OBJECTIVES:

At the end of this lecture, the participant should be able to:
1. make informed decisions regarding use of intravenous vs. inhalational anesthetics during craniotomy.
2. articulate the controversy regarding the use of dexmedetomidine in patients with neurologic injury.
3. identify the potential advantages of hypertonic saline over mannitol for brain relaxation.
4. calculate an effective dose of adenosine to achieve 60 seconds of hypotension during aneurysm clipping.
5. make informed decisions regarding neuroprotective strategies during temporary aneurysm clipping.
6. describe the long-term benefits of scalp block for post-craniotomy analgesia.

INTRODUCTION AND FORMAT

Neuroanesthesiology involves the perioperative care of patients with neurologic disease undergoing surgical intervention. The breadth of neurosurgical practice (from major spine, to cerebrovascular surgery, to awake craniotomy) and neuroscientific investigation could potentially lead to an unwieldy update lecture. As such, the current lecture will be structured around a single clinical case of a patient with subarachnoid hemorrhage presenting for clipping of a ruptured intracranial aneurysm. The case discussion will draw upon recent literature from the past several years as a method of informing clinical decision making. The advantages of this case-based approach are greater coherence and focus; the disadvantage is that other important topics (such as spine or functional neurosurgery) will be excluded. It is hoped that this format will be high-yield for a relatively brief lecture intended to help the participant understand both the fundamentals and current trends of neuroanesthetic practice.

CASE DESCRIPTION

The patient was a 30-year old female with no significant past medical history who was found unresponsive by her father. Two days prior to admission the patient had complained of a headache, which had resolved; on the day of admission she missed work without calling, which prompted further investigation by her family. Of note, her grandfather died of a ruptured intracranial aneurysm. Computed tomography from an outside hospital revealed diffuse subarachnoid hemorrhage and a lesion suspicious for an intracranial aneurysm (Figure 1); subsequent angiography at our institution identified a giant (2.5cm diameter) right middle cerebral artery aneurysm (Figure 2). Due to the size of the aneurysm, coiling was not considered a feasible option and surgical clipping was indicated. You are the on-call anesthesiologist assigned to the case!

Is there an advantage to intravenous vs. inhalational anesthesia?

Lauta et al. conducted a randomized controlled trial to test the hypothesis that a sevoflurane-remifentanil anesthetic was superior to a propofol-remifentanil anesthetic in adult patients undergoing supratentorial craniotomy. There were approximately 150 patients in each group. Sevoflurane was administered at 0.7-2.0% whereas propofol was infused at 6-10 mg/kg/hr. The primary outcome was the time to return to an Aldrete score of ≥9 during the 3 hours after surgery, an endpoint based on Todd et al, 1993. Secondary outcomes included time to eyes open, extubation time, adverse events, intraoperative hemodynamics, opioid consumption, and brain relaxation score. There was no difference in the primary outcome between the sevoflurane and propofol groups. Time to eyes open and extubation were significantly shorter in the sevoflurane group, but only by approximately 2 minutes for each group.
The authors conclude that sevoflurane is not clinically superior to a propofol anesthetic. The decision to use intravenous vs. inhalational anesthesia in the current patient should therefore be dictated by the underlying physiology. Intravenous agents such as propofol may be advantageous in that there remains a tightly coupled decrease of cerebral blood flow in response to decreased cerebral metabolic rate. In this patient, a reduction in cerebral blood flow, cerebral blood volume, and intracranial pressure may be beneficial. Metabolism-flow coupling occurs with sevoflurane, but the ratio is altered due to the cerebral vasodilation caused by potent inhalational agents.

**Is it safe to use dexmedetomidine in a patient with neurologic injury?**

The alpha-2 agonist dexmedetomidine has many potential advantages for the neurosurgical patient undergoing aneurysm clipping, including sympatholysis and a minimum alveolar concentration-sparing effect. However, prior studies in canines have suggested that dexmedetomidine has a cerebral vasoconstrictive effect that is not associated with a coupled reduction in cerebral metabolic rate. In a patient with neurologic insult, this would imply a reduction in much-needed supply without a concomitant reduction in demand, with potentially deleterious effects. However, a recent study in nonanesthetized human volunteers suggested a coupled decrease in cerebral blood flow and metabolism. In 2010, a follow-up report was published on anesthetized humans undergoing cerebrovascular surgery who also had concomitant brain parenchymal \( \text{O}_2 \) measurements. Brain tissue probes were placed in regions at risk of impaired perfusion. Dexmedetomidine was bolused at 1mcg/kg and then infused at 0.5-0.7 mcg/kg/h. Parenchymal \( \text{O}_2 \) measurements were stable after dexmedetomidine infusion. In conjunction with past findings in humans, the current study does not support an adverse cerebral vasoconstrictive effect of dexmedetomidine that is independent of a reduction in cerebral metabolic rate.

The brain is “tight”—is there any advantage to using hypertonic saline vs. mannitol?

