinants of outcome. These observations were confirmed by the Traumatic Coma Data Bank study, which demonstrated that prehospital hypotension was an independent predictor of poor outcome. During the first 24 h after head injury, cerebral blood flow (CBF) is less than half of that of normal individuals and may approach the ischemic threshold. Furthermore, CBF in the vicinity of the posttraumatic contusions and subdural hematoma is reduced even further than global CBF. The reduction in CBF following trauma together with the vulnerability of the traumatized brain to ischemia makes hypotension a potentially lethal complication. In patients who have died from head injury, posttraumatic ischemic lesions have been reported in up to 80% of patients at autopsy.

**Role of Intracranial Pressure and Cerebral Perfusion Pressure**

The cranial vault is a fixed space (closed box) that contains brain tissue, cerebrospinal fluid (CSF), extracellular fluid, and blood. These tissues are largely incompressible. After head trauma, the vol-

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**Figure 3.** CT scan demonstrating multiple hemorrhagic contusions in the bifrontal region, and left temporal and parietal region with surrounding edema (arrows).
ume within the intracranial compartment increases due to blood and tissue edema. Initially, small increases in intracranial volume can be accommodated by the movement of blood and CSF out of the vault. However, with further expansion of its contents, intracranial pressure (ICP) increases sharply. Intracranial hypertension itself is not harmful unless it increases to the point that the cerebral perfusion pressure falls below a critical value. Cerebral ischemia leads to neuronal injury and cerebral edema, which further increases ICP, progressing to irreversible neurologic damage. Raised ICP may also result in pressure gradients that lead to displacement and herniation of brain from areas of higher to areas of lower pressure.

CBF in humans averages approximately 50 mL/100 g of brain tissue per minute. Irreversible neuronal damage occurs if CBF drops < 18 mL/100 g of brain tissue per minute for a prolonged period of time. CBF is equal to the cerebral perfusion pressure (CPP), which is defined as the difference between the mean arterial BP and the ICP, divided by the cerebral vascular resistance. Because the CBF is difficult to measure clinically, the CPP is used as a guide to assessing the adequacy of cerebral perfusion. The normal ICP is between 0 mm Hg and 10 mm Hg. Increased ICP has been defined as a pressure > 20 mm Hg persisting for ≥ 5 min. Normal human values for CPP are between 70 mm Hg and 100 mm Hg. However, as a result of autoregulation, CBF remains relatively constant when CPP is between 40 mm Hg and 140 mm Hg (Fig 4). This phenomenon is due to changes in cerebrovascular resistance probably brought about by a local effect of hydrogen ions on cerebral vessels. Thus, low flow states leading to hypoxia or hypercapnia result in an acidosis that causes cerebral vasodilation and increased blood flow. Chronic hypertension shifts the autoregulation curve to the right, making hypertensive patients susceptible to ischemia at a CPP normally well tolerated by healthy subjects (Fig 4). Cerebrovascular autoregulatory mechanisms are disrupted following head trauma, with CBF dependent largely on the CPP.

While earlier studies and recommendations centered on the importance of the ICP per se in the head-injured patient, current guidelines emphasize the importance of the CPP. The guidelines proposed by the Brain Trauma Foundation recommend that the CPP should be maintained at a minimum of 70 mm Hg in the brain-injured patient, although the exact target number and methodology for achieving that target remains controversial. A higher threshold may be required in patients with chronic hypertension.

CLINICAL EVALUATION OF THE HEAD-INJURED PATIENT

Primary Trauma Survey

The first priority in any injured patient is to stabilize the cervical spine, establish an adequate airway (A, airway), ensure adequate ventilation (B, breathing), and gain venous access to initiate volume resuscitation (C, circulation). These steps are crucial in the head-injured patient to avoid both hypoxia and hypotension, the most important causes of secondary brain insults. The primary survey should conclude with a determination of the level of consciousness and an examination of the pupils (D, disability).

