Management of Intracerebral Pressure in the Neurosciences Critical Care Unit

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KEYWORDS

• Acquired brain injury • Intracranial pressure • Intracranial hypertension • ICP • Neuromonitoring

KEY POINTS

- The management of intracerebral hypertension is a mainstay of neurocritical care, although invasive monitoring remains controversial in certain populations of acquired brain injury.
- Conservative measures to promote improved intracranial compliance should be in place in all patients with acquired brain injury.
- The type of ongoing disease should determine the type of intracranial pressure monitor placed. Limited options exist for noninvasive monitors for intracranial pressure (ICP).
- Interventions for management of ICP involve hyperventilation, hyperosmolar therapy, $CMRO_2$ (cerebral metabolic rate of oxygen)-based strategies, surgical treatment options, and *N*-methyl-D-aspartate receptor antagonists.
- Individual intensive care units should have an established treatment algorithm in place to manage increased ICP.

BACKGROUND REGARDING INTRACRANIAL PRESSURE MONITORING

Introduction

Neurocritical care has evolved to include enhanced diagnostic and treatment options over the past several decades. Central to this care delivered in the neurosciences intensive care unit (ICU) is multimodality monitoring of patients with brain injury. Perhaps second to the bedside clinical examination, the most universal continuous neurologic monitor is likely the intracerebral pressure monitor. The management of increased intracranial pressure (ICP) is discussed.

Neuro-monitoring of patients with acquired brain injury is performed for patients most severely affected by their central nervous system injury. The Glasgow Coma Scale (GCS) allows rapid classification of the severity of the brain injury and fosters

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improved communication regarding a patient's clinical status.[1] This scale classically describes patients with traumatic brain injury (TBI), but can be used to communicate the neurologic status of patients with brain injury from other causes (**Table 1**). Patients with GCS scores of 8 or less have significant neurologic injury. These patients often have abnormal neuroimaging to include computed tomography (CT) scan findings such as a skull fracture, traumatic intracranial hemorrhage, or contusional injury.[2] Rapid evacuation must occur from the point of injury to the ICU for management of the patient's critical care needs, including airway management, mechanical ventilation, neurosurgical evaluation, and neuromonitoring. These modalities may include jugular venous oximetry, brain tissue oxygenation ($Pbto_2$), cerebral microdialysis, electroencephalography (EEG), advanced neuroimaging, and ICP monitoring. Guidelines for the use of multimodality monitoring of patients with severe brain injury are published by the Brain Trauma Foundation and have been instrumental in improving care with evidence-based recommendations.[3] Guidelines are also available for the prehospital management of severe TBI, prehospital care of combat-related head trauma, and surgical management of TBI. These guidelines can be obtained online from the Brain Trauma Foundation at http://braintrauma.org. A tool to assess individual management compliance with published guidelines is available at http://tbiclickandlearn.com.[4] European guidelines for the management of severe head injury have been published by the European Brain Injury Consortium, which also discusses issues of neuromonitoring and ICP.[5] The recommendations in these guidelines have been suggested to serve as a general reference for the management of other mechanisms of brain injury in neurocritical care.[6]

Goals in the critical care management of patients who experience brain injury must address arrest of any ongoing injury, preservation of neurologic function, prevention of medical complications of critical illness, and improvement in overall outcome. These patients should be evaluated in a center with specialized neurologic care, such as neurosurgery and neurointensivist care, where decisions about neuromonitoring, including ICP monitoring, can be best made. Although still controversial, ICP monitoring is the only available technology shown to guide interventions and predict outcomes, especially in TBI.[7] Its use is widely considered a standard tool in the neurocritical care unit.[8] Information obtained by monitoring a patient's ICP can be used to prognosticate and to follow progression of intracranial disease. It also aids in the assessment of global perfusion metrics such as cerebral perfusion pressure (CPP). The merits of ICP monitoring-based treatment protocols and their influence on patient outcome have been recently investigated in a randomized trial,[8] which is further discussed.

