This case illustrates the anesthetic management of radiographically assisted embolization and surgical excision of a large arteriovenous malformation (AVM). Excision resulted in significant blood loss and cerebral edema. This prompted the use of cerebral protection and induced hypotension. The patient was kept in a barbiturate coma postoperatively. On emergence from the barbiturates, the patient demonstrated elevated intracranial pressure and resolving deficits. She was discharged 3 weeks after surgery for rehabilitation.

Arteriovenous malformations can compromise the cerebral parenchyma by mass effect, by hemorrhage, and by "stealing" blood from adjacent tissue. Subarachnoid hemorrhage (SAH) can result in sympathetic stimulation, hydrocephalus, meningeal irritation, fluid and electrolyte disturbances, and cerebral vasospasm. Excision may result in massive cerebral hemorrhage and edema as arterial pressures are abruptly normalized.

Anesthetic management is guided by a full evaluation of the patient's pathophysiology and medical management. The anesthetist must understand the total impact of the AVM, compensatory responses, and the hazard of surgery and anesthesia. The goal is to achieve a balance in oxygen supply and demand at a pressure sufficient to perfuse the brain tissue without exceeding the pressure limits of compromised vasculature. This must be done while providing optimal brain relaxation for excision with minimal bleeding.

Key words: Arteriovenous malformation, cerebrovascular hemorrhage, hyperemia.

Intracranial arteriovenous malformations (AVMs) challenge anesthetists. Anesthesia may be necessary for embolization procedures that are performed prior to open craniotomy.

Intracranial AVMs are congenital in origin. They are composed of an entangled mesh of arteries and veins in direct communication with each other. This arrangement results in high flow through the normally low pressure venous system of the cerebral circulation while limiting flow to the surrounding cerebral capillaries and brain tissue. These lesions gradually enlarge with the ability to increase shunted blood flow and, in some cases, increase cardiac output. Central nervous system effects are most often related to mass effect, cerebral steal, seizures, subarachnoid hemorrhage, or intracranial hematoma. The complex hemodynamic changes associated with an AVM are often coupled with subarachnoid hemorrhage (SAH) and intracranial hypertension. Surgical and anesthetic concerns are related to the potential for hem-
orrrhage and malignant cerebral edema as feeding vessels are being embolized and/or resected.

The purpose of this article is to closely examine the pathologic changes and anesthetic implications related to intracranial AVMs. A case report is presented, followed by a discussion of the pathophysiology, current medical management, and theoretical basis for anesthetic management of these intriguing lesions.

Case report

A 41-year-old woman was admitted to this facility with complaints of a new onset of severe headache and neck stiffness. In 1986, she had been treated for SAH by bilateral craniotomy and two cerebral aneurysms had been clipped. The patient also had a known posterior communicating artery aneurysm that was not surgically treated. Her residual neurologic deficit from these events included mild facial nerve palsy with decreased sensation of the left face. Her social history included a 40 pack-year smoking history and significant alcohol intake (six to eight drinks per day). The patient also had good exercise tolerance as she teaches water aerobics in addition to her full-time job.

The patient was admitted to the neurosurgical service for evaluation. The diagnosis was mild SAH from an AVM of the right middle cerebral artery. Radiologic studies demonstrated a 5-cm, high-flow AVM with feeding vessels from the right anterior communicating and the right posterior communicating arteries.

A consultation with neuroradiology was obtained. The planned management included a three-stage, angiographically guided embolization procedure under sedation preceding a craniotomy for surgical removal of the lesion. Each embolization would be followed by a computed axial tomography (CAT) scan and at least 1 observation day in the neurosurgical intensive care unit. The procedures were staged 3 to 4 days apart to allow the cerebral vasculature to adapt to changes in blood flow following partial embolization of the AVM.