Secondary Trauma Survey

A secondary survey is completed once the patient is relatively stable and includes a complete neurologic examination. The severity of the head injury is classified clinically by the Glasgow Coma Scale (GCS) [Table 1]. A GCS score of 13 to 15 is classified as a mild head injury, as score of 9 to 12 as moderate, and a score of ≤ 8 as severe. Caution should be used in evaluating patients suspected of intoxication with alcohol or other drugs. All too often, an obtunded state in such patients is attributed to the abused substance, when in fact the intoxication may be masking an expanding intracranial mass lesion.

INITIAL MANAGEMENT

The primary brain injuries sustained at the time of trauma cannot be reversed. In order to minimize...
secondary brain damage, the initial management of any patient with TBI is to prevent hypoxia, maintain an adequate BP (ie, CPP), and to recognize and treat surgically correctable intracranial lesions. In addition, other concomitant injuries should be recognized and stabilized.

**Prehospital Phase**

The prehospital phase is perhaps the most important interval in determining the ultimate outcome after TBI. The initial goals are to maintain a patent airway, begin fluid resuscitation, immobilize the cervical and thoracolumbar spine, and assess the level of consciousness, followed by the expeditious transport to a trauma center with neurologic services. Approximately 50% of TBI patients are reported to be hypoxic in the field; this finding is associated with an increased mortality.41–43 A retrospective case control study44 suggested that prehospital intubation was associated with a significant reduction in mortality of patients with TBI. Early orotracheal intubation is therefore recommended in patients with a GCS score \( \leq 8 \) or are unable to protect their airway should be intubated early. Precautions in intubation need to be taken in the patient with an uncleared cervical spine, because the incidence of concomitant spine injury in head-injury patients ranges from 6 to 8%.50,51 Rapid-sequence induction anesthesia is recommended to avoid the increases in ICP that may occur with airway stimulation associated with laryngoscopy and intubation. Hypnotic agents that reduce vascular tone should be avoided. Etomidate, 0.2 to 0.4 mg/kg, a rapidly acting hypnotic agent with a short duration of action and minimal hemodynamic effects, is the preferred agent.52–54 Rocuronium is a short-acting, nondepolarizing muscle relaxant that is devoid of significant hemodynamic effects and does not increase ICP.55,56 Rocuronium is considered the drug of choice for rapid-sequence induction in many trauma facilities.55–57 Etomidate has no analgesic properties and does not blunt the sympathetic response to endotracheal intubation.52 Esmolol, 20 to 40 mg, or fentanyl, 50 to 100 \( \mu \)g, are therefore suggested in combination with etomidate.58

Once the patient is intubated, the patient should be placed on 100% oxygen, with the inspired fraction of oxygen only titrated down once the patient has been transferred to the ICUs. Aggressive hyperventilation (Pa\( \text{CO}_2 \) of 25 mm Hg) has traditionally been considered a cornerstone in the management of TBI because it is causes a rapid reduction in ICP. However, hyperventilation reduces ICP by causing cerebral vasoconstriction with a subsequent reduction in CBF. Skippen and colleagues,27 using xenon-enhanced CT and CBF studies, demonstrated a 2.5-fold increase in the number of regions of brain ischemia in children with TBI who were hyperventilated. In 1991, Muizelaar and colleagues59 published the results of a prospective randomized