Mechanism and Potential Conditions Associated with Increased ICP

Although TBI is the disease process commonly associated with alterations of ICP, different types of brain injury can result in increased ICP. Patients with ischemic and hemorrhagic stroke, aneurysmal subarachnoid hemorrhage, and noncommunicating hydrocephalus encounter issues with intracerebral hypertension.[3,6,9,10] Other critically ill populations with metabolic, infectious, or hemorrhagic space-occupying lesions, postcirculatory arrest, hyperthermia, or electrolyte abnormalities may also have increased ICP, with signs of poor intracranial compliance.[11] The relationship between intracranial volume and ICP was initially described by Monro[12] and later by Kellie[13] in 1783 and 1824, respectively. Given that the skull remains fixed and rigid with a static volume of brain, blood, and cerebrospinal fluid (CSF), any increase in 1 of these 3 components results in the

Table 1
GCS

Eye		Motor		Verbal	
Eyes open spontaneously	4	Follows commands	6	Oriented, alert	5
		Localizes	5		
		Withdraws	4	Confused, appropriate	4
Eyes open to voice	3	Flexion	3	Disoriented, inappropriate	3
Eyes open to pain	2	Extension	2	Incomprehensible speech	2
No response	1	No response	1	No response	1

Data from Monro A. Observations on the structure and function of the nervous system. Edinburgh (United Kingdom): Creech & Johnson; 1783.

displacement of another of the 3 components outside the skull. As volume continues to increase, intracranial compliance, defined as the change in volume/change in pressure, moves from a near-linear relationship to an exponential relationship; small changes in volume result in large changes in pressure (**Fig. 1**). This situation results in alterations of the slope of the ICP waveform.[11] An example of an appropriate ICP waveform is shown in **Fig. 2**.

Basic Principles to Protect a Brain at Risk

A subset of patients in the neurosciences ICU may have clinical signs, a mechanism of injury, a pathophysiologic marker, or imaging findings that suggest that intracranial compliance is not ideal, and consideration should be given for invasive ICP monitoring. Clinical syndromes of increased ICP may be dramatic, such as new focal deficits referable to a localizable or falsely localizable lesion of descending motor tracts.[14] Worsening of ICP from spontaneous intracerebral hematomas can present with focal neurologic deficits such as unilateral motor or sensory findings.[15] Patients with brain injury who develop intracranial hypertension may progress to cerebral herniation. As mechanisms to compensate for increased ICP are exhausted, herniation may manifest in a variety of neurologic syndromes.[16] Although specific clinical presentations and focal findings may occur, patients essentially become more somnolent, with lower GCS scores. Paradoxic herniation, a unique herniation syndrome from a low-pressure phenomenon, has been reported with or without lumbar puncture after decompressive craniectomy (DC).[17,18] If the pressure change is a result of lumbar drainage and subsequent CSF leak, the use of a blood patch has been reported to be

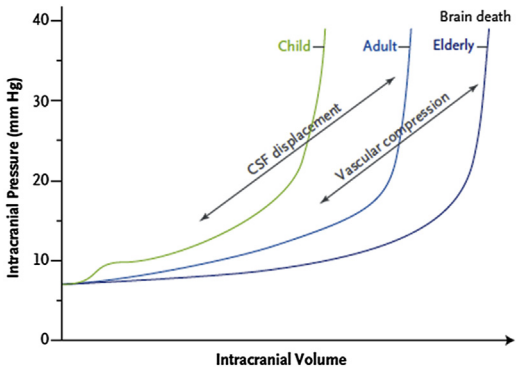

Fig. 1. Theoretic intracranial compliance curves. (*From* Ropper A. Hyperosmolar therapy for raised intracranial pressure. N Engl J Med 2012;367(8):748; with permission. Copyright © 2012 Massachusetts Medical Society.)

lifesaving.[19,20] In addition to the brain parenchymal damage that can occur from herniation, this phenomenon can result in cerebral infarcts secondary to compression of proximate vessels (eg, posterior cerebral artery infarction associated with uncal herniation).[21] These infarcts further increase edema and may affect long-term morbidity. Numerous investigators have published reports regarding outcome of patients with clinical and radiographic herniation from perturbations of ICP who have survived to discharge with variable disability. Prognostication for these patients should be performed after a trial of aggressive medical management has been completed to reduce their ICP.[19,20,22–24]

