Anesthetic management of the head trauma patient

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Abstract

Objective: To describe the optimal anesthetic management of patients with brain injury, with emphasis on the support of oxygen delivery to the brain, and the effects of anesthetic agents on cerebral perfusion.

Data sources: Clinical and experimental studies from both the human and veterinary neuroanesthesia literature.

Summary: The management of patients following primary traumatic brain injury (TBI) significantly impacts outcome. Outcome can be improved by strategies that improve oxygen delivery to the brain and prevent cerebral ischemia. Anesthetic agents have widely variable effects on the blood supply to the brain and, therefore, choice of anesthetic agent can influence neurological outcome. Although in the past, anesthetic agents have been selected for their neuroprotective properties, it is increasingly being recognized that the support of cerebral perfusion during anesthesia contributes more significantly to a positive outcome for these patients. Support of cardiorespiratory function is, therefore, highly important when anesthetizing patients with TBI.

Conclusion: Choice of anesthetic agent is determined by the extent of brain injury and intracranial pressure (ICP) elevation. Factors that should be considered when anesthetizing head trauma patients include the effects of anesthetic agents on the cardiac and respiratory systems, their effects on cerebral blood flow (CBF), ICP, and possible neuroprotective benefits offered by certain agents.

(J Vet Emerg Crit Care 2007; 17(1): 5–14) doi: 10.1111/j.1476-4431.2006.00194.x

Keywords: cerebral blood flow, dog, intracranial pressure, neuroanesthesia, neuroprotection

Introduction

Head trauma is seen frequently in dogs and cats. Vehicular trauma, kick or bite injuries, 'high-rise' injuries, and penetrating wounds are all reported causes.[1,2] General anesthesia is often required during the management of head trauma patients, for purposes such as surgery, diagnostic imaging, or mechanical ventilation. Surgical intervention may be required to repair fractures, thoracic trauma or large skin lacerations, or for investigation and treatment of abdominal hemorrhage. In addition, more severely affected cases may require anesthesia for decompressive craniectomy, which is becoming increasingly common in veterinary medicine for the management of head trauma.[2,3] Analgesics are also usually indicated in head trauma patients. Many anesthetic and analgesic drugs have effects on intracranial physiology, which under certain circumstances may result in further neuronal insult.[4,5] In contrast, agents such as the barbiturates are frequently used therapeutically in head trauma patients to reduce seizure activity and protect neuronal function.[6,7] An understanding of the mechanisms by which anesthetics influence the injured brain is therefore beneficial in the management of patients with head injury.

Intracranial Physiology

When planning an anesthetic regimen for patients with traumatic brain injury (TBI) an understanding of cerebral blood flow (CBF) physiology is beneficial. Many anesthetic agents cause alterations in blood flow to the brain and therefore have the potential to cause further insult. The physiology of intracranial hemodynamics and the effects of head trauma have been reviewed extensively elsewhere.[8–10] However, a review of intracranial physiology as it pertains to brain injury and the implication to anesthetic management are briefly discussed.

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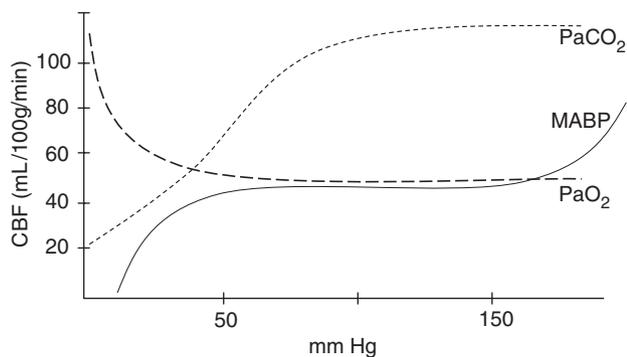E-mail: echan@rvc.ac.uk

Figure 1: Schematic depiction of the effects of arterial partial pressure of oxygen (PaO$_2$), carbon dioxide (PaCO$_2$), and mean arterial blood pressure (MABP) [same scale and measured in mmHg] on cerebral blood flow (CBF) [measured in mL/100 g/min]. (Adapted from Hopkins AL. Head Trauma. Vet Clin N Amer Small Anim Pract. 1996;26(4):875–891, with permission.)[b]