### Table 1—GSC

<table>
<thead>
<tr>
<th>Signs</th>
<th>Score</th>
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</thead>
<tbody>
<tr>
<td>Eye opening</td>
<td></td>
</tr>
<tr>
<td>Spontaneous</td>
<td>4</td>
</tr>
<tr>
<td>To verbal command</td>
<td>3</td>
</tr>
<tr>
<td>To pain</td>
<td>2</td>
</tr>
<tr>
<td>No response</td>
<td>1</td>
</tr>
<tr>
<td>Best motor response</td>
<td></td>
</tr>
<tr>
<td>Obey verbal commands</td>
<td>6</td>
</tr>
<tr>
<td>Localizes to pain</td>
<td>5</td>
</tr>
<tr>
<td>Withdraws to pain</td>
<td>4</td>
</tr>
<tr>
<td>Flexion response to pain</td>
<td>3</td>
</tr>
<tr>
<td>Extension response to pain</td>
<td>2</td>
</tr>
<tr>
<td>No response</td>
<td>1</td>
</tr>
<tr>
<td>Best verbal response</td>
<td></td>
</tr>
<tr>
<td>Orientated</td>
<td>5</td>
</tr>
<tr>
<td>Confused</td>
<td>4</td>
</tr>
<tr>
<td>Inappropriate words</td>
<td>3</td>
</tr>
<tr>
<td>Nonspecific sounds</td>
<td>2</td>
</tr>
<tr>
<td>No response</td>
<td>1</td>
</tr>
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require fluid resuscitation. While lactated Ringer’s solution is generally recommended,1,39 small volume resuscitation (250 mL) with hypertonic saline solution appears very promising in this situation.47,48 In patients with penetrating truncal trauma, Bickell et al49 reported that volume resuscitation initiated only after arrival at the hospital was associated with an improvement in survival compared to immediate prehospital resuscitation. This approach to fluid resuscitation is not applicable to hypotensive patients with TBI who are usually victims of blunt trauma. Delayed volume resuscitation in patients with head injuries is likely to increase the extent of secondary brain injuries.

**Early Hospital Management**

Patients who have not been intubated in the field and have a GCS score \( \leq 8 \) or are unable to protect their airway should be intubated early. Precautions in intubation need to be taken in the patient with an uncleared cervical spine, because the incidence of concomitant spine injury in head-injury patients ranges from 6 to 8%.50,51 Rapid-sequence induction anesthesia is recommended to avoid the increases in ICP that may occur with airway stimulation associated with laryngoscopy and intubation. Hypnotic agents that reduce vascular tone should be avoided. Etomidate, 0.2 to 0.4 mg/kg, a rapidly acting hypnotic agent with a short duration of action and minimal hemodynamic effects, is the preferred agent.52–54 Rocuronium is a short-acting, nondepolarizing muscle relaxant that is devoid of significant hemodynamic effects and does not increase ICP.55,56 Rocuronium is considered the drug of choice for rapid-sequence induction in many trauma facilities.55–57 Etomidate has no analgesic properties and does not blunt the sympathetic response to endotracheal intubation.52 Esmolol, 20 to 40 mg, or fentanyl, 50 to 100 \( \mu \)g, are therefore suggested in combination with etomidate.58

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clinical study in which they demonstrated that hyperventilation after head injury was associated with a significantly worse neurologic outcome when compared to patients who were kept normocapnic. Based on this data, long-term hyperventilation is no longer recommended.\textsuperscript{1,60} Initial target P\textsubscript{aco}_2 should be 35 to 40 mm Hg.\textsuperscript{1,60} Short-term hyperventilation, however, may have a role in reducing cerebral perfusion pressures > 70 mm Hg.\textsuperscript{1} These guidelines use 20 mm Hg as the threshold for intracranial hypertension.\textsuperscript{1}

Previous guidelines\textsuperscript{62} recommended moderate-to-severe dehydration in the treatment of TBI on the basis that this would decrease cerebral edema. However, experimental studies\textsuperscript{63,64} demonstrated that cerebral water content and cerebral edema were not altered by hydration status. Furthermore, this approach failed to recognize the importance of the CPP in preventing secondary brain ischemia. Volume resuscitation with restoration of a normal intravascular volume is therefore essential in all patients with acute cerebral insults.

