Anesthesia for neurosurgery

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The practice of neuroanesthesia is unique in that the target organ of both the surgeon and
the anesthetist is one and the same. Thus, the surgical goals have a profound impact on
the constraints that the anesthesiologist must work within. In order to appropriately
anesthetize the patient for neurosurgery, an understanding of the interrelationships of
neurophysiology, pathophysiology and pharmacology is important. This chapter will
review: 1) basic neurophysiological principles, 2) specific approaches to the management
of intracranial pressure (ICP) as they relate to clinical neuroanesthesia, and 3)
intraoperative management of the patient with a supratentorial mass lesion.

1. Basic principles of neurophysiology

There are six interrelated components that are important to the practice of
neuroanesthesia. They are maintenance of cerebral perfusion pressure (CPP), cerebral
blood flow (CBF), cerebral blood volume (CBV), intracranial pressure (ICP), CO₂
responsiveness (CO₂R) and cerebral oxygen metabolism (CMRO₂).

1. Cerebral Perfusion Pressure. CPP is the difference between mean arterial pressure
(MAP) and intracranial pressure (ICP) \([CPP = MAP - ICP]\), although in the occasional
patient where central venous pressure is higher than ICP, \(CPP = MAP - CVP\). Both
intracranial pathology and drugs may compromise CPP through effects on MAP and/or
ICP. CPP is usually >70 mmHg. An optimal CPP has not been defined but in the context of head trauma, a CPP < 60 is associated with a poorer outcome; a benefit of higher CPP has not been shown [1].

2. Cerebral Blood Flow. The average CBF is ~40-50ml/100gm/min with gray matter having a higher flow than white matter (60 ml/100gm/min and 20 ml/100gm/min respectively). CBF is autoregulated – that is, blood flow is maintained over a wide range (~50 – 150 mmHg) of perfusion pressures in order to avoid ischemia when blood pressure is reduced and edema or hemorrhage at higher blood pressures. Static autoregulation refers to changes in flow that occur slowly (minutes) in response to changes in blood pressure and dynamic autoregulation is used to describe changes that occur within seconds. The autoregulatory range and the relationship between CBF and perfusion pressure can change rapidly as one would want from a homeostatic response. When sympathetic tone is reduced the entire response can shift to lower pressures and when tone is increased such as during stress it moves to a higher pressure range. With hyperventilation the response shifts to lower CBF and covers a wider perfusion pressure range while an increased CO₂ results in a narrower range at a higher CBF.

Volatile anesthetics affect CBF both indirectly and directly. When cerebral metabolism (CMRO₂) is decreased, vasoconstriction occurs to appropriately reduce CBF. However, direct vasodilation also occurs in a dose-dependent fashion [2]; [3]; [4]; [5] but may not manifest as increased CBF except at higher concentrations. Evidence from both animal and humans suggest that the increase in CBF is more pronounced with desflurane and least with sevoflurane [6]; [7]; [8]; [2]].
Both static and dynamic autoregulation remain essentially intact with both sevoflurane and isoflurane up to 1 MAC [9]; [10] but preservation is better and persists to a higher concentration with sevoflurane [11]. Desflurane >1 MAC abolishes autoregulation [10]. Static autoregulation also appears to be intact in children undergoing non-neurosurgical procedures with doses of sevoflurane up to 1.5 MAC [12]. The effect of volatile anesthetics on cerebral hemodynamics including CBF and autoregulation has been well reviewed[6, 8].

Propofol, barbiturates and etomidate are potent cerebral vasoconstrictors reducing CBF secondary to decreasing CMRO₂ [13-15]. The effect on CBF is greater with propofol and thiopental than etomidate. Propofol and thiopental do not alter autoregulation[10].

Opioids have minimal effect on CBF [16].

3. Cerebral Blood Volume. Approximately 15% of CBV is in the arterial tree and ~15% in the major venous sinuses. The remainder is in the capillary and venous systems. CBF is often incorrectly used as a surrogate for blood volume, probably because it has been easier to measure. Changes in CBF and CBV are generally proportional to one another but, for instance, changes in head position from standing to supine to head down can increase CBV without changing CBF.