Changes in intracranial blood flow are a significant cause of cerebral injury after head trauma, and prevention of ischemic damage by maintaining oxygen delivery to the brain contributes significantly to outcome.[11–13] An understanding of the protective mechanisms supporting blood flow to the brain is therefore important in head trauma management. In order to support a high oxygen requirement, the brain normally receives a large percentage of the cardiac output, and CBF is tightly regulated to prevent decreases in perfusion. In a normal brain, constant CBF is maintained by alterations in vasomotor tone regulated according to changes in arterial oxygen (PaO$_2$) and carbon dioxide (PaCO$_2$) partial pressures, and systemic blood pressure (Figure 1). In the injured brain, these protective mechanisms are lost. A decrease in arteriolar pH caused by an increase in PaCO$_2$ results in vasodilation, reduction of cerebral vascular resistance, and an increase in CBF.[14] In contrast, hypocapnia results in intracranial vasoconstriction and a decrease in cerebral perfusion.[15] Alterations of arterial oxygenation have a lesser effect on intracranial hemodynamics unless severe hypoxemia occurs. When PaO$_2$ decreases below 50 mmHg, vascular resistance decreases in order to increase CBF and maintain cerebral oxygen delivery.[15] Changes in systemic blood pressure are usually prevented from causing alterations in CBF by cerebral pressure autoregulation. Pressure autoregulation maintains constant CBF when mean arterial blood pressure (MABP) varies within a physiological range (50–150 mmHg).[15] Following TBI, pressure autoregulation may be lost causing mildly decreased systemic blood pressures that otherwise might be considered safe to result in markedly reduced CBF. The increased dependency of CBF on MAP may explain the worsened outcome associated with hypotension in patients with TBI.[13–17]

Clinical assessment of CBF is difficult and as a result, cerebral perfusion pressure (CPP), a variable that is more easily ascertained and a clinical correlate of CBF, is used to predict a patient's risk for cerebral ischemia.[18] CPP is the pressure gradient driving CBF. It is calculated as the difference between MABP and intracranial pressure (ICP):

$$CPP = MAP - ICP$$

ICP is defined as the pressure exerted between the skull and the intracranial tissues.[7] Since the skull is rigid and poorly compliant, an increase in volume by any of its contents without a concomitant reduction in the other components results in an increase in pressure. Increases in intracranial volume and pressure may result from an increase in volume of brain tissue (e.g., by formation of cerebral edema), blood (e.g., due to hemorrhage or vasodilation), or cerebrospinal fluid (e.g., by obstruction to fluid outflow). As ICP increases, systemic blood pressure must increase to prevent a decrease in CPP and a resultant decrease in CBF. Excessive unregulated cerebral vasodilation such as that which may arise during anesthesia of TBI patients may also increase ICP, reduce CPP, and may lead to cerebral ischemia.

Under normal circumstances, vasomotor tone is coupled to the oxygen requirement of the brain by flow-metabolism coupling. This phenomenon describes the ability of the cerebral vasculature to respond appropriately to changes in oxygen demand. Provided flow-metabolism coupling remains intact, a reduction of cerebral metabolic activity leads to a decrease in oxygen demand, followed by vasoconstriction and a subsequent decrease in ICP. Because anesthetic agents reduce brain metabolism when a state of unconsciousness is reached, oxygen demand is reduced, minimizing the risk of ischemia.[4] Flow-metabolism coupling is disrupted by any event causing a change in vasomotor tone that is not reflected by a similar alteration in cerebral metabolism. Therefore, the induction of vasoconstriction without a parallel decrease in the cerebral metabolic rate, for example by hyperventilation, can actually increase the risk of cerebral hypoxia.[19] The high metabolic demands of the brain result in poor tolerance to reduced oxygen delivery. Ischemic injury leads to abnormal nerve function (e.g., unregulated sodium and calcium flux across cell membranes), release of the excitatory neurotransmitter glutamate (causing an increase in oxygen requirement and generation of seizures), and neuronal cell death.[20,21]

