Anesthetic approach in pediatric brain injury

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ABSTRACT

Traumatic brain injury (TBI) is defined as an insult to the brain resulting from external force, leading alteration in brain function, permanent or temporary impaired cognition, wide-spread impairments in motor and behavior function. TBI is not only a leading cause of death but it is a significant contributor to disability in pediatric age group. Its sequelae is an important health problem throughout the world. The patients face numerous difficulties to return to a productive life. Improvements in the prognosis continue with its elucidated pathophysiology, technological developments in its monitorization, and sustained scientific research. In 2003, the Society of Critical Care Medicine published the Guidelines for the Acute Medical Management of Severe Traumatic Brain Injury in Infants, Children, and Adolecents and updated the guidelines in 2012 with some significant changes. Pediatric anesthesiologists are frequently faced with the perioperative management of such patients. This article reviews pathophysiology, anesthetic management, hemodynamic support, management of intracranial hypertension of pediatric patients with TBI in the light of current evidence-based medicine. Informing the anesthetists confronting TBI patients in the intensive care unit, during preoperative and peri-operative periods, about important issues related to pathophysiology and treatment of TBI will contribute to the improvements in the prognosis of these patients.

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1. Introduction

Head traumas are the most frequent cause of trauma-specific hospital stays and mortality. Because of anatomical development and changes in head and neck biomechanics in parallel with age, head traumas result in different types of injuries in various age groups (Wing and James, 2013). In small children, head traumas may accompany with other organ injuries (Soriano et al., 2002). According to the data released by the National Center for Injury Prevention and Control, every year 510.000 children aged between 1-14 years in the U.S are exposed to traumatic brain injury (TBI), and 35.000 of them are hospitalized, while the injuries are fatal in 2.000-3.000 cases (Schneier et al., 2006). The most frequent cause of TBI is motor accidents. Fall from height and child abuse are responsible for 30-50% of the cases in children younger than 4 years of age (Vavilala Monica and Chesnut, 2008).

Pediatric head injuries differ from those seen in adults in some aspects. In children, the head is larger and heavier than other parts of their bodies relative to the adult body, their occiputs and foreheads are more conspicuous, and their facial bones are smaller. Their skulls are more compliant and absorb external forces without fracturing, but create greater tensile forces between dura, subdural vessels, and the brain. Since children's necks are weaker than those of adults, when exposed to trauma, their heads move more rapidly in the

opposite direction of the neck. In children, the water content of the brain is higher and their myelinization is incomplete (Hulke, 1998). Since the brain has a relatively lower density, acceleration-deceleration injuries are more frequently seen in comparison with adults (Wing and James, 2013).

Informing the anesthetists confronting TBI patients in the intensive care unit, during preoperative and perioperative periods, about important issues related to pathophysiology and treatment of TBI will contribute to the improvements in the prognosis of these patients. The aim of this review is to inform anesthetists about anesthetic management in patients with TBI in the light of current recommendation in literature.

2. Pathophysiology of TBI

Primary and secondary injuries play an important role in the pathophysiology of TBI and its resultant sequelae. Primary injuries occur at the onset of the traumatic event. Primary injuries, which emerge under the impact of acceleration, deceleration, or rotational forces, can result in skull fracture, cerebral contusion, intracranial hematoma, and diffuse axonal damage (Werner and Engelhard, 2007; Greve and Zink, 2009).

Inflammatory and excitotoxic processes caused by primary injuries can lead to secondary injury with edema, an increase in intracranial pressure (ICP), and a decrease in cerebral perfusion. Hypoxemia and hypotension that occur during primary injury may cause secondary injuries. The effects of acute posttraumatic onset of injury may last for days or even months, and inadequate delivery of oxygen and glucose to neurons may induce progression of the traumatic damage (Chesnut et al., 1993; Wing and James, 2013).

In most children with multiple traumas, TBI is present, which represents a very high percentage of posttraumatic death and morbidity. In 15% of TBI cases seen in infants and small children, serious injuries occur with mortality rates of 50%. Mortality rates in pediatric cases are lower than those encountered in adults. However, the presence of hypoxia ($PaO_2 < 60$ mmHg), hyperventilation ($PaCO_2 < 35$ mmHg), hyperglycemia (glucose>250 mg/dL), hyperthermia (body temperature>38°C), hypotension (systolic blood pressure; 5 percentiles lower compared with their age-matched peers), intracranial hypertension (ICP>20 mmHg), and multiple traumas may worsen the prognosis (Vavilala Monica and Chesnut, 2008).