A preoperative anesthetic assessment and management plan were made prior to each embolization procedure. Approximately 1 week had elapsed between the onset of symptoms and the first preanesthetic evaluation. Physical examination was unremarkable. Weight was 69 kg and height was 165 cm. Nuchal rigidity was much improved. Baseline blood pressure ranged from 100/60 to 118/72 mmHg. Heart rate was regular at 58 to 70 beats per minute. Her airway was evaluated and a Mallampati class of I was assigned. Hematologic studies, electrocardiogram (ECG), and chest x-ray were noncontributory. Medications included nimodipine, phenytoin, dexamethasone, and ranitidine. Nifedipine was administered, as needed, to maintain systolic blood pressure at less than 130 mmHg. The patient was quite anxious. A thorough explanation of the events to follow was given and the patient was encouraged to ask questions and express concerns.

Embolization of feeding arteries to the AVM is performed to limit the blood flow through the lesion, thus minimizing loss during excision. Staged procedures allow the vasculature to adapt to changing pressures as vessels are occluded. Intravascular thrombosis is accomplished by introduction of a foreign body or a sclerosant substance into the feeding vessels. This particular procedure was accomplished with polyvinyl alcohol and absolute ethanol. These agents denature proteins, lyse cells, and irritate the intima of the vessel to produce clotting (personal communication, Philip B. Long MD, September, 1994). Angiography is used to locate the vessels, introduce an irritant, and confirm embolization. The neuroradiologist may wish to assess the patient's neurological response at any time during the procedure. A CAT scan is performed after each procedure to identify cerebral edema or bleeding that may result as the flow through the vasculature is altered.

Prior to each embolization procedure, the patient was greeted in a preoperative holding area where an intra-arterial catheter and an intravenous line were placed. Family members stayed with the patient until transport to the radiology department (except during the performance of invasive procedures). Once in the radiology department, monitors were applied for continuous ECG, arterial blood pressure, pulse oximetry, and capnography. A pretracheal stethoscope was also applied. Supplemental oxygen at 3 L/min via nasal canula with a CO2 sampling port was placed on the patient. An intravenous infusion of propofol mixed with alfentanil (propofol 9.1 mg/mL and alfentanil 45.5 µg/mL) was started at 20 mL/hr. The infusion rate was titrated to effect throughout the procedure and periodically discontinued to allow neurologic assessment. The alfentanil concentration was gradually reduced throughout the day to avoid cumulative effects that could result in hypventilation and hypercapnia. During the last embolization procedure, labetalol was titrated to maintain a systolic blood pressure below 130 mmHg. Although not needed, nitroprusside was available.

At the end of each embolization procedure, the patient was transported to the CAT scanner for evaluation and then taken to the neurosurgical intensive care unit for monitoring. The first CAT

Journal of the American Association of Nurse Anesthetists
scan was unchanged from that which was obtained on admission. The CAT scan following the second embolization procedure demonstrated new blood in the Sylvian fissure and the patient again developed a severe headache. She also expressed new complaints of visual changes. These symptoms resolved spontaneously within 24 hours. The CAT scan, following the third and final embolization procedure, revealed an increase in cerebral edema. Despite these changes, the patient had no further neurological deficits, and a right parietal-occipital-temporal craniotomy to excise the AVM was scheduled 4 days after the last embolization.

A preoperative assessment was made the evening before surgery, and an anesthetic plan was developed to include high doses of narcotic combined with an inhalation agent. Neuromuscular blockade would be used to facilitate endotracheal intubation, assure immobility, and facilitate controlled ventilation throughout the procedure. Routine monitoring would include ECG with ST segment analysis, noninvasive blood pressure, pulse oximetry, mass spectrometry, capnography, and heart sounds and temperature (via an esophageal stethoscope and temperature probe). Invasive monitoring would include arterial and central venous pressure lines. Extra, large-bore, intravenous lines would be inserted to allow management of blood loss and provide access for medication infusions.

On the day of surgery, the patient was greeted in the operating room by the anesthesia team and the operating room nurses. The chart was given a final review and no changes had occurred since the presanesthetic assessment. Noninvasive monitors were applied and baseline data were noted. Midazolam was titrated to alleviate anxiety. An arterial catheter was inserted and baseline arterial blood gases, electrolytes, hemoglobin, and hematocrit were obtained.