Selection of Anesthetic Agent

In selecting anesthetic agents for use in patients with TBI, specific properties of the agent that must be
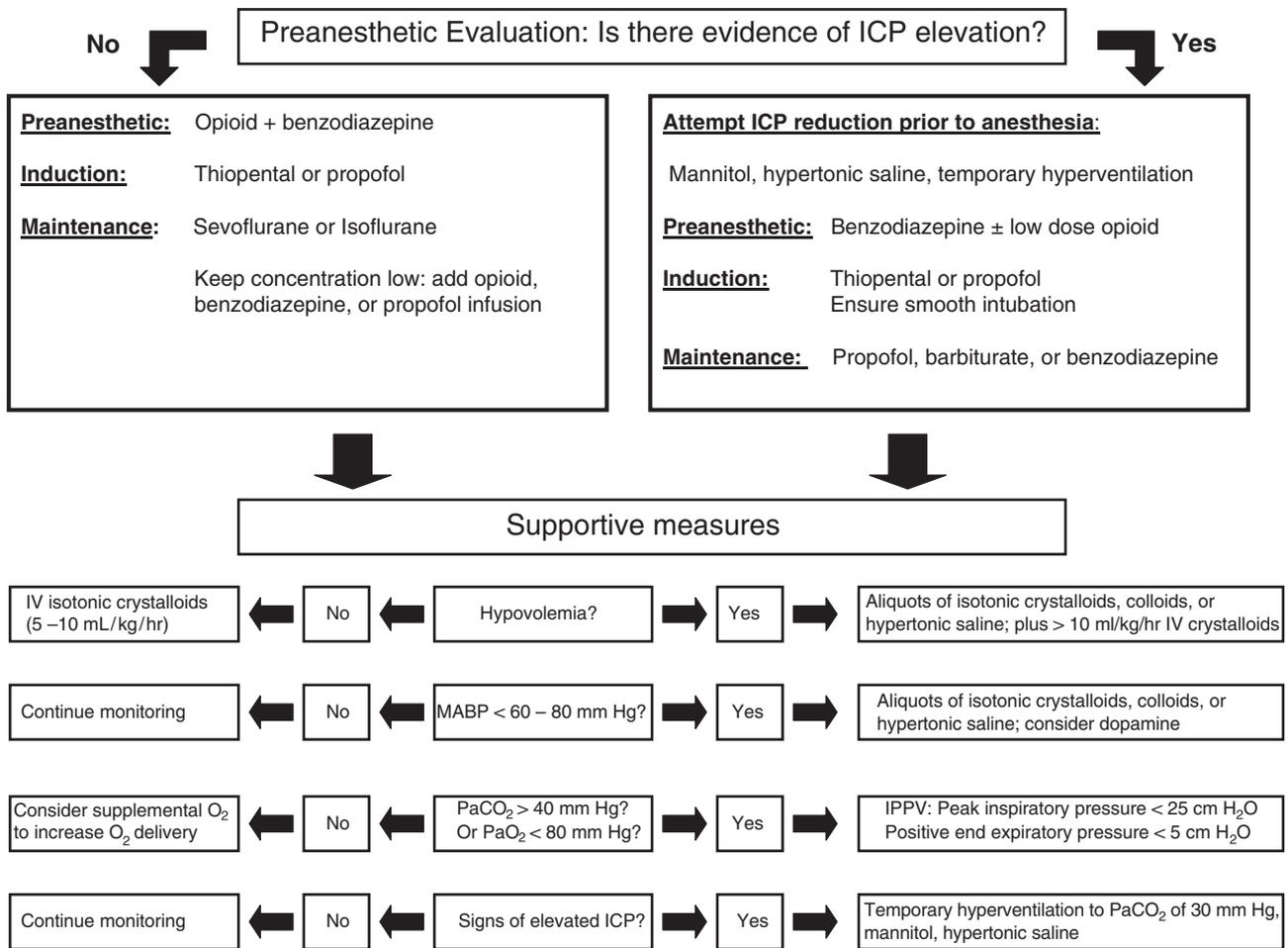
Figure 2: Selection of anesthetic protocol for use in head trauma patients.

considered include the effects on cardiovascular and ventilatory function, effects on intracranial hemodynamics, and potential neuroprotective properties. These neuroprotective properties include reduction of brain ischemia by decreasing cerebral oxygen demand and enhancing cerebral pressure autoregulation.[22,23] Agents that have been investigated for their potential neuroprotective properties include volatile anesthetics, barbiturates, propofol, benzodiazepines, and ketamine.[21,24] However, despite much research, evidence for long-term beneficial anesthetic-induced brain protection is scarce.[24] A simple algorithm for selection of anesthetic agent in head trauma patients is shown in Figure 2. The importance of minimizing cardiovascular and respiratory compromise cannot be overemphasized, and maintaining CPP remains a top priority when selecting an anesthetic protocol.[24]

Volatile anesthetics
Most volatile anesthetics, including halothane, isoflurane, sevoflurane, and desflurane have dose-related

effects on ICP. Low concentrations of all these agents reduce cerebral metabolism; and if flow-metabolism coupling is intact, there is a resultant decrease in cerebral blood volume and a reduction in ICP.[25] As the dose is increased over 1–1.5 MAC (minimum effective alveolar concentration), suppression of metabolic activity persists; however, the predominant effect becomes increased ICP and decreased CPP.[26] This is primarily caused by a direct vasodilatory effect; however, it is augmented by anesthetic-induced hypoventilation and hypercapnia. The systemic hypotensive effects of volatile anesthetics cause an additional detrimental effect on cerebral perfusion. Additionally, at higher alveolar concentrations, cerebral pressure autoregulation is disrupted. Perfusion therefore becomes dependent on systemic blood pressure and is decreased if blood pressure is not supported.[27]