Propofol decreases CBV in humans and sevoflurane increases it but less than isoflurane [17, 18].
4. Intracranial Pressure. Maintenance or reduction of ICP (normal value ~10 mm Hg) of ICP is one of the important aims of neuroanesthesia. ICP is a critical determinant of CPP and by extension CBF and brain function. As ICP increases above ~20 mmHg, focal reductions in CBF occur and further increases eventually result in global cerebral ischemia. The three major components of the intracranial cavity are brain (~80%), cerebrospinal fluid (CSF) (~10%) and CBV (~10%). If one component increases its volume, it must be compensated for by a decrease in another to prevent ICP from increasing.

5. CO₂ responsiveness. CO₂R of the cerebral arterial tree is important in that hypercarbia results in vasodilation and increased CBV. Conversely, hyperventilation causes cerebral arterial vasoconstriction, decreased CBF & CBV and a decreased ICP. While the reduction in ICP is beneficial, the reduced CBF can result in ischemia so that caution must be exercised with the extent and duration of hyperventilation (see below).

CO₂ reactivity is maintained with both sevoflurane and isoflurane up to 1.5 MAC in adults [3, 19, 20] and with sevoflurane, isoflurane and halothane up to 1.0 MAC in children[21, 22]. Intravenous anesthetics do not influence CO₂ R significantly.

6. Cerebral oxygen metabolism. CMRO₂ is a key determinant of the risk of ischemic insult. If metabolic rate is high, then a reduced CBF is more likely to disrupt neuronal function and integrity. This is the rationale behind decreasing CMRO₂ in order to prevent ischemia. While this notion is appealing in its simplicity, there are no clinical trials in neuroanesthesia to support such a practice and animal studies indicate that any benefit from anesthetics probably reflects both intra- and extra-cellular effects[23].
Intravenous anesthetics potently reduce CMRO$_2$. As CBF is closely coupled to CMRO$_2$, CBF is reduced in parallel with an associated reduction in CBV and ICP which makes them very useful agents in patients with intracranial hypertension. Volatile anesthetics in contrast reduce CMRO$_2$ but increase CBF through direct effects on the vasculature. Although often referred to as “uncoupled,” experimental studies in rats suggest that flow and metabolism continue to track in the same direction but with CBF at a higher “set point”[24].

II. Clinical neuroanesthesia

The common types of neurosurgery can be divided into excision of intracranial mass lesions, especially supratentorial tumors, decompressive procedures in major head trauma and aneurysm clipping. This review will focus on managing elevated ICP as this is a problem common to all types of intracranial surgery and then specifically the management of supratentorial masses.

1. Management of Intracranial Pressure

ICP may be affected by four major variables in the operating room - hyperventilation, anesthetic drugs, diuretics such as mannitol, and head position.

A. Hyperventilation constrains the cerebral arterioles with concomitant decreases in CBF and CBV. The effect takes place rapidly and may be especially useful for decreasing ICP in situations in which ICP is critically elevated or the surgeon is having difficulty with brain bulk. However, cerebral vasoconstriction may lead to critical hypoperfusion and
brain ischemia with no improvement or worsened outcomes especially with prolonged use [25-28].

Therefore, current recommendations are that hyperventilation: 1. should not be used prophylactically in the traumatically brain injured patient and should only be used for brief periods to manage significant increases in ICP not responsive to alternate treatments[25, 26]. 2. Similar concerns prevail in the operating room although no trials have addressed outcomes in this context. In either case, unless neurosurgical conditions demand it, ventilation to moderate levels of hypocapnia (PaCO2 32-35 mmHg) rather than severe (PaCO2 < 32 mmHg) should be used.

B. Anesthetic drugs

Volatile anesthetics produce direct vasodilatation and thus have the potential to increase ICP. However the effect on ICP, in both pediatric and adult patients with space-occupying lesions is clinically insignificant when anesthetic concentrations are maintained below 1.2 MAC and if the ICP is not critically elevated [4, 29-32].

Propofol, barbiturates (thiopental) and etomidate have minimal effect or decrease ICP [32]. Few randomized controlled trials have compared intravenous and inhalation agents and their effect on ICP. In a trial of 117 patients with supratentorial tumors undergoing elective resection, subjects received propofol or isoflurane or sevoflurane as well as a fentanyl infusion (2-3 μg/kg/hr). ICP was lower, brain swelling less, and CPP better preserved in the propofol group[33]. An earlier trial on 121 patients undergoing elective removal of supratentorial tumors found no difference in mean ICP amongst propofol/fentanyl, fentanyl/nitrous oxide, or isoflurane/nitrous oxide[34]. However, there
were significantly more patients in the isoflurane/nitrous oxide group that had an intraoperative ICP $\geq 24$ mm Hg.