General measures for patients with acquired brain injury should be in place. For example, the head should be kept in midline position and increased 15° to 30°.[6] This strategy allows optimal venous drainage, which if compromised, can exacerbate intracranial hypertension. With traumatic acquired brain injury, patients often have cervical immobilization collars in place, because of the risk of concomitant cervical spine trauma.[25] If these collars are fitted properly, they assist in keeping the head midline and minimize jugular venous obstruction. Routine placement of internal jugular central lines has been discouraged, although at least 1 study suggests that brief access to the central circulation via the internal jugular vein is well tolerated by patients at risk for increased ICP.[26] The use of jugular venous bulb oximetry in neurotrauma patients ranges from 8% to 12% in the United States to 21% in Japan.[27,28] Because of the potential problems of internal jugular line-associated thrombosis, routine or nonemergent cannulation of the internal jugular vein is avoided (P Nyquist, personal communication, 2013). In addition, central lines that require the Trendelenburg position should not be used during herniation. Trendelenburg positioning may acutely increase ICP.[29]

Other conservative measures that may help protect the injured brain include avoidance of circumferential neck dressings, such as tracheostomy ties or other apparatus to secure the endotracheal tube, in patients on mechanical ventilation. This strategy allows maintenance of venous outflow from the intracranial circulation. Seizures, pain, agitation, and bladder or bowel distention should all be treated.[3] Patients with brain injury should not be overstimulated, because there is evidence to suggest that a quiet and therapeutic environment may improve sleep and restoration of normal circadian rhythms in some types of brain injury, and this may have secondary effects on outcome.[30] Fever should be controlled.[9,10,31] Mild hyperthermia has been shown to worsen proximal

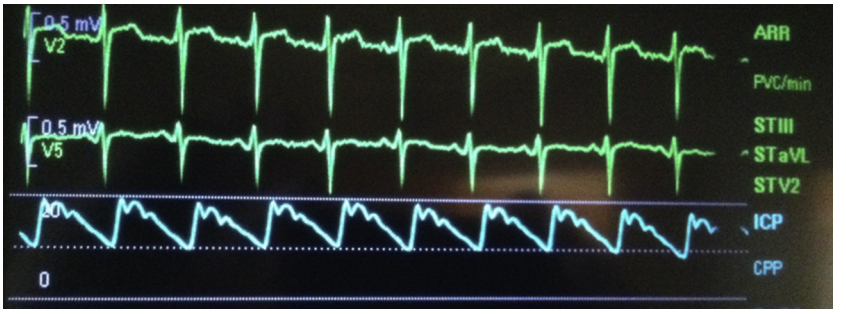

Fig. 2. Typical ICP waveform reading on the bedside monitor showing P1, P2, and P3 subpeaks of the ICP waveform. These waveforms are in descending order of amplitude. As intracranial compliance worsens, the P1 and P2 subpeaks may merge or the P2 subpeak may show a higher amplitude than the P1 subpeak. (*Data from* Asgari S, Bergsneider M, Hamilton R, et al. Consistent changes in intracranial pressure waveform morphology induced by acute hypercapnic cerebral vasodilatation. Neurocrit Care 2011;15(1):55–62.)

outcome in multiple mechanisms of brain injury, including TBI, ischemic stroke, hemorrhagic stroke, and subarachnoid hemorrhage.[31–35] It is reasonable to avoid hypotension and hypoxia in patients with acquired brain injury, because protective autoregulatory mechanisms are known to be abnormal in this setting.[36] Increases in ICP have been shown to worsen this phenomenon of impaired autoregulation.[36]

Indications for ICP Monitoring

Accurate monitoring of ICP is invasive and not without risk of complications. Specific to the setting of TBI, a level II recommendation to invasively monitor ICP given certain clinical and radiographic findings has been proposed. The merits of ICP monitoring as an evidence-based practice have been challenged. To answer the question of whether or not ICP should be treated, it is unlikely that a rigorous clinical trial will occur in which patients in whom ICP is known are randomized to receive or not receive treatment if they experience intracerebral hypertension. Regarding the question of monitoring, a recent trial was completed in South America[8] in which ICP monitoring is available but not routinely used. Patients with TBI were randomized to ICP-based treatment or to treatment decisions based on clinical examination and concurrent imaging findings. Intracranial hypertension was treated in both groups. The patients in the ICP monitoring group had a significantly shorter length of ICU stay and decreased times of ICU-administered brain-specific treatments, whereas the clinical and imaging-monitored group used significantly more mild hyperventilation (P_{CO_2} [partial pressure of carbon dioxide] 30–35 mm Hg) and more absolute hypertonic saline (HTS) for a longer period. The mortality, adverse events, and the primary outcome of functional and cognitive scores at 6 months were not significantly different between monitoring groups. These conclusions regarding mortality are different from other prospective studies using ICP monitor-directed care.[37] Death and worsened outcomes in patients with brain trauma are often attributed to intractable ICP, and for critically ill patients at risk of increases in ICP, consideration for invasive monitoring and specific management based on monitored ICP are still recommended.[3,6,9,10,37]