The dose/effect response varies between the different inhalant agents. Most of the detrimental effects are significant at 1.0 MAC, although the increase in ICP seen with halothane is greater than that observed with new-

er inhalant anesthetics.[26] For example, sevoflurane does not impair pressure autoregulation until concentrations exceeds 1.5 MAC (3.3%), while isoflurane disrupts autoregulation at 1.0 MAC (1.3%).[28] Other studies, however, comparing sevoflurane to isoflurane at up to 1.5 MAC have failed to show any benefit to the use of sevoflurane in patients with intracranial disease.[29,30] These differences may emphasize the fact that disease states may influence drug responses. An additional benefit of sevoflurane includes its lower solubility, producing a more rapid anesthetic recovery compared to the use of isoflurane, permiting earlier neurological assessment following anesthesia. This has been demonstrated in people even after prolonged neurosurgical procedures lasting longer than 6 hours.[31] Effects of desflurane on intracranial blood flow and CO_2 vasoreactivity in dogs and pigs have also been investigated. Desflurane use was associated with higher ICP, greater degree of vasodilation, and decreased responsiveness to hypocapnia when compared to isoflurane and sevoflurane.[32] This agent may therefore be less suitable for use in patients with intracranial disease.

The intracranial effects of inhalant anesthetics can be minimized when low anesthetic concentrations are used and with appropriate support of ventilation and blood pressure. In the absence of ICP elevation, the vasodilatory effects of these agents may even improve cerebral perfusion.[33] However, if ICP is already elevated, an anesthetic protocol that does not include volatile anesthetics is recommended.[34]

Injectable anesthetics and analgesics
Injectable anesthetic agents such as propofol and the barbiturates are widely used in people following head trauma.[22,35] Beneficial properties of barbiturates include neuroprotection conferred by their reduction of cerebral oxygen requirements, cerebral vasoconstriction, reduction of ICP, and increased protection from excitatory neurotransmitter-induced neuronal damage.[24,36] Other potential neuroprotective properties include reduction of sodium channel conduction and intracellular calcium entry, enhancement of cAMP production, and antioxidant effects.[21] Their main disadvantages include delayed anesthetic recovery, hypotension, and potent respiratory depressant effects, which are detrimental in TBI patients, particularly those with disrupted pressure autoregulation.

Neuroprotective properties of propofol under investigation include modulation of GABA receptors and antioxidant effects.[21] Clinically, advantages to propofol in head injured patients include more rapid recovery compared to thiopental, allowing earlier assessment of neurological status and easier titration to desired anesthetic depth. In the authors' experience, however, a small percentage of cats (some with and some without evidence of intracranial disease, based on cerebrospinal fluid analysis and magnetic resonance imaging) have had prolonged recoveries after propofol anesthesia, and therefore care should be taken when this drug is used for anesthetic maintenance in this species. Because of the negative cardiovascular effects of propofol, blood pressure should be supported during its use. Although propofol does not directly disrupt pressure autoregulation, this may be absent in TBI patients, making cerebral perfusion dependent on systemic blood pressure. Propofol can cause respiratory depression and therefore care should be taken to avoid hypercapnia and hypoxemia. A recent investigation in patients at risk for cerebral hypoperfusion indicated that propofol use leads to disruption of flow-metabolism coupling and vasoconstriction in excess of that resulting from suppression of brain activity.[23] The significance of this is unclear, although increased cerebral ischemia has been associated with propofol use when compared to both isoflurane and sevoflurane.[37,38] Until more is known about the effects of propofol on cerebral vasculature, long periods of high doses of propofol should be used cautiously in patients at risk for ischemic brain injury.

Despite the controversy associated with the use of some injectable anesthetics, propofol and barbiturates offer a number of advantages over the use of volatile anesthetics when ICP elevation is present. Compared to volatile anesthetics, barbiturates have been shown to produce superior reduction of cerebral edema and ICP.[39,40] In patients with intracranial disease, comparisons of propofol and volatile anesthetics (sevoflurane and isoflurane) have demonstrated improved cerebral perfusion and better maintenance of pressure autoregulation when total intravenous anesthesia was used.[28,34,41] In addition, in contrast to volatile anesthetics, cerebral pressure autoregulation is maintained by the use of these agents.[42] However, it is important to remain cognizant that pressure autoregulation may be disrupted focally or globally in cases of intracranial disease and that in such cases, hypotension may not be tolerated. Under conditions of preexisting ICP elevation, total intravenous anesthesia, such as that achieved with propofol or fentanyl is recommended.