The benefits of high dose barbiturate coma in the management of elevated ICP have not been demonstrated while deleterious outcomes including increased mortality have been shown [35].

Opioids do not increase or decrease ICP[36]. However, when blood pressure decreases, the cerebral vasculature dilates to maintain CBF; this dilation may increase ICP if it is critically increased [16].

**C. Mannitol** has become the mainstay of ICP management protocols. An osmotic diuretic, mannitol draws water from the brain and other tissues into the intravascular compartment. Mannitol may also lower ICP by decreasing blood viscosity and expanding plasma volume which increase CBF. When autoregulation is intact this prompts vasoconstriction to restore CBF towards normal [37].

A small, randomized trial concluded that there may be a mortality benefit to using mannitol instead of barbiturate infusion in cases of elevated ICP [35]. Other prospective, randomized studies evaluated long-term outcomes in TBI patients. In each study, one group received early, pre-operative treatment of high-dose mannitol whereas the other group did not. The early, high-dose mannitol groups had clinical reversal of impending signs of brain death, better postoperative control of ICP, and better cerebral perfusion [38-41]. Thus current guidelines advocate use of high-dose mannitol boluses for elevated ICP as long as hypovolemia and excessive serum osmolalities ($>320$ mOsm) are avoided.
The use of mannitol to reduce brain bulk in the OR has not been as well investigated; current practice guidelines are drawn from the head trauma literature.

Hypertonic saline is being investigated as an alternative to mannitol [42]. It has been suggested that by using a hypertonic saline solution, a similar ICP lowering effect to mannitol may be achieved with better outcomes, better preservation of MAP and a potentially longer duration of effect [42, 43].

D. Head-up position is an effective intervention to reduce ICP although there is concern that MAP and consequently CPP would drop. There have been two cohort craniotomy trials examining 10 degree head up position. One involved 40 patients, the other 15. Head-up position of 10 degrees significantly decreased ICP and MAP but left CPP unaffected [44]. Similar results have been found in head trauma patients subjected to 30 degree head up [45].

2. Anesthesia for a patient with a supratentorial mass

The most common mass is a supratentorial tumor. Resection of the tumor requires maintenance of adequate cerebral perfusion to prevent ischemia while ensuring that ICP is not dangerously elevated. Timely wake-up is desirable in order to facilitate neurological evaluation soon after surgery.

Pre-operative evaluation. Besides the routine assessments the patient should be assessed for signs of elevated ICP (nausea/vomiting, papilledema, headache, visual changes, altered mental status, altered breathing patterns, hypertension, bradycardia) and the
neurological deficits documented. It is better if the anesthesiologist does his/her own examination but the neurologist or neurosurgeon’s examination may be more complete. The diagnostic imaging should be seen so as to identify the type of tumor, its location, vascularity, evidence of midline shift and presence of hydrocephalus. Often, patients are taking steroids and anti-epileptic medications which can have an impact on glucose homeostasis and pharmacodynamics of neuromuscular blockers respectively. Pre-medication for anxiolysis may be offset by sedation that may hamper neurological assessment and hypercarbia which may increase ICP. In most patients, a carefully titrated dose of intravenous benzodiazepine can safely be given if needed.

Monitors consist of standard monitors. Continuous blood pressure measurement, preferably via peripheral artery catheter is useful in detecting and treating abrupt hemodynamic changes that might compromise CPP or ICP. Core temperature should be monitored and kept in the normal range. A Foley catheter is important if diuretics are to be used or the surgery will be long.

