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Anesthetic Management of Patients with Intracranial Aneurysms

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ABSTRACT

Background: Stroke is a leading cause of death and disability worldwide. Aneurysmal subarachnoid hemorrhage (aSAH), a significant cause of hemorrhagic stroke, continues to have poor prognosis. Early diagnosis and treatment are key to improving outcomes. Subarachnoid hemorrhage (SAH) and aSAH are often accompanied by multiple comorbidities, making anesthetic management of these patients complex.

Methods: This article summarizes the goals of anesthetic management of patients with cerebral aneurysm, including preoperative considerations, intraoperative management, and postoperative considerations.

Results: Hemodynamic monitoring is an important aspect of management. Use nicardipine, labetalol, and esmolol to avoid increases in blood pressure that may cause aneurysm rupture, and avoid low blood pressure as this may decrease cerebral perfusion pressure. Nimodipine is recommended for vasospasm prophylaxis in all patients with aSAH. The hypertension arm of Triple H therapy (hypertension, hypervolemia, hemodilution) is the most important to improve cerebral perfusion. Erythropoietin has shown some promise in lowering the incidence of vasospasm and delayed cerebral ischemia. Albumin is the preferred colloid.

Conclusion: Anesthetic management of patients with aSAH and SAH is a complex endeavor. Careful consideration of individual patient status, optimal techniques, and the safest evidence-based methods are the best options for successfully treating these life-altering conditions.

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INTRODUCTION

Stroke and cerebrovascular disease are the second leading cause of death worldwide and account for significant healthcare costs and morbidity among survivors.[1] Hemorrhagic strokes result from the rupture of weakened blood vessel walls, usually aneurysms or arteriovenous malformations. Often a subarachnoid hemorrhage (SAH) results from the rupture of these vessels. Risk factors for an aneurysmal SAH (aSAH) include female sex, African American ethnicity, first-degree relative with SAH, low high-density lipoprotein (HDL) cholesterol level, hypertension, obesity, alcohol abuse, and tobacco use.[2-7]

Classically, patients with SAH present with acute onset of what they describe as the worst headache of their lives. Other presenting symptoms include nausea, vomiting, photophobia, altered or lost consciousness, seizures, meningismus, and focal neurologic deficits. Unfortunately, many patients die prior to presentation. For diagnosis, computed tomography (CT) has the highest sensitivity during the first 3 days after the onset of bleeding; magnetic resonance imaging (MRI) has better sensitivity than CT after 3 days.[8-10] Lumbar puncture can also confirm clinical suspicions of SAH.

Surgical treatment involves obliterating the aneurysm by surgical clipping via the intracranial route or coiling via the endovascular route. If both treatment options are possible for a particular patient, endovascular coiling is the preferred method.[10]

PERIOPERATIVE CONSIDERATIONS

The aSAH is often complicated by rebleeding, hypertension, cerebral edema, delayed cerebral ischemia (DCI), electrolyte abnormalities, hydrocephalus, seizure activity, and cardiopulmonary dysfunction.[11,12] Monitoring for and consideration of each of these complications should guide anesthetic management from preoperative through postoperative treatment.

Upon diagnosis of SAH, prompt treatment is recommended as the risk of rebleeding is highest within the first 12 hours of initial rupture. Early rebleeding and cerebral vasospasm can lead to cerebral ischemia, which is the major cause of morbidity and mortality after aSAH, and early rebleeding has worse outcomes than later rebleeding. Hypovolemia and increased intracranial pressure (ICP) heighten the chance of cerebral vasospasm and possible ischemic events.[13]

Hypertension, which may be the precipitating event that led to the rupture of the aneurysm, is often a long-standing issue for patients with SAH. Thus, blood pressure control may be relative to the patient's baseline blood pressure. To avoid lowering blood pressure excessively, cerebral perfusion pressure (CPP) must be maintained at adequate levels. The American Heart Association (AHA) 2012 Guidelines for the Management of Aneurysmal Subarachnoid Hemorrhage do not give any specific blood pressure recommendation. However, general recommendations call for systolic blood pressure $<$160 mmHg because of the risk of rebleeding; administering short-acting, titratable, continuous intravenous (IV) agents with a favorable safety profile such as nicardipine, labetalol, and esmolol to control hypertension when needed; and avoiding sodium nitroprusside.[7]