Patients with severe acquired brain injury from any cause with a strong clinical suspicion of increased ICP and a nonreassuring clinical examination should be considered for ICP monitor placement.[3,6,9] Invasive monitoring devices include the extraventricular drain (EVD), intraparenchymal fiber-optic monitor, subdural bolt, and epidural fiber-optic catheters.

Types of Invasive Monitors

Monitoring of ICP is perhaps best achieved with the use of either ventriculostomy or an intraparenchymal monitor.[3,38] ICP monitoring is required for calculation of CPP (CPP = mean arterial blood pressure – ICP). The ventriculostomy or EVD is a fluid-coupled system that is accurate, inexpensive, and reliable. This modality allows measurement of ICP as well as the ability to reduce ICP by removal of CSF.[39] The EVD has a catheter attached to an external microstrain gauge and an external transducer, which allows intermittent ICP measurement. Pressure can be measured only when the drain is closed. Although imperfect, the recent development of in-line catheters that contain pressure transducers within their lumen allows simultaneous pressure monitoring and drainage.[40,41]

A variety of intraparenchymal monitors are in use. However, they are more expensive, have a shorter dwell time, and are believed to be less

reliable than the EVD.[7] These devices are less technically challenging to place and can record pressure continuously, but cannot be rezeroed once inserted or used to drain CSF from the intracranial space. The technology used in these monitors varies, and they can incorporate either fiber-optic, strain gauge, or pneumatic technologies.[42] The placement of these monitors varies and depends on the site of the maximal injury in focal lesions. For example, in diffuse injury, the monitor is usually positioned in the frontal lobe of the nondominant hemisphere.[42] A small burr-hole is created to place these monitors, which may allow for the placement of other intraparenchymal monitors, such as brain tissue oxygen monitors or microdialysis probes. Some of the devices in use include the following[42]:

- Camino or Ventrix (Integra Neurosciences, Plainsboro, NJ)
- Codman microsensor (Codman, Raynham, MA)
- Spiegelberg ICP sensor and compliance device (Spiegelberg, Hamburg, Germany)
- Raumedic ICP sensor and multiparameter probe (Raumedic, Münchberg, Germany).

Subdural and extradural monitors were used in the past. These modalities are now less frequently used in modern neurocritical care units. Other invasive monitoring devices such as brain tissue oxygenation monitors, microdialysis catheters, and jugular venous saturation monitors can be used to tailor therapy and are described elsewhere in this issue Bullock et al. and LeRoux et al. Routine application of these devices awaits further study.[3] The use of brain tissue oxygen monitors has recently been reported to be associated with increased fluid and vasopressor use and pulmonary complications such as acute respiratory distress syndrome.[3] As with any monitor, the monitor itself does not alter outcome, but the information obtained influences the clinician's decisions and possibly outcome, a general principle most poignantly shown in the landmark ESCAPE (Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness) trial published in 2005.[43]

Noninvasive Measures of ICP

The search for an accurate and noninvasive monitor of ICP is ongoing. Two of the better options for nonabsolute measurement of ICP are the optic nerve sheath diameter (ONSD) and the pulsatility index (PI) calculated from transcranial Doppler studies (TCD). TCD is a portable and noninvasive tool widely used in the assessment of cerebral blood flow and screening for vasospasm in aneurysmal and traumatic subarachnoid hemorrhage.[10,44–46] Use of the PI can approximate a noncontinuous estimation of ICP, where an ispilateral/contralateral PI ratio greater than 1.25 is suspicious for compartmentalized ICP and mass effect.[47] Use of TCDs as a surrogate for ICP requires further study and is not routinely implemented.[48,49]