Induction of anesthesia is a critical time because of the highly stimulating effects of direct laryngoscopy and intubation which is followed a short time later with pinning the head for optimal positioning which is painful. Excessive increases in blood pressure and coughing should be avoided. The most common induction agents are propofol or thiopental with etomidate or ketamine occasionally used in the hemodynamically unstable patient. These are supplemented with an opioid such as fentanyl 2-3 ug/kg or a remifentanil infusion [46]. In addition 1-1.5 mg/kg lidocaine IV or esmolol 5-10 mg IV may help blunt the hemodynamic effect on ICP but the effect may be incomplete [47].
Either succinylcholine or a nondepolarizing muscle relaxant may be used. There has been controversy about succinylcholine in patients with elevated ICP but the effects are usually of short duration and can be buffered by some additional propofol. The efficacy of lidocaine has not been demonstrated [48]. Level 2 evidence exists to support use of a defasciculating dose of a nondepolarizing relaxant to blunt the increase in ICP with succinylcholine [49]. Expeditious intubation followed by oxygenation and hyperventilation is much preferred to the avoidance of succinylcholine but with a delayed and problematic intubation. Neuromuscular blockade may not be needed during the procedure but should be used during positioning and head pinning.

**Maintenance of anesthesia.** There needs to be constant attention to the balance between ICP and CPP together with adequacy of anesthetic depth. Attention to ICP is especially important before the dura is opened; once the dura is open, ICP is effectively zero. Another important consideration is the need for neuromonitoring, e.g. somatosensory or motor evoked potentials which are used with increasing frequency during neurosurgical procedures. Good communication between anesthesiologist, neurosurgeon and monitoring technician is essential as local preferences tend to dictate drug choices. This is especially true for direct stimulation of the motor cortex as there is a paucity of clinical studies to support the use of one drug over another. SSEPs are only minimally influenced by total intravenous anesthesia (TIVA) and are suppressed by inhalational agents in a dose dependent manner although good signals can be obtained with <0.75MAC vapor.
A typical maintenance anesthetic might consist of a vapor anesthetic at <1 MAC and an opioid (fentanyl, sufentanil or remifentanil) infusion or alternatively a TIVA. The latter is especially appropriate where ICP is markedly elevated or there is acute decompensation.

**Recovery.** If the patient is to be extubated at the end of surgery, the anesthetic drugs should be appropriately tapered as the scalp is sutured. If fentanyl or sufentanil have been used by infusion, these are usually terminated at dural closure. Remifentanil should be continued till scalp closure and transitional analgesia such as fentanyl 50–100 μg given[46]. The goal is a comfortable patient in whom a neurological examination can be conducted early after the surgery.

**III. Summary & recommendations**

Management of the patient for neurosurgery requires a good understanding of the interrelationships of neurophysiology, pathophysiology and pharmacology. Good data (mostly level 1) exist to describe the effects of volatile and intravenous anesthetics on cerebral hemodynamics (CBF, autoregulation, CBV, CO2 reactivity). Based on this data, one would recommend using < 1 MAC sevoflurane or isoflurane over desflurane in adults with elevated ICP with a slight preference for sevoflurane. In children, a similar recommendation can be made. For patients with critically elevated ICP, a TIVA anesthetic may be preferred. Most studies, however, have used physiological measurements such as CBF or ICP intraoperatively. No level 1 study exists which measured clinical outcomes.
Induction of anesthesia may be achieved with IV agents normally used (e.g. propofol, thiopental or etomidate). There is level 2 data to support pre-treatment with lidocaine to minimize elevation in ICP (Grade B recommendation). There is also level 2 data to support the use of a defasciculating dose of non-depolarizing muscle relaxant if succinylcholine is to be used.

The clinical data for management of ICP come mostly from studies of patients with head trauma. Level 2 Data (Grade B recommendation) support the use of the head-up position for significantly reducing ICP without compromising CPP. With respect to hyperventilation and mannitol, this data has been subjected to formal Cochrane reviews and review by the Brain Trauma Foundation. There are Grade A recommendations for the use of: 1) brief, moderate hyperventilation (PaCO₂ 32-35 mm Hg) in cases of acutely elevated ICP, and 2) high-dose mannitol (1.2-1.4 g/kg) in place of conventional dose mannitol (< 1 g/kg) for the treatment of acutely elevated ICP (in comatose patients). These guidelines can be applied to the OR for non head trauma patients. More randomized control trials that explore these interventions for elevated ICP specifically in this setting are needed.

REFERENCES:


48. Robinson, N. and M. Clancy, In patients with head injury undergoing rapid sequence intubation, does pretreatment with intravenous lignocaine/lidocaine lead