Nimodipine is recommended by AHA for all patients with aSAH for vasospasm prophylaxis. Although it has not been shown to improve cerebral vasospasm by angiogram, nimodipine has decreased delayed ischemia and improved neurologic outcomes.[14,15] Verapamil has been shown to improve neurologic outcomes without increasing ICP.[16]

DCI associated with vasospasm is a major cause of death and disability in patients with SAH. Vasospasm and DCI are common after SAH and occur most frequently 7-10 days after aneurysm rupture. No preventive therapy for DCI has been determined to date. Maintaining normovolemia is recommended to prevent DCI, and prophylactic hypervolemia is not.[7] When DCI is diagnosed, CPP should be maintained with hemodynamic augmentation. Induced hypertension to treat DCI is recommended if cardiac status allows and baseline blood pressure is not elevated.[7]

The triple H therapy, aimed at achieving hypervolemia, hypertension, and hemodilution, is often used to increase cerebral blood flow (CBF) following repair of the aneurysm. Although triple H therapy is a traditional method for prophylaxis and treatment of cerebral vasospasm, few randomized clinical trials were conducted to prove its efficacy and some recent studies have questioned this technique.[17]

Administration of triple H therapy can be risky for patients with significant cardiopulmonary compromise, so it must be tailored appropriately to avoid exacerbating any existing dysfunction. Volume expansion decreases cerebral oxygenation and only mildly increases CBF, while vasopressor-induced elevation of mean arterial pressure (MAP) increases CBF significantly.[18] Hemodynamic augmentation focus has shifted away from traditional triple H therapy toward maintenance of normovolemia and induced hypertension.[19] The Neurocritical Care Society recommends vasopressor therapy to augment blood pressure when necessary.[20] Commonly used vasopressors include phenylephrine, norepinephrine, and dopamine. For a symptomatic vasospasm unresponsive to hypertensive augmentation, the AHA has deemed cerebral angioplasty and/or selective intra-arterial vasodilator therapy reasonable.[21,22] In the presence of vasospasm, intraaortic balloon pump therapy has been shown to successfully improve cardiac function and cerebral blood flow for patients with SAH and to reverse vasospasm-induced DCI.[21,22]

Erythropoietin has shown some promise in lowering the incidence of vasospasm and DCI. It also has shown improved outcomes, but further studies are needed to confirm this result.[23]

According to AHA guidelines for aSAH, treating volume imbalances with crystalloid or colloid is reasonable. Monitoring fluid volume status via central venous pressure, pulmonary wedge pressure, and/or fluid balance may be necessary. Albumin has been shown to improve cerebral perfusion and is the colloid of choice because of its neuroprotective properties and minimal effect on coagulation.[24-27]

Compared to synthetic colloids, albumin has minimal effect on coagulation. Additionally, albumin has neuroprotective effects in models of cerebral ischemia, improves cerebral perfusion that helps normalize the changes in diffusion-weighted MRI, and reverses postischemic microvascular stasis.[24-27] Albumin also binds platelet-activating factor with high affinity and decreases responses induced by platelet-activating factor.[28] Electrolyte abnormalities are seen frequently with SAH, most commonly hyponatremia that may occur in up to 30% of cases.[29] Administering normal saline intravenously can help attenuate hyponatremia while maintaining appropriate normovol-

emia.[7] Vasopressin is not commonly used as a vasopressor for patients with SAH because of its ability to further deplete blood sodium levels.[9]

Patients with hydrocephalus may need urgent ventricular drainage. Often, significant clinical improvement occurs after external ventricular drain (EVD) placement or lumbar drainage; therefore, upon appreciation of acute hydrocephalus, clinicians should initiate cerebrospinal fluid diversion.[30-38]

Up to 26% of patients with aSAH experience seizure-like episodes.[39-41] Some small, nonrandomized studies have shown that prophylactic use of anticonvulsant therapy in the immediate posthemorrhage period may be beneficial, but definitive research suggesting its efficacy is lacking. The reported benefit may be the result of a reduction in possible reinjury or rebleeding related to seizure-like activity.[42-44] Therefore, clinicians should consider using anticonvulsant therapy prophylactically in this time period, while weighing the risks, including possible worse cognitive outcomes.[45] If such therapy is used, only a short course (3-7 days) is recommended. Phenytoin may worsen outcomes.[46]