Anesthesia was induced with sufentanil 1 μg/kg, sodium thiopental 375 mg in divided doses, pancuronium 7 mg, and desflurane 2%. Sympathetic response to laryngoscopy was attenuated with esmolol in 10-mg increments (total 20 mg). The airway was secured and the patient's eyes were protected. An esophageal stethoscope and temperature probe, nasogastric tube, and a right internal jugular central venous line were placed. Postinduction arterial blood gas analysis correlated end-tidal CO₂ with Paco₂. Two additional 14-gauge peripheral lines were placed.

The anesthetic was maintained with sufentanil infusion at 3.5 μg/kg per hour initially, desflurane 2% to 7% and N₂O 70% and O₂ 30%. Pancuronium was titrated to maintain one twitch in a train-of-four. Higher doses than normal were anticipated based on prior anesthetic experiences and on the assumption that a history of significant alcohol intake and phenytoin therapy can increase dosage requirements of anesthetics and nondepolarizing neuromuscular blockers. Three hours after induction, the sufentanil infusion was tapered to .217 μg/kg per hour to avoid cumulative effects. The Paco₂ was maintained at 27-28 mmHg. In anticipation of the need for cerebral protection, the patient temperature was allowed to cool to 34°C. As expected, there was significant blood loss, and the procedure was difficult to perform. The patient began bleeding with the initial manipulation of the AVM. Two hours later, the surgeons moved to a more easily controlled area of the AVM. Eight hours into the case, the surgeons were ready to move back to the area of greatest blood loss. The plan was changed to include barbiturate coma for the next few days. The sufentanil drip was decreased to .159 μg/kg per hour, and sodium thiopental 500 mg was given. A sodium thiopental infusion was initiated at 1.74 mg/kg per hour and increased over the next 4 hours to 13.5 mg/kg per hour. The exact dose of thiopental needed was difficult to determine since electroencephalographic (EEG) monitoring was not being done and cerebral protection was desirable due to the extensive cerebral bleeding. The patient maintained stable hemodynamics as the dosage was increased. As the surgeons neared the end of the resection, the patient's temperature was actively warmed to 35.5°C. The skull was cemented 12 hours into the case, and the surgeons were ready to normalize the Paco₂. Before transporting the patient to the CAT scanner, an intracranial pressure monitor was placed and the central venous pressure catheter was changed to a pulmonary artery catheter. The entire procedure lasted 16 hours.

The patient's blood pressure was controlled to a moderate hypotension (systolic pressure 85-100 mmHg) using labetalol titrated to 1 mg/kg and sodium nitroprusside 6-15 μg/kg per minute. The total blood loss was estimated to be 3,500 mL. Replacement therapy consisted of a combination of crystalloids (7,000 mL), 5% albumin (1,500 mL), and packed red blood cells (2,075 mL). This was titrated according to blood loss, central venous pressure, urine output, serum electrolytes, hematocrit, serum osmolarity, and colloid oncotic pressure measurements.

The patient was kept in a barbiturate coma, and EEG monitoring was performed over the next 5 days. As anticipated, the initial postoperative CAT scan demonstrated extensive right hemisphere edema and a slight midline shift. The barbiturates were discontinued with only mild in-
creases in intracranial pressure (ICP) initially. The patient was successfully extubated on the seventh postoperative day. By the tenth postoperative day, she was able to communicate effectively with intermittent episodes of confusion. She demonstrated weakness and sensory deficits on the right side of her body. Her condition continued to improve, and she was discharged to a rehabilitation facility 3 weeks after her surgery.

Discussion

Intracranial AVMs are relatively uncommon, having an estimated incidence of 1 per 500 persons in North America.1 They are congenital lesions of the cerebral vasculature characterized as expanding vascular mesh with direct communication between arteries and veins or by fistulous communication. This results in high-flow arterial blood shunted to the low-resistance venous system that may be sufficient to increase cardiac output.2 Arteriovenous malformations produce symptoms by direct mass effect, by rupture, and by "stealing" blood flow from surrounding tissue. These lesions are often located deep in the brain parenchyma and, unless completely obliterated, they are likely to reestablish growth.7

The most common initial symptom of an AVM is hemorrhage. Bleeding occurs in 40-80% of all patients with an intracranial AVM. Of those that bleed, 70% will do so by age 40. More than half of small, unruptured AVMs will bleed within 5 years as opposed to only one-tenth of large AVMs. However, once they do bleed, large AVMs are far more likely to bleed again.2 Seizures, the second most frequently encountered initial symptom, occur in 8-46% of this population,2 and the risk of hemorrhage is less. Other initial symptoms include headache, focal neurologic deficits, and cerebral ischemia.7