3. Anesthetic management

Because of the potentially poor prognosis of TBI, the treatment strategy should aim to prevent secondary injury and stabilize the patient's health condition. Since the effects of secondary injury are preventable, operative time is of vital importance for early onset of treatment on patient survival. The physiological effects of intraoperative anesthesia and the use of surgical intervention can cause secondary injuries. The main components of the treatment approach for a patient with TBI can be listed as resuscitation of the patient, urgent evaluation of the surgically excisable mass lesion, control of the ICP, support of cerebral perfusion (SPP), multimodal monitorization, optimization of physiological media, adequate anesthesia, achievement of analgesia, and prevention of hypotension, hypoxemia, hypocarbia, hypercarbia, hypoglycemia, and hyperglycemia (Bhalla et al., 2012).

In children with TBI, cervical vertebral injuries can also occur. In small children and children over 12 years of age, maximum cervical mobility is achieved by C1-C3 and C5-C6 cervical vertebrae, respectively. Therefore, the upper and lower vertebral levels are injured in small children and older children, respectively (Dickman and Rekate, 1992).

The first evaluation and intervention in TBI are generally performed in the intensive care unit. The respiratory, circulatory, and neurological systems and airways should be evaluated, and the potential involvement of other organ systems should not be forgotten in trauma patients. In particular, the presence of newly developed hemodynamic instability, anemia, and respiratory distress should suggest an injury to other organ systems.

4. Airway management

Endotracheal intubation should be performed in patients with the Glasgow Coma Scale (GCS)<9 to protect the airway and for the management of ICP. In cases with suspected cervical injury, hyperextension of the neck during intubation should be avoided (Davis et al., 2010, Davis et al., 2011). Recent studies have not detected any difference between prehospital mask ventilation and intubation regarding the survival of patients with TBI (Gausche et al., 2000). Uncertainties in the diagnosis of cervical spinal injury, blood, and vomitus in the mouth, laryngopharyngeal injury, full stomach, and intracranial hypertension can cause complications during airway management. Nasotracheal intubation is contraindicated in cases with basilar skull fractures (Tobias, 1996).

5. Intravenous access

It is very difficult to achieve intravascular access in a pediatric trauma patient. Before induction of anesthesia, it is appropriate to open an intravenous route using a≥20 G peripheral catheter. Generally, saphenous veins are used. After induction of anesthesia, a second intravenous route should be opened. If a peripheral catheter can not be inserted after two attempts, the interosseous route should be used and experienced hands should implant a central catheter (Soriano et al., 2002).

6. Anesthetic technique

In TBI, the selection of the sedation/analgesia and neuromuscular blocker is critical. Intravenous and volatile agents exert diverse effects on cerebral blood flow (CBF) and cerebral metabolic rate (CMR). However, up to now, any marked difference between these two groups in terms of survival rates has not been detected.

7. Intravenous agents

Analgesic, sedative, and neuromuscular agents decrease CMR and increase ICP, with stress response and shivering, with the potential induction of a secondary cerebral injury. Intravenous agents including thiopental, propofol, and etomidate decrease CMR. This causes cerebral vasoconstriction with a resultant reduction in CBF, cerebral blood volume (CBV), and ICP. However, propofol and thiopental induce marked hypotension and can decrease cerebral perfusion pressure (CPP). In response to a reduction in mean arterial pressure, cerebral vasodilation developed via autoregulation, which aims to maintain CBF, can induce increases in CBV and ICP (Brussel

et al., 1989). Similar effects can be seen when fentanyl and sufentanyl are used. To annihilate these effects a vasoactive agent (i.e., phenylephrine), which can increase mean arterial pressure, can be used (Albanese et al., 1999).

Generally in the induction of anesthesia, sodium thiopental, etomidate, and propofol are used. Since all intra venous (IV) sedative-hypnotic agents are potent cerebral vasoconstrictors, they decrease both CBF and CMR, which can also reduce ICP. Because of their vasodilatory and negative inotropic effects, which can increase patients' preexisting comorbidities, the use of thiopental and propofol might not be appropriate in intensive care unit patients (Brussel et al., 1989, Tritapepe et al., 1999).

In trauma patients, frequently etomidate and ketamine are preferred (Tobias, 2000). Limited information is available about the potentially deleterious effects of etomidate in patients with sepsis (Annane, 2005). Despite well-known adrenal suppressive effects of etomidate, data on related with its unfavorable effects on survival are lacking. It has a limited effect on mean arterial pressure. Besides, it decreases CMR and hence ICP, with a net increase in CPP. Etomidate is a beneficial drug thanks to all of these effects in patients with TBI (Bhalla et al., 2012).

Previously, because of its ICP-increasing effects, ketamine use was avoided in patients with TBI; however, recent data recommend the effectiveness of ketamine in decreasing ICP in painful interventions (Takeshita et al., 1972; Bar-Joseph et al., 2009).