Other anesthetic and sedative agents available for use in head trauma patients include benzodiazepines, ketamine, and etomidate. Benzodiazepines (midazolam and diazepam) are advantageous due to their lack of adverse intracranial effects and lack of adverse effects on cardiovascular and respiratory function. Although they do not appear to decrease ICP, mild reductions in cerebral oxygen requirement are reported.[43] Their use also enables dose reduction of other agents, such as propofol or barbiturates, thereby reducing depression of

cardiovascular and respiratory systems. Etomidate is another agent that is frequently selected for cardiovascular and respiratory stability and has previously been thought to produce neuroprotection by decreasing cerebral metabolism.[44] However, in contrast to the benzodiazepines, use of etomidate has been associated with cerebral hypoxia and ischemic injury.[44] The mechanism by which etomidate decreases brain tissue oxygen tension is not known; however, the changes observed are consistent with cerebral vasoconstriction, possibly due to hemolysis and nitric oxide scavenging by free hemoglobin.[44] It is, therefore, suggested that etomidate be avoided in patients with head injury.

Ketamine is an alternative anesthetic and analgesic agent that has recently gained interest for use in neurosurgical patients. It is typically avoided in the presence of intracranial disease, since the sympathetic stimulation it produces may increase ICP. However, studies in head trauma patients have demonstrated that administration of ketamine under propofol sedation decreases ICP.[45] This agent, unlike other commonly used anesthetics, acts by inhibiting the NMDA receptor. Because this is the predominant receptor type responsible for ischemic injury, ketamine use may theoretically have beneficial neuroprotective properties. An additional advantage is the lack of cardiovascular or respiratory depressant effects. Ketamine administration, however, has also been demonstrated to increase cerebral oxygen consumption, possibly by inhibition of the GABA receptor (the major inhibitory neurotransmitter system within the brain).[46] It is possible that the detrimental effects of ketamine on cerebral activity may be reduced by co-administration of a GABA agonist such as propofol. Further investigation of the beneficial and detrimental effects of ketamine and other NMDA antagonists is required before their use can be recommended for use in head injured patients.

The provision of adequate analgesia is essential to prevent further ICP elevation. Opioids are widely used to provide analgesia for critically ill patients due to their relative lack of adverse cardiovascular effects and ease of reversal. Adverse effects of opioids, such as respiratory depression and hypotension, have greater significance in the presence of ICP elevation, especially when used at high doses. As a result opioids were previously withheld from head trauma patients. However when carefully titrated to patient analgesia and when ventilation is supported, opioids are safe to use in cases of intracranial hypertension.[47] In the presence of cardiovascular shock or damage to the blood–brain barrier (BBB), dose requirements may be decreased and so care should be taken to avoid overdose. Opioid agonists, such as fentanyl and morphine, can be administered as a continuous rate infusion (CRI) to avoid peaks and troughs in analgesia and the adverse effects seen at higher blood levels. Recommended CRI dosages for fentanyl include 0.2–0.7 µg/kg/min and 0.1–0.5 mg/kg/hr for morphine. These drugs may be reversed using an opioid antagonist, such as naloxone, if significant respiratory or cardiovascular depression occurs. Opioid agonist/antagonists such as butorphanol and buprenorphine are analgesics used to treat mild to moderate pain. They are generally thought to be safer than opioid agonists because they cause less cardiovascular and respiratory depression.[48,49] When considering administering these agents to patients with TBI at risk for rapid changes in neurological status, it is important to consider that the effects of buprenorphine are difficult to reverse with standard doses of naloxone.[48] It is also important to remember that the duration of analgesia from butorphanol is relatively short and, if used, should be repeated every 2 hours.[49]

Medetomidine, an α_2 agonist used for sedation and analgesia, appears not to influence ICP in dogs.[50] Reduction in heart rate and cardiac output may impair cerebral perfusion however, and therefore it should only be administered at a very low dose (1–2 µg/kg/hr) and only used if analgesics with less adverse cardiovascular effects are unavailable or are providing insufficient pain relief.

New Neuroprotective Anesthetic Adjuncts

A number of drugs are under investigation for their possible neuroprotective properties. Lidocaine may reduce secondary brain injury by preventing sodium influx into ischemic neurons.[17,51] There is some experimental evidence that infusion of antiarrythmic doses (1.5–2 mg/kg) of lidocaine after the onset of brain ischemia reduces neuronal death and improves neurologic outcome.[52] Xenon is another agent that is gaining interest as a potential neuroprotective agent.[52] This is a volatile anesthetic, but unlike other inhalant agents, it produces its effect via NMDA receptor antagonism and produces no adverse hemodynamic effects. Finally, amantadine, also an NMDA antagonist, may prove to be beneficial in head trauma. A small population of head injury patients showed a significant improvement in neurological outcome and mortality when administered amantadine compared to a group which did not receive this drug.[53] More studies are necessary, however, before amantadine can be recommended for use in a clinical setting.