In 2007, Rozet and colleagues conducted a blinded, randomized controlled trial in 40 patients undergoing craniotomy in order to compare equiosmolar mannitol and 3% saline. The investigators found that the two osmotic agents were comparable in achieving brain relaxation (using a four-point scale: 1-perfectly relaxed, 2-satisfactorily relaxed, 3-firm, 4-bulging). Mannitol was associated with increased urine output and rising lactate levels compared to 3% saline. In 2010, Wu et al. conducted a larger trial of supratentorial craniotomy in which 122 patients were randomized to 3% saline and 116 patients were randomized to mannitol. The Wu et al. study demonstrated that 3% saline was more effective at achieving brain relaxation (using a three-point scale: 1-tight, 2-adequate, 3-soft). Like the Rozet et al. study, Wu and colleagues found that mannitol was associated with significantly more urine output. Both studies found that 3% saline increased serum sodium and mannitol decreased serum sodium. Hypertonic saline may therefore have advantages as an osmotic agent for brain relaxation and maintenance of fluid balance.

**How much adenosine should I use to facilitate aneurysm clipping or in the event of rupture?**

Adenosine is a purine nucleoside that slows conduction through the atrioventricular node and has a negative chronotropic effect at the sinoatrial node. Retrospective clinical reports in 2010 by Bebawy and colleagues and 2011 by Guinn and colleagues have contributed to our understanding of adenosine dosing to facilitate surgical management of complex aneurysms. Bebawy et al. reviewed cases over a 3-year period in which adenosine was used to facilitate intracranial aneurysm clipping. Patients were not given adenosine if they had significant coronary artery disease (left main >80% stenosed, multi-vessel disease), conduction defects, pacemakers, or severe reactive airway disease. In order to achieve systolic blood pressure <60mmHg for approximately 60 seconds, a median dose of 0.34mg/kg ideal body weight was used during propofol-induced burst suppression. This also resulted in systolic blood pressure less than baseline for approximately 2 minutes. Of the 24 patients who received adenosine, 2 developed stable intraoperative atrial fibrillation and 2 other patients developed mild troponin elevation. The study by Guinn et al. was also retrospective and evaluated 27 patients over 2 years who received adenosine. A median dose of 0.53mg/kg was associated with systolic blood pressure <60mmHg for 60-90 seconds; this was not dosed to ideal body weight. Both articles suggested that pacing pads be placed after induction and prior to the use of adenosine, given the reported 4% incidence of temporary pacing required in a study of endovascular aortic aneurysm repair. Taken together, these studies suggest that an adenosine dose of approximately 0.4mg/kg may be needed to achieve the hemodynamic conditions required for aneurysm clipping.

**Will cooling or pharmacologic interventions during temporary clipping improve outcome?**

Before permanent clipping of an intracranial aneurysm, a temporary clip is often placed on the parent vessel. The advantage of the temporary clip is that it allows the surgeon to manipulate the aneurysm without fear of rupture; the disadvantage is that this “proximal control” can potentially result in focal cerebral ischemia in the brain parenchyma normally supplied by the clipped vessel. Thus, a neuroprotective intervention that could reduce the risk of cerebral ischemia during temporary clipping would be of clinical benefit. Techniques that have been employed for this purpose include mild hypothermia, titration of an intravenous anesthetic to burst suppression, and induced hypertension for improved collateral flow. In 2010, Hindman and colleagues published a secondary analysis of the Intraoperative Hypothermia for
Aneurysm Surgery Trial (IHAST). IHAST found that mild hypothermia (33°C) did not improve neurologic or neuropsychologic outcome in patients who underwent surgical clipping of a ruptured intracranial aneurysm. However, cases in which temporary clipping occurred were not analyzed separately in the original study. Of those receiving temporary clipping in IHAST (n=441), there were 208 patients assigned to intraoperative hypothermia and 233 patients to normothermia. Furthermore, of the 441 patients, 263 received no additional protective intervention and 178 did (157=thiopental, 20=etomidate, 1=other). The main findings of Hindman et al. were that neither mild hypothermia nor supplemental pharmacologic intervention had any meaningful association with early or late neurologic outcome in the setting of temporary clipping. Of note, longer temporary clip times (>20 minutes) were associated with less favorable outcomes.

Will scalp block facilitate postoperative pain control?

Despite common misconceptions, craniotomies can be painful and can lead to chronic pain. In 2009, Batoz et al. published the results of a randomized study in which patients undergoing craniotomy received scalp infiltration with ropivacaine 0.75% vs. a control in which patients undergoing craniotomy received no additional protective intervention. The primary outcome was pain at 2 months. There was no statistically significant reduction in pain between the two groups, but there was a significant reduction in pain scores in the 24 hours following surgery. At 2 months, the group receiving scalp block had significantly reduced pain scores in the 24 hours following surgery. At 2 months, however, the group receiving scalp block had significantly reduced pain scores in the 24 hours following surgery. In 2010, the group receiving scalp block had significantly reduced pain scores in the 24 hours following surgery. At 2 months, however, the group receiving scalp block had significantly reduced pain scores in the 24 hours following surgery.

CONCLUSION

The patient in this case received adenosine boluses and temporary clipping during a total intravenous anesthetic and had her aneurysm successfully clipped despite technical challenges—she is now making an excellent recovery. This case served as a vehicle to discuss several recent studies related to cerebrovascular surgery and craniotomy in general. For a comprehensive update in neuroanesthesiology, the reader is referred to the excellent annual review article by Pasternak and Lanier.18

REFERENCES