Currently, lactated Ringer’s solution or normal saline solution are recommend for volume resuscitation in head-injured patients.\textsuperscript{39} Hypotonic solutions should not be administered, as these will increase cerebral edema.\textsuperscript{65,66} Hypertonic saline solution has a number of beneficial effects in head-injured patients, including the expansion of intravascular volume, the extraction of water from the intracellular space, a decrease in the ICP, and increase in cardiac contractility.\textsuperscript{67–70} Despite serum sodium concentrations as high as 170 mEq/L, hypertonic saline solution is well tolerated in head-injured patients.\textsuperscript{71–73} Wade and colleagues\textsuperscript{74} performed a cohort analysis of individual patient data from prospective, randomized, double-blind trials to evaluate the effect on survival after initial treatment with hypertonic saline solution in patients with TBI. Using logistic regression analysis, these authors\textsuperscript{74} concluded that hypertonic saline solution significantly improved survival (odds ratio, 2.12; p = 0.048). The indications as well as the optimal timing, concentration, and volume of hypertonic saline solution have yet to be determined by prospective clinical studies. However, hypertonic saline solution appears to have promise in the initial resuscitation of head-injured patients. The prophylactic use of mannitol is not recommended due to its volume-depleting diuretic effect.\textsuperscript{75} Mannitol should only be used initially in patients demonstrating signs of transtentorial herniation.\textsuperscript{61}

Diagnostic Studies: Historically, imaging of the head-injured patient relied on skull radiographs.\textsuperscript{76} With the widespread availability and advancement of head CT scanning, the CT scan has become the diagnostic procedure of choice when evaluating acute head trauma. CT scanning is recommended in patients considered to be at high risk for intracranial injury. This includes all patients with a GCS score < 15 and patients with focal neurologic deficits or clinical signs of basilar or depressed skull fractures. While it is generally recommended to scan patients with a GCS score of 15 and a history of loss of consciousness or amnesia, not all investigators believe this to be a cost-effective approach.\textsuperscript{77–79} A CT scan without contrast will enable visualization of most major types of injuries.

Abnormalities noted on CT imaging associated with intracranial hypertension include subdural hematomas, subarachnoid hemorrhage, intracerebral hematomas, cerebral infarcts, diffuse brain injury, and generalized cerebral edema often with shift of midline structures, effacement of cortical sulci, and ventricular compression.\textsuperscript{80–82} However, it should be emphasized that a normal initial CT scan does not exclude significant intracranial hypertension.\textsuperscript{17,82}

Neurosurgical Consultation: Once the patient’s condition is stabilized, neurosurgical consultation is required. The critical factors in deciding whether to proceed directly with surgical evacuation of an intracranial hematoma are the patient’s neurologic status and the CT scan findings. In general, all acute traumatic extra-axial hematoma ≥ 1 cm in thickness warrant evacuation; a subdural or epidural hematoma > 5 mm in thickness with an equivalent midline shift in a comatose patient (GCS score ≤ 8) should also be evacuated urgently. Surgical evacuation has been recommended in patients with intracerebral hematomas > 20 mL with mass effect.\textsuperscript{83,84} Surgical repair is also required in patients with depressed, open, and compound skull fractures.

Disposition: Head-injured patients with no loss of consciousness, no amnesia, no palpable fractures, and a GCS score of 15 can be discharged home to a reliable caretaker without brain imaging. Written instructions on how to evaluate the patient at home should be given. The patient should undergo follow-up with his primary care physician, with instructions to return to the emergency department if there
are any signs indicating increased ICP, such as change in mental status. Patients with loss of consciousness, amnesia, or a GCS score of 13 to 14 must undergo an immediate head CT. If this noncontrast study finding is negative, the patient can be discharged with instructions as above. If there is a focal neurologic examination, GCS score < 13, or an intracranial lesion on head CT, the patient should be admitted to an ICU or neurologic observation unit for continuing care.

**Continuing Management in the ICU**

Once the patient is stabilized and has been transferred to the ICU, the establishment of physiologic monitoring facilitates and directs the further management of these patients. Although no randomized controlled studies have been performed demonstrating that ICP monitoring improves outcome, ICP monitoring has become an integral part of the management of patients with severe head injuries in virtually all trauma centers in the United States. The improved outcome of patients with severe head injuries in the United States has been ascribed to intensive management protocols that include ICP monitoring. Furthermore, several studies have shown that under conditions of aggressive ICP management, the probability of a good outcome is inversely proportional to the maximum ICP and the percentage of the time spent at levels of > 20 mm Hg. ICP monitoring is therefore recommended in patients with a GCS score < 8, since intracranial hypertension in this population is > 60%. Currently, available methods for ICP monitoring include extradural, subdural, intraparenchymal, and intraventricular catheters. Intraventricular catheters are preferred when possible, as these allow for continuous measurement of ICP and for drainage of CSF to control raised ICP. The role of continuous monitoring of jugular venous oxygen saturation in head injured patients is unclear.