Supportive Care for the Anesthetized Patient

Of equal importance to the selection of an anesthetic agent is the support of cardiovascular and respiratory

function. Prevention of cerebral ischemia during anesthesia is vital to a successful outcome for a patient with head injury. To ensure adequate oxygen delivery to the brain, PaO_2, $PaCO_2$, hemoglobin concentration, and systemic blood pressure must be maintained within normal ranges.

Blood pressure support

In head injured patients, where cerebral pressure auto-regulation may be impaired by disease or the effect of anesthetic agents, systemic blood pressure should be supported to maintain a CPP between 60 and 70 mmHg.[54,a] Normal ICP in dogs and cats is between 7 and 12 mmHg.[55–57] The necessary MABP required to support a CPP of 60–70 mmHg in the absence of ICP elevation can, therefore, be calculated as approximately 70–80 mmHg. Without the benefit of ICP monitoring devices, exact values of CPP cannot be calculated. However, blood pressure targets should be increased if signs of severe ICP elevation, such as cranial nerve deficits (e.g., nonresponsive pupils, strabismus, lack of menace response), changes in mental status or seizures become apparent. Improved brain oxygenation in head trauma patients has been demonstrated by maintaining MABP above 90 mmHg, compared to patients managed similarly but using 70 mmHg as the minimum acceptable blood pressure.[54] However, use of vasopressors to achieve targeted blood pressures in head trauma patients have also been associated in increased risk of developing adult respiratory distress syndrome and therefore should be used judiciously.[58,a] During anesthetic procedures, hypotension is avoided by the selection of anesthetic agents that do not reduce cardiac output, the use of intravenous fluid therapy, and the careful administration of vasopressors. Care should be taken to avoid inducing excessive intracranial vasoconstriction, which may negatively impact cerebral perfusion. Dopamine has been shown to improve CBF after head trauma without causing detrimental vasoconstriction.[59] In the authors' experience, dopamine infusions of 5–10 μg/kg/min effectively improve blood pressure. Vasopressin has also been used successfully in acute brain injury, although widespread clinical use in head injury is not reported.[60] Reports of the use of norepinephrine in TBI are variable. Its use has been associated with detrimental effects on CBF after damage to the BBB.[61] In contrast, more recent reports suggest that norepinephrine use is not associated with cerebral perfusion compromise.[62] Because of this controversy, dopamine is the vasopressor agent most frequently recommended for use in head trauma patients.

Intravenous fluid management

Intravenous fluid administration during anesthesia is necessary to maintain blood volume and promote cerebral and systemic perfusion, but should be performed judiciously as fluid overload may exacerbate vasogenic cerebral edema.[63] Vasogenic edema is formed by leakage of protein and fluid across blood vessel walls and can be reduced by maintaining serum osmolarity and colloid osmotic pressure (COP).[64] Selection of fluid type may, therefore, be guided by measurements of serum osmolarity and COP, as well as sodium and total protein levels. Isotonic crystalloids (e.g., lactated Ringer's solution), hypertonic fluids (e.g., 3–7% hypertonic saline), and artificial colloids (e.g., 6% hetastarch) are all suitable fluid choices; hypotonic fluids (e.g., 0.45% saline) should be avoided as these may contribute to edema formation.[64] Glucose-containing fluids should also be avoided, unless there is significant hypoglycemia, since hyperglycemia drives cerebral lactate production and has been associated with worse neurological outcome.[1,13,14,65,66] The use of hypertonic saline (e.g., 3–7%) for blood volume support is being increasingly described in the treatment of head trauma in people.[67–71] This has been associated with greater ICP reduction, thereby improving CPP, when compared to the use of lactated Ringer's solution or mannitol in both human head trauma patients and in dogs.[68,72–75]

The volume of fluid administered should be carefully considered, because of a possible association between excessive hydrostatic pressure (i.e., overhydration) and edema formation. In the past, fluid restriction and reduction of systemic blood pressure were advocated to decrease formation of vasogenic edema.[76] However, negative fluid balance has since been associated with poor outcome, and more aggressive fluid resuscitation to support intravascular volume is now recommended.[63,77] It is possible that in certain, well-hydrated euvolemic patients with no evidence of ongoing blood loss, the commonly recommended anesthetic maintenance fluid rate of 10 mL/kg/hr of isotonic crystalloid may be excessive and lead to fluid overload. Conversely, care should be taken to avoid compromising cardiac output by inadvertent fluid restriction. Fluid therapy should be adjusted according to markers of systemic perfusion and cardiac output. Parameters such as heart rate, pulse quality, mucous membrane color, urine output, and serum lactate concentration should be monitored frequently and used to guide fluid administration. In the absence of clinical parameters suggesting preanesthetic hypovolemia (tachycardia, weak or bounding pulses, pale mucous membranes, and oliguria), infusion of isotonic crystalloids at 5 mL/kg/hr during the anesthetic period is likely sufficient to

meet anesthetic fluid requirements, although monitoring parameters of intravascular volume should be continued. Preoperative administration of osmotic diuretics should also prompt titration of fluid rates to maintain euvolemia. The presence or development of hypotension or other indicators of hypovolemia during anesthesia should be aggressively treated with careful titration of intravenous fluids (e.g., isotonic, hypertonic crystalloids, and colloids) until acceptable clinical parameters are achieved. Aliquots of isotonic crystalloids (10–20 mL/kg) or 6% hetastarch (5 mL/kg) should be given to effect.