The use of ultrasonography in assessing the ONSD has also been studied.[50] In patients with increased ICP, the ONSD reliably increases as a result of its intimate relationship with CSF. Ultrasonography using a point-of-care linear array probe is placed on the superior and lateral aspect of the orbit against the upper eyelid. With the eye closed and angled slightly caudally and medially, the ONSD can be reliably measured.[51,52] For detection of ICP greater than 20 mm Hg, an ONSD greater than 0.48 cm has been found to have a sensitivity of 95% and specificity of 93%.[50,53] Trials are ongoing to further characterize this modality of monitoring ICP and clarify its role in ICP management.[54]

ICP Treatment Goals

The ICP goal in acquired brain injury is to maintain a normal pressure state, which is generally less than 20 cm H_2O or 15 mm Hg. Increased ICP is associated with poor outcome in TBI, ischemic stroke, subarachnoid hemorrhage, and intracerebral hemorrhage.[3,55–57] Current guidelines recommend instituting measures to control ICP when pressures of 20 mm Hg are reached, and to use aggressive means to prevent ICP increases to more than 25 mm Hg or CPP less than 60 mm Hg.[3,6,9] Awareness of CPP, as described earlier, is important, because many interventions to decrease ICP may also have systemic effects on peripheral hemodynamics. The maintenance of a CPP of at least 60 mm Hg with intravenous (IV) fluids or vasopressors is strongly recommended.[6,9] CPP goals may initially be satisfied with IV fluids, but if CPP cannot be maintained with a reasonable amount of IV fluids alone, norepinephrine and phenylephrine are commonly used. Overaggressive use of pressors and fluids to manipulate CPP greater than 70 mm Hg has been associated with increased incidence of pulmonary complications and acute lung injury.[58,59]

MANAGEMENT OF INCREASED ICP

Given the multiple different mechanisms by which ICP may be increased, its treatment can be nuanced with respect to different ongoing

pathologic processes.[11] In general, treatment of intracranial hypertension is accomplished by manipulation of vasoreactivity, brain/blood osmotic gradient, metabolic rate of oxygen consumption, or physical/surgical means that affect intracranial compliance.

Hyperventilation

Hyperventilation may be a helpful short-lived and temporary intervention for increased ICP.[3,5,29] Prolonged hyperventilation has been associated with exacerbation of cerebral ischemia.[60] Short durations of mild hyperventilation (Pco_2 30–35 mm Hg) may be acceptable as a temporizing measure until other methods of managing ICP are available.[6] If hyperventilation is continued for longer than 12 hours, metabolic compensation negates any helpful effects of hyperventilation.[60] During a herniation event, hyperventilation acutely and reliably lowers Pco_2, as well as ICP, within seconds. The recommended Pco_2 goal is to maintain levels higher than 25 mm Hg.[3,61]

Conversely, hypoventilation must be monitored for its potential to increase ICP, a relationship that has been described in both preclinical and clinical models.[11] Procedures and different ventilator strategies have been shown to increase ICP via hypoventilation and hypercarbia.[62] Rescue ventilator modes (eg, airway pressure release ventilation) aimed at improving oxygenation at the expense of ventilation may require close monitoring of Pco_2, although success with 1 such mode in the setting of monitored ICP has been reported.[63,64] It may be helpful to use end-tidal CO_2 ($Etco_2$) monitoring in these patients, with the awareness that $Etco_2$ and Pco_2 may be discordant in the setting of chest trauma, hypotension, or metabolic acidosis.[65] Classically, a large pulmonary embolism or decreased cardiac output may also cause the $Etco_2$ to be lower than the Pco_2, in which case the latter may be higher than anticipated.[66,67] In these settings, it may be useful to correlate an arterial to alveolar CO_2 gap on a regular interval to assess for hypoventilation and hypercarbia (J Klein, personal communication, 2013).

Hyperosmolar Therapy

Creation of a relative increase in osmotic content in the bloodstream relative to the brain parenchyma causes efflux of fluid from intracellular and extracellular compartments of the brain into the vasculature. This situation effectually decreases the volume of the cranial compartment, thus reducing ICP and improving intracranial compliance.[29] Mannitol and HTS are the mainstays of hyperosmolar therapy.[3] Mannitol should be given IV via a peripheral or central IV line at a dose of 0.25 to 1.0 g/kg. Small doses of mannitol (0.25 g/kg) have been shown to effectively reduce ICP in patients with TBI.[68] Earlier data show that mannitol use in TBI correlates with decreased ICP and improved cerebral blood flow and CPP.[69] Mannitol can be given while following serum osmolality, and although a serum osmolality of 320 mOsm/L is generally accepted as a treatment end point, some investigators and experts advocate that higher levels can be obtained with caution.[70–72]