Patients should undergo aggressive fluid resuscitation to maintain the mean arterial BP > 90 mm Hg. Volume replacement with Ringer’s lactate or normal saline is suggested. The central venous pressure should not be used as a guide to fluid replacement, as there is no correlation between central venous pressure and intravascular volume. A volumetric pulmonary artery catheter is recommended in patients who respond poorly to volume expansion, demonstrate hemodynamic instability, or have underlying cardiovascular disease. The role of vasopressor agents in TBI is controversial. While the data suggests that a decline in BP should be avoided in the head-injured patient, even when the baseline BP is high, induced hypertension may either increase or decrease ICP depending on the ability of the cerebral circulation to autoregulate. Furthermore, because of their potential vasoconstrictory effect on intracerebral vessels, vasopressors might impair local CBF, despite adequate CPP elevation. Induced hypertension with vasopressor agents should, therefore, be used with extreme caution and only with invasive hemodynamic monitoring. Dopamine is the preferred pressor, as experimental data have shown this agent to increase CBF within and around the injured brain without increasing ICP or cerebral edema. Phenylephrine, however, may increase ICP and decrease cardiac output. A potentially promising approach to increasing CBF in head-injured patients is the use of cerebral vasodilators, such as L-arginine.

Colloid solutions do not reduce ICP or cerebral water content. This is because cerebral capillaries have extremely tight intercellular junctions and few microvesicles and, as such, are impermeable to most ions. It is the osmotic pressure, rather than the plasma oncotic pressure, that is the major determinant of water movement between the vascular and the extravascular compartments of those areas where the blood-brain barrier is intact. In patients with leaky capillaries, albumin has been demonstrated to increase interstitial fluid volume. Albumin administration may therefore leak into the interstitium in areas where the blood-brain barrier is compromised and increase ICP. Furthermore, as albumin has been associated with an increased mortality in critically ill patients, this solution cannot be recommended.

The ventilator settings should be adjusted to maintain the PaCO$_2$ between 35 mm Hg and 40 mm Hg and the PaO$_2$ > 70 mm Hg. While it has been suggested that a high PaO$_2$ may improve brain tissue oxygenation, this goes against our understanding of human physiology, as tissue oxygen unloading is dependant primarily on the hemoglobin concentration, the position of the oxygen dissociation curve (partial pressure at which hemoglobin is 50% saturated), and the hemoglobin saturation. The dissolved oxygen fraction makes an insignificant contribution to oxygen transport. A high fraction of inspired oxygen may, however, promote the formation of reactive oxygen species and increase lipid peroxidation. While it has been suggested that positive end-expiratory pressure and modes of ventilation that increase mean intrathoracic pressure be avoided in patients with elevated ICP, studies do not support this contention. However, in accord with current guidelines, the lowest level of positive end-expiratory pressure that maintains adequate oxygenation and prevents end-expiratory alveolar collapse should be used. Continuous pulse oximetry is recommended, with the arterial saturation main-
tained > 94%. Although endotracheal suctioning does cause a transient rise in ICP, it does not produce cerebral ischemia and is required to prevent atelectasis.115

Even though head-injured patients may be comatose, they require analgesia and sedation as they still respond to painful and noxious stimuli, often with an increase in ICP and BP. Narcotics (morphine or fentanyl) should be considered first-line therapy since they provide both analgesia and depression of airway reflexes, which is required in the intubated patient. Fentanyl has the advantage of having minimal hemodynamic effects. Propofol is the hypnotic agent of choice in patients with an acute neurologic insult, as it is easily titratable and rapidly reversible once discontinued. These properties permit predictable sedation yet allow for periodic neurologic evaluation of the patient.116,117 Propofol has additional properties that may be beneficial in the head-injured patient, including a decrease in cerebral metabolic rate, potentiation of γ-aminobutyrate A (GABAergic) inhibition, and inhibition of methyl-D-aspartate glutamate receptors and voltage-dependent calcium channels.118 Propofol is also a potent antioxidant and inhibitor of lipid peroxidation.119