Ventilatory support

Assisted ventilation is often required for head trauma patients under anesthesia. Since many anesthetic agents cause hypoventilation, either manual or mechanical positive pressure ventilation is necessary to prevent hypercapnia-induced cerebral vasodilation and increased ICP. Although the application of positive pressure ventilation may increase ICP by decreasing venous return from the head, studies have shown that maintaining peak inspiratory pressure below 25 cmH$_2$O and positive end expiratory pressure less than 5 cmH$_2$O prevents a clinically significant increase in ICP.[78] Increasing arterial oxygenation by the provision of supplemental oxygen also helps support cerebral oxygen delivery. Previously, hyperventilation leading to hypocapnia was recommended as a method of causing vasoconstriction and prophylactically reducing ICP. However, this strategy reduces cerebral perfusion, increases the risk of ischemia, and is no longer recommended for routine use in anesthetized head trauma patients.[19,22,79] Additionally, cerebrovascular CO$_2$ reactivity following severe traumatic brain is variably depressed, potentially limiting the usefulness of hyperventilatory therapy in TBI patients.[80] Recent studies indicate that there is an increased risk of ischemic damage with even mild hypocapnia (PaCO$_2$ = 30–35 mmHg).[80] Head trauma patients under anesthesia should, therefore, be ventilated to eucapnia (PaCO$_2$ = 40 mmHg) to avoid inducing either vasodilation or vasoconstriction.

Management of ICP Elevation During Anesthesia

Despite careful patient management, acute increases in ICP may occur during anesthesia, necessitating emergency treatment to prevent decreased CPP, cerebral ischemia, and ultimately, herniation of brain tissue. Timely identification of ICP elevation during anesthesia is essential, but hampered by the effects of the anesthetic agent. In particular, proper assessments of mental status and many cranial nerve reflexes are often impossible. Clinical parameters indicative of ICP elevation that remain detectable in the anesthetized patient include miotic pupils, pupil asymmetry, and loss of palpebral and corneal reflexes.[7] As the palpebral reflex may be lost in patients at a surgical plane of anesthesia, this may not be a reliable indicator of increasing ICP. In addition, the perianesthetic use of anticholinergics may interfere with assessment of pupil size by causing pupil dilation, and therefore pupil size must be interpreted in light of anticholinergics use. These difficulties can be overcome by lightening the plane of anesthesia or discontinuing administration of anesthetic agents if increasing ICP is suspected. If the patient is not being ventilated, altered breathing patterns such as apneustic or Cheyne–Stokes breathing may also be seen in the presence of rising ICP. The Cushing's reflex is a cardiovascular phenomenon associated with increased ICP. In response to ICP elevation, systemic blood pressure increases, often to a systolic pressure greater than 200 mmHg, to maintain CPP. Reflex bradycardia prevents tissue damage resulting from such severe hypertension. This is a protective mechanism and treatment with anticholinergics (atropine or glycopyrrolate) may cause further ICP elevation and increase ischemic brain injury. Rather than treating the bradycardia, the anesthetist should therefore consider the possibility of rising ICP, and perform the treatments described below to reduce ICP and avoid further brain swelling and ischemia.

Methods to rapidly reduce ICP include hyperventilation and administration of hypermolar agents. Hyperventilation is one of the most rapid and effective methods of reducing ICP. Decreasing PaCO$_2$ by 10 mmHg can reduce ICP by up to 30% within 15 seconds.[81] Because of the adverse effects of hypoventilation on cerebral perfusion, hyperventilation is regarded as an emergency therapy only, and should be discontinued when clinical signs of ICP elevation improve. Hyperventilation to maintain a PaCO$_2$ of 30 mmHg for up to 30 minutes, with concomitant administration of other therapies can be attempted initially. In the absence of significant pulmonary disease or reduction in cardiac output, the difference between PaCO$_2$ and end-tidal CO$_2$ (ETCO$_2$) will be less than 5 mmHg and ETCO$_2$ values can be used as a noninvasive measure of arterial CO$_2$. When using ETCO$_2$ to guide hyperventilatory therapy, a target of 35 mmHg is recommended. Hyperventilation to a PaCO$_2$ less than 30 mmHg should be only be used for intractable intracranial hypertension and for the shortest duration possible.