Management of patients with intracranial AVMs varies, and options are based on the risk of morbidity and mortality associated with conservative therapy versus surgical intervention. Surgery is considered to be the best option if there is little risk of creating insurmountable neurological deficits.1 Other options include no intervention, embolization, high energy therapy (proton beam, gamma rays, or conventional x-rays), or a combination of therapies.1

Current treatment for large lesions is often staged with obliteration of some of the arterial feeding vessels of the AVM and eventual surgical excision of the entire mass of vessels. This may be accomplished surgically or by angiographic embolization to reduce intraoperative blood loss and cerebral edema.1 Arteriovenous malformations that are only partially removed or embolized may actually increase in size after intervention.2

Initial symptoms, surgical complications, and current treatment of AVMs are related to their vascular nature and the hemodynamic pathophysiology. Although much debate exists in the literature, most theorists agree upon some basic concepts. Blood flow through the AVM passing through tortuous vessels and a poorly developed capillary bed. The arterial feeders, with high-flow rates, shunt blood away from the surrounding brain parenchyma and send it to low-resistance, venous draining vessels.8 This translates to a lower than normal arterial pressure in the AVM and excessive venous pressure.9 These pressure differences may be exaggerated in AVMs that are large with long tortuous vessels.9 The surrounding brain parenchyma suffers from vascular steal as blood is shunted through the AVM.9 Autoregulation is probably compromised to some extent in the presence of ischemia because blood vessels are already maximally dilated to facilitate gas exchange and metabolite removal.3 9

Surgical excision results in normalization of flow as blood is diverted back to the cerebral vasculature. Because the previously ischemic vessels are maximally dilated in response to low perfusion pressure from the feeding AVM, sudden normal perfusion pressure can exceed the limits of autoregulation in the surrounding vasculature.3 8 10 If autoregulation is completely impaired, the effect could be massive cerebral edema and hemorrhage.3 8 10 In an attempt to prevent this phenomenon, the AVM flow is often decreased in staged procedures by partial surgical ligation or radiological embolization. The hope is to allow the vasculature to adapt to gradually increasing pressures.9 10

Management of AVMs may be complicated by SAH and the physiologic consequences of such an insult. Severity of cerebral bleeding may range from mild, with symptoms of severe headache, to life-threatening, massive hemorrhage. Subarachnoid hemorrhage is associated with sympathetic nervous system activation, hypertension, elevated ICP, meningeal irritation (related to the presence of blood in the subarachnoid space), ECG changes, vasospasm, hydrocephalous, and changes in body fluid composition.5,11,12 Transient increases in ICP are associated with mild bleeding and may actually help tamponade the lesion.7 Larger areas of bleeding are associated with sustained elevation of ICP. Measures to protect the brain and reduce ICP may be necessary if the patient is to survive. As many as 50% of patients have ECG changes as a result of SAH, which may include T-wave changes,
ST segment changes, U wave formation, and dysrhythmias. These may or may not be associated with ischemia and, in some cases, they may be associated with myocardial infarction. Hydrocephalus is also associated with SAH, as basal cisterns are blocked with red blood cells and their remnants, which may further elevate ICP. Caution must be exercised in the management of intracranial hypertension to avoid losing the possible benefit from tamponade. Disturbances in fluid and electrolyte balance may present as syndrome of inappropriate antidiuretic hormone secretion or as central salt-wasting syndrome. The former results in hyponatremia with an excess of free water, and the latter results in hyponatremia with loss of free water.

It has been reported in the literature that 60–70% of patients suffering from SAH have vasospasm shown on angiogram and one-third to one-half of these patients develop clinical symptoms of vasospasm. Vasospasm appears to be biphasic. The initial spasm is short in duration, immediately follows the SAH, and may be protective in reducing the hemorrhage. The second vasospasm may occur 3 to 14 days later, may persist for a week to nearly a month, and does not respond to cerebral vasodilators, such as nitroprusside. Vasospasm may result from the release of vasoactive substances in the brain as hemoglobin is broken down. These substances may also have neurotransmitter effects that potentiate central nervous system depression. Potential mediators of vasospasm include histamine, serotonin, catecholamines, prostaglandins, angiotensin, and free radicals.