Concentrations of 1.5% to 23.4% HTS represent an option for osmotic therapy.[3] These varying concentrations of HTS have been studied versus mannitol, and the use of HTS seems to have better overall efficacy in terms of ICP control and avoidance of complications, such as hypotension. Two recent meta-analyses concerning the use of HTS in TBI, pediatrics, and nontraumatic acquired brain injury confirm the benefit of HTS over mannitol in reduction of ICP and improved CPP.[73,74] Bolus doses of 30 to 60 mL of 23.4% HTS have been used to emergently reverse a herniation event.[24] The ameliorative effect of 23.4% HTS on ICP has been shown to last longer than that of mannitol.[75] Such high concentrations of HTS must be administered via a central venous line during a 10-minute to 15-minute period to prevent phlebitis and hypotension. A reasonable initial treatment goal is to achieve supranormal serum sodium levels of 145 to 155 mEq/L, which is likely equivalent to a serum osmolality of 300 to 320 mOsm/L in most patients.[29] This level can then be titrated to effect to achieve optimal CPP and ICP goals. A 23.4% solution of HTS is effective in reducing ICP by a mean value of more than 8 mm Hg when given for ICP greater than 20 mm Hg and can increase CPP values by 6 mm Hg when pretreatment values are less than 70 mm Hg.[76] A continuous IV infusion of 1.5% to 3% HTS can be used to maintain high serum osmolality, as discussed earlier, but solutions of greater than 3% HTS should be given via a central line. If continuous infusions of HTS are used, serum sodium should be monitored every 4 hours, avoiding rapid changes in serum sodium so as not to precipitate cerebral edema or central pontine myelinolysis.[29] This complication is rare, likely because of clinician awareness regarding monitoring of serum sodium while patients are receiving HTS.[73] The phenomenon of rebound cerebral edema, which may occur with withdrawal of HTS, requires further study.[73] A recent review[72] discussed frequent questions that arise regarding the use of HTS in the setting of intracranial hypertension.

Agents to Reduce the Cerebral Metabolic Rate of Oxygen ($CMRo_2$)

Despite optimal osmotic gradients and therapies, ICP may remain poorly controlled, and other options for treatment must be considered. Reductions in ICP may be achieved by alterations in the metabolic rate of the brain via induction of a pharmacologic coma.[77] The reduction in cerebral metabolism occurs through global reductions in cerebral blood flow and reduced tissue oxygen demand. Pentobarbital is in widespread use for induction of pharmacologic coma for this purpose.[28] This barbiturate is administered IV at a loading dose of 10 mg/kg during a 30-minute period, followed by a 5 mg/kg/h infusion for 3 hours, and maintenance therapy for 1 mg/kg/h titrated to therapeutic goals of either burst suppression on continuous EEG monitoring or a satisfactory reduction in ICP.[78] Smaller loading doses combined with an increase in the infusion dose can be given until burst suppression is seen or ICP is controlled. If ICP continues to increase and a patient has adequate burst suppression on EEG, further increases in pentobarbital may not be effective.[79] The use of pentobarbital coma can be associated with a large percentage of favorable outcomes in those patients who survive, although a recent Cochrane review was not supportive of this therapy to improve outcome.[80,81] Other barbiturates have been used in the past, such as the shorter-acting thiopental for acute exacerbations of ICP or during surgical procedures.[37] This medication is not currently available in the United States.

Another option for reducing $CMRo_2$ is the anesthetic propofol, which can be given at an IV loading dose of up to 2 mg/kg, followed by a titrated infusion of up to 2 to 75 μg/kg/min. The use of propofol for this indication is controversial and this drug has several side effects, the least of which includes dose-related hypotension. A study using propofol for ICP reduction showed a failure of an improvement in 6-month functional outcome, and long-term and high-dose propofol infusions have been associated with the development of propofol infusion syndrome (PRIS), which consists of renal failure, rhabdomyolysis, hyperkalemia, myocardial failure, metabolic acidosis, lipemia, hepatomegaly, and often death.[82] Patients receiving continuous infusions of propofol must be monitored for signs of PRIS, and long-term infusions more than 4 mg/kg should be avoided.[3,83] Laboratory monitoring for lactic acid, creatine kinase, and serum triglycerides to detect early signs of PRIS is recommended, although early detection and withdrawal of propofol does not guarantee survival if PRIS occurs.[83,84] Continuous EEG monitoring may be helpful to monitor for burst suppression or titrated control of ICP.