Hyperosmolar agents such as mannitol can be used to decrease ICP. Mannitol acts as an osmotic diuretic to reduction cerebral edema. Other benefits attributed

to mannitol include reduction in blood viscosity, improved perfusion of ischemic regions, free radical scavenging properties, and possible reduction of subsequent edema formation.[81] Twenty-five percent mannitol (osmolarity = 1372 mOsm/L) is administered at a dose of 0.25–1 g/kg over 20 minutes.[6] Because the osmotic effects of mannitol are dependant on an intact BBB, its use when the BBB is disrupted, for example, following intracranial hemorrhage, may worsen cerebral edema. When the BBB is no longer intact, mannitol may leak into brain interstitium, increase tissue osmolarity, and therefore increase fluid accumulation. While a disruption of the BBB will increase its permeability to all ions, the higher membrane reflection coefficient for sodium chloride ($\sigma = 1$) compared to mannitol ($\sigma = 0.9$) suggests that the use of saline-based hyperosmolar agents may be preferable over mannitol in certain intracranial pathologies such as intracerebral hemorrhage.[72,82] Additionally, because of the tendency of mannitol to deplete the intravascular volume, repeated doses are not recommended and use of alternative hyperosmolar agents may be preferred. Hypertonic saline (7.2% hypertonic saline; osmolarity = 2464 mOsm/L), given at a dose of 4 mL/kg administered slowly IV, can be used to reduce ICP and cerebral edema.

Other management strategies including the prevention of hyperthermia, head elevation, and avoiding occlusion of jugular veins may also be employed to prevent increases in ICP. In experimental models, moderate hypothermia (31–34 °C) reduces the effects of global ischemia, decreases cerebral metabolic rate, and decreases ICP.[83] While clinical induction of hypothermia in patients with TBI cannot be recommended currently, avoidance of hyperthermia may be prudent.[13,24,84] Elevation of the head by 15–30° may limit venous congestion and thereby reduce ICP without decreasing CPP or CBF.[85] Jugular vein occlusion impairs venous drainage from the head and can cause increased intracranial blood volume; jugular catheters, twisting the neck, and tight neck bandages should be avoided in head trauma patients. Coughing and gagging during endotracheal intubation can also contribute to ICP elevation, and therefore a smooth anesthetic induction is beneficial. This is easily accomplished by administering a premedication that causes sedation (e.g., a benzodiapine or opioid), applying lidocaine to the larynx and administering sufficient anesthetic induction agent that laryngeal reflexes are suppressed prior to attempting intubation. Additionally, rough anesthetic recovery may cause sympathetic stimulation elevating ICP; therefore, providing sedation during the anesthetic recovery phase is recommended.

Summary

The effects of anesthetic agents on intracranial hemodynamics and neuronal injury are complex. The overall effect on CPP is a result of a number of specific effects that include ICP elevation, vasomotor effects, disruption of autoregulation, and secondary effects via alterations of cardiovascular and respiratory function. Low concentrations of isoflurane and sevoflurane are likely to have minimal effects on cerebral perfusion as long as blood pressure and ventilation are supported; however, their tendency to increase ICP is a concern, especially if the patient shows signs of ICP elevation prior to anesthesia. Barbiturates produce minimal adverse intracranial effects and therefore are suitable agents for use in head trauma patients if blood pressure is supported; however, delayed anesthetic recovery can complicate neurological assessment. Propofol has been a useful alternative to barbiturates due to its short half-life leading to rapid recovery from anesthesia. It remains a useful agent in neuroanesthesia with appropriate physiologic support; however, it is probable that it has less neuroprotective properties than barbiturates, and there is a concern it may exacerbate ischemic injury. Use of agents such as opioids and benzodiazepines allows the dose of the selected anesthetic maintenance agent to be reduced. This minimizes adverse cardiovascular, respiratory, and neurological effects and can provide an anesthetic protocol which is less likely to cause further neuronal damage. More important than the anesthetic drugs selected, careful monitoring and support of cardiovascular and respiratory functions remains of primary importance when managing an anesthetized head trauma patient.

Footnotes

[a] Brain Trauma Foundation, American Assoc Neurological Surgeons, Congress of Neurological Surgeons, Joint Section on Neurotrauma and Critical Care. Management and prognosis of severe traumatic brain injury: Cerebral perfusion pressure – update 2003. http://www2.braintrauma.org/guidelines/index.php

[b] Adapted from Hopkins AL. Head trauma. Vet Clin North Am: Small Anim Pract 26(4):876. Copyright (1996), with permission from Elsevier.

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