Paralytic agents have traditionally been used in patients receiving mechanical ventilation. There are, however, no data to support this practice. Indeed, in patients with TBI, paralytic agents have been demonstrated to increase the risk of pneumonia.120 In addition, paralytic agents are associated with significant neuromuscular complications.121 The use of adequate doses of propofol together with fentanyl may obviate the need for paralysis. The routine paralysis of patients with TBI can no longer be recommended.122 However, as it may take up to 30 min to carefully load a patient with sufficient sedation and analgesia to control airway reflexes in response to mechanical ventilation, early paralysis may be helpful in preventing ventilator dysynchrony with gagging and coughing that produce ICP surges. However, once the patient has been stabilized and adequate sedation and analgesia achieved, the neuromuscular blocker should be stopped.

Other general principles in the management of patients with head injury include lowering the body temperature of patients with fever and prevention of jugular venous outflow obstruction (keeping the patient’s head midline, avoiding extrinsic compression of the jugular veins by hematomas, masses). While some studies37,121 have suggested that CPP is optimal when patients are nursed flat, others124 have demonstrated that head elevation to 30° lowers ICP without decreasing CPP or CBF. However, elevation of the head of the bed (to 30°) has been demonstrated to reduce the risk of ventilator-associated pneumonia.125 Erosive GI lesions are common after severe head injury; therefore, routine stress ulcer prophylaxis is required.126 Seizure prophylaxis is currently recommended for 7 days following the injury in patients with severe TBI.127 The agent most commonly recommended is phenytoin, with a loading dose of 18 mg/kg and usual maintenance dose of 5 mg/kg/d following serum drug levels to a goal of 10 to 20 mg/L.

In patients with TBI, corticosteroids have been shown to lack efficacy and carry the risks of potential side effects (ie, hyperglycemia, increased risk of infections), and their use must be avoided.128–130 Experimental and initial clinical data suggested that moderate hypothermia (33°C) for 24 h after severe head injury may improve outcome.131–133 However, a recently completed, randomized, placebo-controlled, multicenter study134 demonstrated that hypothermia initiated within 8 h after injury was ineffective in improving outcomes in patients with severe brain injury. The lack of efficacy of induced hypothermia may be related to the use of neuromuscular blockers (to prevent shivering) in the hypothermic group. However, the active warming of patients who are hypothermic on hospital admission may be detrimental, and is therefore not recommended.134

Management of Established Intracranial Hypertension: If the ICP remains >20 mm Hg, despite adequate sedation and elevation of the head of the bed (to 30°), additional measures are required to lower the ICP.135 When a ventriculat catheter is being used for ICP monitoring, CSF drainage should be used for ICP elevations.136 If CSF drainage is ineffective, a hyperosmotic agent such as mannitol should be used next.136,137 The dose used is 0.25 to 0.5 g/kg administered every 2 to 6 h to increase the serum osmolarity to 310 to 320 mOsm/kg H2O.138 Mannitol acts acutely by expanding intravascular volume and decreasing blood viscosity, thereby increasing CBF.139,140 The osmotic movement of fluid out of the cellular compartment is followed by a diuresis that is delayed for 15 to 30 min while gradients are established between plasma and cells.141 The osmotic diuresis following mannitol lasts between 90 min and 6 h.142,143 The prolonged administration of mannitol may lead to intravascular dehydration, hypotension, and prerenal azotemia.144 The benefit of mannitol in head-injured patients has yet to be determined, and remarkably only one placebo-controlled study has been reported to date.145 In this study, which compared the prehospital administration of mannitol against placebo, mannitol was associated with an increased relative risk for death (1.59; 95% confidence interval, 0.44 to 5.79). Mannitol, in common with other osmotically
active agents, is known to cause “opening” of the blood brain barrier, meaning that both mannitol and other small molecules may pass into the brain. This effect becomes harmful after many doses have been administered because mannitol may accumulate in the brain, causing a reverse osmotic shift and raising brain osmolarity, thus theoretically exacerbating ICP. The accumulation of mannitol in the brain may be most marked when mannitol is in the circulation for long periods, as occurs with continuous infusion administration. Thus it has been recommended that mannitol should be administered as repeated boluses rather than as a continuous infusion. Hypertonic saline solution has been demonstrated to decrease ICP and increase CPP in patients with refractory intracranial hypertension, and should be considered an alternative to treatment with mannitol. High-dose barbiturate coma may be used as last resorts in patients with persistently elevated ICP; however, this therapy has not been proven to change neurologic outcome. Indeed, in the University of Toronto Head Injury Study, those patients with an elevated ICP and no intracranial hematoma who were treated with pentobarbital had a 77% mortality rate, compared to a 41% mortality for those patients treated initially with mannitol. Finally, there is a resurgence of interest in decompressive craniectomy for intractable ICP elevations, and craniectomy is an option to consider in selected cases.