SAH may trigger the sympathetic discharge of catecholamines. Electrocardiogram (ECG), troponin levels, and creatine kinase levels should be monitored. If cardiac dysfunction and/or myocardial injury are present, other treatment therapies (triple H therapy for acute onset of symptomatic cerebral vasospasm) must be weighed for their benefit vs the risk of exacerbating tenuous cardiopulmonary status. ECG abnormalities and cardiac dysfunction in these cases have not been shown to directly affect morbidity and mortality and may not require adjustment to overall anesthetic management, although the cardiac function may influence the choice of treatment modality (clipping vs coiling).[47] Elevated troponin levels have been associated with increased mortality and disability at discharge. Because of possible cardiac dysfunction and its negative effect on outcomes, treatment of cardiac insufficiency should be considered.[12,48-50]

When aneurysm obliteration is delayed, antifibrinolytic drugs such as aminocaproic acid or tranexamic acid have been shown to reduce the incidence of rebleeding,[51] although neither of these drugs is approved by the United States Food and Drug Administration for this use.

Data suggest that treatment with statins may help reduce the size and growth progression of cerebral aneurysms, but more investigation is necessary to determine dosing, as conflicting data show that statins may increase aneurysm size at higher doses.[52,53]

Papaverine has been shown to reverse arterial narrowing, but it has not been shown to improve outcomes and its use is not recommended.[54]

GOALS OF INTRAOPERATIVE ANESTHETIC MANAGEMENT

The anesthetic goal in the treatment of cerebral aneurysms and SAH is a balancing act of maintaining adequate CPP to prevent ischemia, while also controlling excessively high blood pressures to prevent aneurysmal rupture and further bleeding. No catch-all anesthetic technique exists for treatment of aSAH, and no adequate research exists to recommend a particular anesthetic approach. Patient-specific considerations must guide the tailoring of anesthetic management.

SURGICAL CLIPPING VS ENDOVASCULAR COILING

The International Subarachnoid Aneurysm Trial (ISAT) is the only multicenter randomized trial yet to have compared microsurgical and endovascular repair. This study included 2,143 patients with aSAH in 42 neurosurgical centers. The results of this trial showed that the risk of death or dependency was 24% with endovascular coiling compared to 31% with surgical clipping.[55,56] However, the incidence of late rebleeding was 2%-9% with endovascular coiling compared to 0.9% with clipping, and only 58% of coiled aneurysms were completely obliterated compared to 81% of clipped aneurysms.[56] The latest guidelines from the AHA/American Stroke Association recommend endovascular coiling as the preferred method of treatment for ruptured aneurysms that are amenable to both clipping and coiling. However, middle cerebral artery aneurysms are sometimes difficult to treat with coiling, so clipping might be a better option.

ANESTHETIC CONSIDERATIONS FOR CEREBRAL ANEURYSM OBLITERATION CASES

In general, the anesthetic principles are the same for both the surgical clipping and endovascular coiling methods of cerebral aneurysm obliteration. The likelihood of blood loss is higher and the need for brain relaxation is greater in clipping compared to coiling procedures. Careful consideration of comorbidities, patient immobilization, facilitation of clear visualization and access to the aneurysm, standard and cerebral function monitoring, blood and intracranial pressure management to maintain adequate cerebral perfusion and oxygenation, and rapid emergence are the anesthetic goals in both aneurysm coiling and/or clipping cases.

Premedication administration should be tailored to patient status and comorbidities. For example, the risk of an anxious patient becoming hypertensive, increasing the risk of aneurysm rupture, must be weighed against the goals of resuming adequate respiratory status and facilitating quick determination of neurologic status at emergence. Nimodipine or vasopressor therapies can be used for vasospasm prophylaxis and/or blood pressure control and CPP management.[11]

Anemia is common in SAH patients. The average drop in hemoglobin concentration in SAH patients is 3 g/dL. Higher hemoglobin levels have been associated with positive functional outcome. Blood transfusions, however, carry associated risks, such as an impaired immune system and increased incidence of infection. The Neurocritical Care Society recommends maintaining hemoglobin between 8-10 g/dL and maintaining higher levels (up to 12 g/dL) for patients at risk for DCI. More research is needed to investigate prophylactic blood transfusions to elevate hemoglobin levels in SAH patients because of the inherent risks.[19,57-60]