8. Inhalation agents

All inhalation agents (isoflurane, sevofluorane, and desfluorane) cause a decrease in CMR. As cerebral vasodilators, they can cause increments in CBF, CBV, and ICP. However, these effects are generally at a minimal level in concentrations lower than 1 minimum alveolar concentration (MAC). Therefore, lower concentrations can be used in patients with TBI. However, nitrous oxide should be avoided since it increases ICP via increments in both CMR and cerebral vasodilation (Werner and Engelhard, 2007).

9. Muscle relaxants

When rapid neuromuscular blockade is required to achieve optimal intubation conditions, as muscle relaxants, succinylcholine and rocuronium can be used. Though minor increases in ICP are known with succinylcholine use, increased ICP, which might develop secondary to hypoxia and hypercapnia, is clinically more important. Therefore, rapid intubation of the patient to achieve oxygenization carries more importance compared with an increase in ICP induced by succinylcholine. It is more appropriate to have sugammadex at hand when using rocuronium. The use of lidocaine has been thought beneficial while intubating patients with increased ICP; however, evidence-based data demonstrating the effectiveness of lidocaine are lacking. Bradycardia can be observed in a pediatric patient group with increased ICP during endotracheal intubation with laryngoscopy. To refrain from bradycardia, administration of atropin has been recommended, despite the lack of supporting evidence. Incidences of bradycardia increase with hypoxemia, hypothermia, and succinylcholine use (Tobias, 1996; Robinson and Clancy, 2001; Vavilala and Chesnut, 2008).

10. Steroids and glycemic control

In children with serious TBI, corticosteroids do not induce improvements in functional survival or decrease mortality and ICP; contrarily, they suppress endogenous cortisol levels with a resultant increase in the risk of pneumonia. Therefore, the use of corticosteroids is not recommended in pediatric patients with TBI (Kochanek et al., 2012).

Another debatable issue related to patients with TBI concerns the association between hyperglycemia and poor prognosis. Diverse opinions have been asserted about aggressive treatment of hyperglycemia. Increased gluconeogenesis, glycolysis, cortisol release, and glucose intolerance following TBI can lead to the development of hyperglycemia. Especially in small patients (<4 years) with serious TBI, hyperglycemia is more frequently seen. An increase in the rate of glycolysis and reactive oxygen species, acidosis of cerebral parenchyma, alterations in immune, inflammatory, and mitochondrial functions, and cell death all related to hyperglycemia can result in the emergence of secondary injury. Many studies on hyperglycemia detected in adults and children have demonstrated its correlation with poor neurological survival. However, limited data are available, which suggests that treatment of hyperglycemia improves survival (Rovlias and Kotsou, 2000; Sharma et al., 2009; Smith et al., 2012).

11. Monitorization

According to the monitorization standards of the American Society of Anesthesiologists, invasive arterial blood pressure monitorization has been recommended (Hardcastle, 2014). To evaluate intravascular volume status, monitorization using central venous pressure is helpful. Since intracranial hypertension might induce secondary injury, its prevention and treatment are essential. In children with serious TBI with ICP (GCS<8), monitorization is recommended. In cases with coagulopathy, its use is contraindicated. ICP≥20 mmHg requires intervention. Cerebral blood pressure (CBP) should be kept over 40 mmHg (Adelson et al., 2003).

Use of noninvasive transcranial doppler pulsatile index as an indicator of ICP is debatable. Since it has a higher sensitivity in the detection of intracranial bleeding at first admission of the patient, its use has been recommended (Melo et al., 2011). Measurement of jugular venous oxygen saturation using a catheter, which is retrogradely inserted into internal jugular vein, provides information about cerebral oxygen supply. Monitorization of retrograde jugular venous saturation can be used to evaluate the degree of hyperventilation in cases with TBI; however, this method is not used routinely. Urine output should be monitored (Bhalla et al., 2012).

12. Position

Many studies have been performed on the potential effects of the position and elevation of head on ICP. The patient's head should be kept in a midline neutral position to prevent jugular venous obstruction as far as possible. Flexion, right or left rotation of the head, and the Trendelenburg position will result in marked increase in ICP, especially in patients with altered intracranial compliance (Ng et al., 2004). Elevation of the patient's head to 15°-30° is recommended to decrease ICP and achieve adequate CBF. Elevation of the patient's head is also beneficial in decreasing ventilation-related pneumonia in the intensive care unit (Adelson et al., 2003).

13. Fluid resuscitation

Despite the risk of hypovolemia and hypotension in patients with TBI, at baseline, normovolemia should be achieved with volume resuscitation. In the majority of cases, isotonic saline solutions should be used at baseline, and for maintenance of fluid resuscitation. Since serum sodium concentration and osmolality is reduced in patients receiving lactated Ringer's solution rather than normal saline, as an isotonic fluid, normal saline should be used (Williams et al., 1999). When potential advantages and disadvantages of crystalloid and colloid solutions are analyzed, recent data related to adult patients have tended to demonstrate that resuscitation with albumin containing solutions can effect survival adversely, and mortality rates increase in patients receiving albumin solutions relative to those treated with normal saline (Myburgh et al., 2007).