Experimental Drug Therapies

There have been many attempts to reduce brain damage after severe head trauma using pharmacologic therapy. Free-radical scavengers, amino-steroids, calcium antagonists, glutamate antagonists, ion-channel blockers, and adenosine agonists have been evaluated in patients with TBI. To date, none of these agents have been demonstrated to be beneficial.

Other Management Issues in the ICU

Electrolyte Derangements: Hyponatremia lowers the seizure threshold and can exacerbate cerebral edema. Hyponatremia is relatively common after head injury. The etiology of the hyponatremia is complex, with both cerebral salt wasting and the syndrome of inappropriate antidiuretic hormone being implicated. Urine electrolytes and osmolarity are helpful in the evaluation of hyponatremia. The distinction between these two syndromes is critical, as the former is treated with volume replacement while the latter is treated by fluid restriction.

Magnesium levels should be closely followed in patients with TBI. Hypomagnesemia lowers the seizure threshold, and in experimental brain injury hinders recovery. Postinjury administration of magnesium has been shown to improve neurologic outcome in an experimental model of head injury.

Nutritional Support: TBI results in a generalized hypermetabolic and catabolic state. Early enteral nutrition maintains the integrity of the GI mucosa, has beneficial effects on immunocompetence, and attenuates the metabolic response to stress. A meta-analysis that compared early (within 36 h) with delayed initiation of enteral nutrition demonstrated a 55% reduction in the risk of infections in head-injured patients who received early enteral nutrition. Parenteral nutrition should be avoided, as it is associated with profound metabolic, immunologic, and GI changes and an increase in mortality. Although gastric emptying is frequently impaired following TBI, this route of feeding is generally well tolerated in head-injured patients. We recommend placement of a standard 14-gauge to 16-gauge oro gastric tube followed by the immediate initiation of an immune-enhancing nutritional formula at a rate of 20 mL/h, increased at 6-h intervals by 20 mL until the nutritional goal is achieved. Additionally, we recommend erythromycin, 250 mg IV q8h, as a promotility agent at the time of initiation of tube feedings. The gastric residual volume should be checked every 6 h; a small bowel feeding tube should be placed in patients with a residual volume > 150 mL.

Deep Venous Thrombosis Prophylaxis: Deep vein thrombosis and pulmonary embolism are frequent complications in head-injured patients. The incidence of deep-venous thrombosis in patients with major head injuries who are not receiving thromboprophylaxis is reported to be as high as 54%. Low-dose heparin and low-molecular-weight heparin are considered to be contraindicated in patients with head injuries. Sequential compression devices should be used (if possible) in all patients with TBI. However, the optimal prophylactic regimen and the indications for prophylactic vena caval filter placement in these patients remains unclear.

Conclusion

The management of patients with severe head injury is complex and requires a coordinated, comprehensive, and multidisciplinary approach. Central to the management of the head-injured patient is the prevention of secondary neuronal injury by avoiding hypotension and hypoxemia. Considering the enor-
mous costs to society, we need to invest greater resources in the prevention of this pandemic.

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