General anesthesia is the preferred technique for both endovascular coiling and surgical clipping procedures.[10] General anesthesia allows for patient immobilization via neuromuscular block or deep sedation and helps provide a stationary focal point for surgical manipulation and for visualization of the target area during the endovascular procedure.[11]

Standard monitoring includes 5-lead ECG, intra-arterial blood pressure monitoring, pulse oximetry, capnography, urinary output, and temperature.[11] Invasive blood pressure monitoring is necessary to keep tight blood pressure control and to facilitate blood gas analysis. For patients with increased ICP, some type of ICP monitoring is beneficial for anesthesia induction and postoperative blood pressure management of patients who remain unconscious. EVDs can also facilitate cerebrospinal fluid drainage for the purpose of reducing ICP and brain bulk and for achieving brain relaxation.[11]

The neurosurgeon may wish to monitor cerebral function via cortical somatosensory evoked potentials (SSEPs) and brainstem auditory evoked potentials (BAEPs). Such monitoring can guide surgical cessation or application of temporary vascular occlusion (clipping) and can guide adjustment of blood pressure management for perfusion augmentation if cerebral ischemia is detected.[11]

When SSEP and/or BAEP monitoring is used, total IV anesthesia (TIVA) should be considered because IV anesthetics interfere with evoked potentials less than volatile anesthetics. Propofol and remifentanil infusion can be used to facilitate TIVA.[61,62]

At certain points (temporary clipping) during cerebral aneurysm surgery, induced hypertension may be requested and considered to increase cerebral perfusion pressure for the duration of the clipping, especially if the temporary clipping is to be longer than 120 seconds. Brief periods of temporary clipping of aneurysms have been shown not to affect outcomes, but the duration should not be greater than 15-20 minutes. Longer periods can increase the likelihood of postoperative ischemic events.[63,64] Common vasopressors used for inducing hypertension in patients with aSAH include phenylephrine, norepinephrine, and dopamine.

BRAIN RELAXATION TECHNIQUES

Brain relaxation and the creation of a slack brain environment in which brain bulk is reduced can lessen the force necessary for retraction of the brain by the surgeon and can aid in visualization and access to the aneurysm for surgical clipping. Mannitol is the drug of choice to decrease brain water content, and consequently ICP, by creating an osmotic gradient. The recommended dose ranges from 0.25-2 g/kg, and its peak effect occurs approximately 30-45 minutes after the start of infusion. Slow administration of mannitol over 20 minutes is recommended to avoid occasional transient increase in ICP. Mild hyperventilation can counteract the undesired transient effect, if observed. If the area of intact blood-brain barrier is sufficiently reduced, so is the effectiveness of this drug.[11]

Furosemide is an alternative for decreasing ICP and brain water content and can be used in combination with mannitol to achieve greater effect.[65] Because of the combination of drugs' greater effect, particular attention should be paid to the patient's fluid volume, electrolytes, acid-base, and serum osmolality levels.[11]

Cerebrospinal fluid volume management via ventricular drains can also facilitate creation of slack brain. Vigilant monitoring of drainage volume and speed is necessary to eliminate abrupt ICP decreases and brain sagging that may lead to rebleeding, reflex hypertension, bradycardia, and possible asystole, as well as significant clinical deterioration postoperatively.[66] Acute volume drainage should not exceed 20-30 mL. Lumbar cerebrospinal fluid drainage is contraindicated in patients with intracerebral hemorrhage because of the risk of brainstem herniation.

Mild hyperventilation (30-35 mmHg $PaCO_2$ with intact dura and 20-30 mmHg with open dura) can be employed to facilitate a reduction in brain-blood volume via cerebral vasoconstriction in patients with intact CO_2 cerebrovascular activity. However, hyperventilation should be used only in patients with increased ICP and in moderation. Normoventilation

is the general goal, because prolonged hyperventilation can cause cerebral ischemia.[67] Use of nitrous oxide and volatile anesthetics can increase cerebral vasodilation and interfere with evoked potential monitoring and should be discontinued or avoided in cases in which brain relaxation and reduction in brain bulk are desired. Other than ketamine, most IV anesthetic drugs show some cerebrodepressant or cerebral vasoconstrictive properties, and their use is advised.[11]

Induced hypotension is not recommended, and the degree and duration of hypotension should be minimized because of the increased risk of neurologic deficits.[11,68,69]