14. Management of intracranial hypertension
Hyperosmolar treatment

In patients with serious TBI, mannitol or hypertonic saline is used to treat intracranial hypertension. With the use of hypertonic saline, dehydration, central pontinemyelinosis, and rebound increase in ICP can be seen. The 2012 guideline recommends both bolus and IV infusion of 3% saline for management of TBI (Bell and Kochanek, 2013). In pediatric patients with increased ICP following TBI, the effective dose range varies between 6.5-10 mL/kg. When compared with bolus doses of 0.9% saline, administration of bolus doses of 3% saline ensures further decreases in ICP, fewer complications, and lower requirements for additional interventions to control ICP (Fisher et al., 1992). When lactated Ringer's and 1.7% saline solutions were compared, better ICP control with lower complication rates and shorter intensive care unit (ICU) stay were achieved with infusions of hypertonic saline solution in pediatric cases (Simma et al., 1998). To maintain ICP under 20 mmHg, 3% saline infusions were administered at a dose range of 0.1-10 ml/kg/hr and more improved management of ICP was achieved without any adverse effects (Peterson et al., 2000).

Limited clinical data are available on mannitol use in the treatment of ICP. With mannitol use, natriuresis, dehydration, acute renal failure, adverse osmotic cerebral effects with resultant increase in ICP can be seen (Segal et al., 2001). Placebo-controlled clinical studies comparing mannitol with other osmotic diuretics in the pediatric patient groups have not been performed (Kochanek et al., 2012).

Therapeutic hypothermia

The 2012 treatment guideline emphasized that, if indicated, hypothermia should be maintained for 24 hours, and the temperature should be raised gradually at 0.5°C increments per hour (Kochanek et al., 2012). Moderate hypothermia decreases CMR with resultant decreases in cerebral vasoconstriction, CBF, CBV, and ICP. Adverse effects of hypothermia include hypotension, bradycardia, arrhythmia, sepsis, and coagulopathy (Bhalla et al., 2012).

Corticosteroids

For years, steroids have been used in patients with brain tumors for their edema decreasing effects, with the aim of increasing survival. However, in studies performed on patients with TBI, any favorable effect of steroids has not yet been demonstrated on the survival of these patients. Crash study demonstrated increased mortality rates with methylprednisolone use in adult patients with TBI (Edwards et al., 2005).

Hyperventilation

Hyperventilation can decrease the oxygen supply of CBF to a level that induces cerebral hypoxemia and ischemia. Prophylactic hypocapnia has been shown to decrease the buffering capacity of cerebrospinal fluid. The 2012 treatment guideline recommends avoiding dropping $PaCO_2$ below 30 mmHg with prophylactic hyperventilation within 48 hours of the traumatic injury. If hyperventilation is to be used for the treatment of serious intracranial hypertension, the degree of cerebral ischemia should be evaluated using neuromonitorization. Despite all of these recommendations, currently, hyperventilation therapy is the most frequently used method in the treatment of pediatric TBI (Kochanek et al., 2012).

Barbiturate coma

The 2012 treatment guideline recommends a barbiturate-induced coma in cases with intractable increases in ICP refractory to medical and surgical interventions (Kochanek et al., 2012). If barbiturates have to be used, continuous monitoring of blood pressure levels and cardiovascular support to achieve adequate CPP are recommended (Kasoff et al., 1988).

Decompressive craniectomy

The 2012 treatment guideline recommends craniectomy at the early onset of clinical manifestations of herniation and in cases of intracranial hypertension refractory to medical therapy (Kochanek et al., 2012).

15. Anticonvulsant therapy

Children are more frequently exposed to the risk of posttraumatic seizures, and this risk increases 2.5-fold in children younger than 2 years of age. Convulsive activity can induce increases in CMR and ICP and cause fluctuations in blood pressure. Besides, seizures can aggravate secondary injuries. During the 7 days following a trauma, prophylactic anticonvulsants should be used (Bhalla et al., 2012).

16. Conclusion

In conclusion, TBI and its sequelae are important health problems. Owing to well-known pathophysiology of TBI and the opportunity to utilize advanced monitorization with technological developments, improvements in the prognosis of TBI have been observed. During the perioperative period, avoiding hypocarbia, hypercarbia, hypoxemia, hypoglycemia, and hyperglycemia, and maintaining hemodynamic stabilization will prevent secondary injury and its ensuing sequelae, which will therefore contribute to further improvement of the prognosis.

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