Induced hypothermia to improve outcomes in patients with intractable increases of ICP is promising but controversial. Preclinical data show induced hypothermia to be associated with improved neurophysiologic metrics in a hypoxic brain injury model, and there are randomized prospective data in TBI that induced mild hypothermia may improve outcome after TBI.[85,86] Hypothermia as a neuroprotectant strategy is appealing because of the multiple mechanisms by which hypothermia may protect the brain from secondary injury, including by the reduction of $CMRo_2$.[87,88] Current use of induced hypothermia for treatment of ICP in severe TBI is a second-tier therapy but may be helpful in refractory cases.[29] The potential of coagulopathy and antiplatelet effects of induced hypothermia should be considered, especially in the setting of hemorrhagic-acquired brain injury.[89–93] Shivering may negate the benefit from therapeutic hypothermia and must be controlled.[87] It is argued that induced hypothermia perhaps should be considered more of a first-tier therapy in some disease states that increase ICP, such as metabolic processes and fulminate liver failure.[94] If performed for ICP control, the optimal temperature may be closer to 35° rather than the typical 32° to 33°, although the optimal duration and depth of mild hypothermia remains unclear. It seems reasonable to use mild hypothermia for the period when ICP and cerebral edema are expected to peak, and rewarming from mild hypothermia should be performed sufficiently slowly (ie, 0.1° per hour). Infectious complications of prolonged mild hypothermia should not be dismissed, because the incidence of pulmonary infections (ie, ventilator-associated pneumonia) is high in some series.[95–97] Its use is advocated by some authorities because of strong evidence of its effectiveness on ICP, and although no clear consensus exists regarding whether there is an influence on long-term outcome for any treatment that reduces ICP, hypothermia is likely at least as effective at improving this metric in patients with acquired brain injury.[98] Two excellent review of the practical use of therapeutic hypothermia, including different modalities for the application of hypothermia, is referenced.[87,89]

Where great controversy seems to be lacking is the potential benefits of maintaining normothermia in patients with acquired brain injury. Avoiding hyperthermia in patients with severe acquired brain injury is recommended by numerous authorities.[9,10,31–35,99,100] Induced normothermia, just as therapeutic hypothermia, can be achieved in

several ways, via antipyretics, ice-cold saline, airway cooling, invasive intravascular cooling, or various methods of surface cooling.[87,101–103]

Other Medial Options to Treat Increased ICP

Remote preclinical data suggest improved outcomes for females in some models of acquired brain injury.[104] Follow-up work has helped to define progesterone as a potentially protective compound from the standpoint of slowing the development of malignant cerebral edema and increased ICP.[105–108] The following 2 ongoing clinical trials are recruiting to examine the potential benefit of administered progesterone therapy in TBI: ProTECT III trial (Progesterone for Traumatic Brain Injury, Experimental Clinical Trial III) and SyNAPSe (Study of the Neuroprotective Activity of Progesterone in Severe Traumatic Brain Injury). Together, these 2 studies have a planned enrollment of more than 1100 patients, with expected completion dates of 2015 and 2013, respectively.[54] The use of progesterone outside the setting of Institutional Review Board-approved research protocols is not advocated.

The anesthetic ketamine offers yet another, if perhaps underused, option for the medical management of ICP. Ketamine, an inhibitor of the *N*-methyl-D-aspartate receptor, has long been reported to cause increases in ICP and was generally avoided in the anesthetic management of patients with acquired brain injury, although the validity of the science on which this practice was based has been subsequently questioned.[109–112] Perhaps because of its more generally prevalent use in children, research began to emerge in the pediatric critical care literature that ketamine appeared safe to use in patients with intracranial hypertension on controlled mechanical ventilation, and may even be beneficial for reducing ICP.[113] A large body of literature has helped to clarify the effects of ketamine on $CMRO_2$, ICP, CPP, and cerebral blood flow in preclinical models, which seem favorable from a neuroprotectant standpoint in acquired brain injury.[114] However, the use of ketamine for control of ICP is not advocated in any of the published treatment guidelines for TBI, aneurysmal subarachnoid hemorrhage, ischemic stroke, or intracerebral hemorrhage.[3,6,9,10,100] If used, doses of 1 to 1.5 mg/kg may be appropriate in mechanically ventilated patients and followed for its effects on ICP.[113]