TECHNIQUES FOR BLUNTING THE EFFECTS OF STIMULATION

The anesthesia provider should be aware of periods of high patient stimulation and low patient stimulation to prevent acute increases or decreases in blood pressure and ICP, so adequate CPP is maintained and possible rebleeding or aneurysmal rupture is avoided. Using IV medications such as lidocaine, esmolol, or labetalol to reduce stimulation and the cardiac response to laryngoscopy and endotracheal intubation is a practical way to avoid overly elevated ICP and MAP. Administration of a local anesthetic at scalp incision and pin sites can help reduce responses to stimulation during head pinning and bone flap creation. Clinicians can administer prophylactic boluses of propofol or a short-acting opioid prior to stimulation or administer a continuous infusion of an ultra–short-acting opioid such as remifentanil to maintain CPP and ICP near baseline during periods of stimulation.[11] When the dura is open, this is a period of relatively low stimulation. Anesthesia should not be reduced enough to result in patient awareness or sudden movement (if not neuromuscularly relaxed). If blood pressure decreases during periods of low stimulation, vasopressor therapy should be administered to maintain baseline blood pressure.[11]

Short-duration cardiac pause induced by adenosine administration may be requested to facilitate aneurysm clipping or to help control bleeding during acute intraoperative rupture.[51,70]

Routine use of induced hypothermia is not recommended but may be reasonable in specific instances. Intraoperative hypothermia has not been determined to be beneficial in surgical/endovascular correction of SAH or cerebral aneurysm.[71-74] Further investigation is needed to determine if achieving mild hypothermia (33°C) by the time of coiling or clipping has beneficial results and if a passive rewarming approach instead of an active and rapid rewarming of the patient after procedure completion has benefits.

GENERAL RECOMMENDATIONS

- Hemodynamic monitoring is integral to management.
- Blood pressure and heart rate should be closely controlled during induction.
- Control blood pressure with nicardipine, labetalol, and esmolol to avoid increases in blood pressure that may cause aneurysm rupture. Avoid low blood pressure as this may decrease cerebral perfusion pressure.
- Nimodipine is recommended to control hypertension for all patients with aneurismal subarachnoid hemorrhage.
- Triple H therapy may be needed to improve cerebral perfusion, although its use is still controversial.
- Erythropoietin has shown some promise in lowering the incidence of vasospasm and delayed cerebral ischemia.
- Albumin is the preferred colloid.
- Normal saline is the crystalloid of choice, if needed.
- Mannitol and furosemide are recommended to lower intracranial pressure to facilitate surgical exposure.
- Maintain a hemoglobin level between 8-10 g/dL throughout surgery.

Proper control of blood glucose levels should be considered, especially if hypothermia therapy is employed because blood glucose regulation by insulin is impaired at lower temperatures. Tight glucose control with insulin infusions showed an increased incidence of hypoglycemia that increased the incidence of vasospasm.[75] The Neurocritical Care Society recommends blood glucose levels $<$200 mg/dL and $>$80 mg/dL, compared to the old recommendation of levels $<$129 mg/dL.[19,76,77]

During patient emergence, continued control of MAP and ICP is important to prevent hemorrhage, prevent vasospasm, and maintain CPP. Adequate analgesia, antiemetic, antishivering, and antihypertensive medications should be administered. Emergence should be controlled but swift. Upon emergence, the patient's neurologic status should be determined to direct diagnostic testing (CT and angiography) and treatment interventions (cerebral vasospasm therapy) as necessary. Anesthetic agents

with a short duration (remifentanil) coupled with avoidance of longer-acting agents can facilitate swift emergence.[11]

POSTOPERATIVE CONSIDERATIONS

Consideration of risk factors, continued treatment for stroke-related conditions, and behavior modification are all necessary in the postoperative period and beyond for prevention of recurrence.

In the immediate postoperative period, cerebrovascular imaging may be necessary to identify any remnants or further occurrence of aneurysm. High vigilance for heparin-induced thrombocytopenia for patients treated endovascularly and preventive measures for venous thrombosis should be employed while recovering from SAH.

Initiation or continued use of nimodipine for blood pressure control and maintenance of normovolemia is recommended to help prevent DCI.[14,15]

CONCLUSION

Anesthetic management of patients with aSAH and SAH is a complex endeavor. Careful consideration of individual patient status, optimal techniques, and the safest evidence-based methods are the best options for successfully treating these life-altering conditions.

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