Surgical Treatment Options

In the setting of polytrauma, the phenomenon of ICP that does not respond to conventional treatment may represent a multiple compartment syndrome (MCS) of the intracranial, intra-abdominal, and intrathoracic compartments.[115] Antecedent trauma or the required fluid or blood product resuscitation required to maintain CPP and mean arterial pressure (MAP) may play a role in the development of MCS. Published reports show that decompressive laparotomy performed in this setting resulted in improvements in intracranial compliance and ICP.[115–117] Whether decompressive laparotomy offers benefit to patients with intractable increases in ICP from other causes of acquired brain injury is unclear.

DC represents another clinical approach to the management of increased ICP. Reported results using this therapy are conflicting.[118–120] However, the role of DC in treating brief increases in ICP in TBI was evaluated in the recently published DECRA (Decompressive Craniectomy) trial.[121] ICP control was significantly improved in the surgical treatment arm, but 6-month outcome was worse compared with medical therapy. Patients with focal space-occupying lesions were excluded from the study, and the surgical arm cohort had a statistically significant difference in loss of pupil reactivity compared with the medically treated patients. This significant difference in the 2 treatment groups, combined with the choice of the surgical procedure performed, may limit the ability to generalize the conclusions of the study. Another study, RESCUEicp (Randomized Evaluation of Surgery with Craniectomy for Uncontrollable Increase of Intra-Cranial Pressure), may help further define the role of DC in the management of severe TBI.[122] RESCUEicp recently completed its enrollment of approximately 400 patients comparing DC with medical management (including barbiturates) in severe TBI.[122] The subject of the surgical management of increased ICP and the role for DC in other causes of refractory ICP is discussed in detail elsewhere in this issue.

Common clinical approaches for increased ICP management

Recognition of an ICP emergency should result in an algorithmic approach to treatment.[23] The management of acute increases in ICP initially involves ensuring that the waveform and ICP value are accurate. Respiratory derangements, ongoing seizure activity, hyperthermia, and metabolic causes need to be ruled out if suspected. Imaging with CT should be considered in any new episode of increased ICP without explanation. Physical interventions such as ensuring the head is midline and the head of the bed is up to at least 30°, establishing normothermia, and cessation of noxious stimuli such as suctioning may help to acutely lower temporary spikes in ICP. If this is unsuccessful

and the ICP is believed to be accurate, brief hyperventilation of intubated patients may be performed to a P_{CO_2} of 30 to 35 mm Hg. If the ICP is measured with an EVD, then drainage of 5 to 10 mL of CSF may improve compliance and the overall treatment plan for ongoing drainage of CSF evaluated. If the patient with an intraparenchymal ICP monitor has moderately sized ventricles, then placement of an EVD should be considered. If central access exists, then 30–60 mL of 23.4% HTS may be given via a central line over a 15-minute period. This solution may need to be given faster, and if so, then a small dose of phenylephrine may help to augment the MAP so that the patient's CPP is maintained higher than 60 mm Hg. As an alternative to HTS, mannitol may be given via a peripheral line, with the dose tailored to the clinical situation. A dose of 1 g/kg is given for clinical signs of herniation and doses of 0.25 to 0.75 g/kg for less severe increases in ICP. In a herniation event, central access should be obtained, with consideration of a femoral central venous catheter or avoidance of extreme Trendelenburg positioning for subclavian lines.[29] If ICP continues to be increased after these maneuvers, then additional HTS can be given as well as further boluses of mannitol, treating up to a serum osmolality in the range of 320–340 mOsm/L. Standing infusions of 3% HTS can be used, with goal sodium values that may exceed 155 to 160 mEq/L if required. Further medical management includes use of bolus doses of propofol and consideration given to pharmacologic coma, induced hypothermia, ketamine, or surgical intervention.

SUMMARY

The management of patients with increased ICP in acquired brain injury from multiple potential causes may offer the potential to reduce secondary injury and improve outcomes. Controlling intracranial hypertension may maintain brain perfusion and alter the potential morbidity associated with acquired brain injury. Multimodality treatments in neurocritical care offer the potential to improve patient outcomes, both proximal and long-term.

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