There are many theories regarding the best management of vasospasm. The most promising new treatment includes cerebroselective calcium channel blockers, nimodipine, in particular. The exact method by which these drugs improve outcome is not known. It is theorized that they may decrease smooth muscle contractility, increase red blood cell degradation, and retard platelet aggregation. They may also have direct cerebral protective effects. Exogenous insulin may be given if serum glucose is elevated by nimodipine.

Augmentation of blood volume has been demonstrated to aid in the management of vasospasm. This is usually done with a combination of crystalloids and colloids to increase cardiac output, improve perfusion pressure, and improve the viscosity of blood. Positive inotropes and peripheral vasoconstrictors may also augment cerebral perfusion pressure.

The clinical scenario that accompanies an AVM is a complex situation in and of itself. When associated with SAH, it may produce a situation that can overwhelm the adaptive mechanisms of an otherwise healthy individual.

**Anesthetic considerations**

Anesthesia will most certainly be required for any craniotomy procedure for AVM management and may be required for embolization procedures. The anesthetist needs to have an understanding of the underlying pathology, the consequences of interventions, and the techniques currently available to meet the complex needs of each patient. The anesthetic plan must exploit adaptive mechanisms that are present in each situation and control any maladaptive responses and/or reduce the severity of their impact. Current techniques employed in the neurologic and anesthetic management of AVMs are intended to promote the fine balance of oxygen supply and demand at a pressure sufficient to perfuse brain tissue and yet not exceed the transmural pressure of its vulnerable vasculature. This must be done while providing optimal brain relaxation for visualization and access to the lesion. The anesthetic plan must consider the potential need for induced hypotension and cerebral protection in light of potential imbalances in cerebral oxygenation.

Induced hypotension may be used intermittently to reduce the incidence and severity of hemorrhage by reducing lesion size and blood flow during excision. If uncontrolled bleeding occurs, it may be necessary to acutely reduce the blood pressure to facilitate location and control of the offending vessel. After excision, blood pressure may need to be reduced below the normal limits of autoregulation to avoid normal perfusion pressure breakthrough (bleeding in the AVM bed, rupture of associated aneurysms, and hyperperfusion) in the surrounding vessels.

Induced hypotension is not without risks. The ramifications of this depend on the degree of hypotension needed and what other significant risk factors exist. The lower limit of cerebral autoregulation is generally considered to be a mean arterial pressure (MAP) of 50 mmHg. This limit is approximately 25 mmHg above the level that produces electrical silence and membrane ionic pump failure in neuronal tissue. In a patient with chronic hypertension, the autoregulatory curve is shifted to the right, and a 30% reduction in MAP is considered to be within the limits of adaptability. In the event of intraoperative hemorrhage, the blood pressure may need to be lowered to a MAP of 50 mmHg, and in extreme situations, transient reductions to a MAP as low as 20 mmHg may be done.

The situation is confounded when the hemo-
dynamics of an AVM are such that the most vulnerable vessels are not autoregulated (maximal dilation) and the patient has suffered SAH. Subarachnoid hemorrhage results in volume contraction and may be unrecognized. Such contractions may be due to sympathetic responses, fluid restrictions, diuretic therapy, central self-wasting syndrome, and/or coexisting hypertension. Hypotension induced with vasodilators, in the presence of hypovolemia, will obliterate ongoing vasoconstrictive responses and cause a precipitous drop in blood pressure. Complications of induced hypotension are related to end-organ perfusion. Tissue damage can be worse in oliguric hypotension than in drug-induced hypotension. It is also important to note that anesthetic agents can increase shunting due to inhibition of hypoxic pulmonary vasoconstriction and that induced hypotension can have an additive effect. In the brain, increased ICP and prolonged retractor pressure can reduce cerebral perfusion pressure. Vigilant, direct arterial pressure monitoring and assurance of well-oxygenated blood can reduce the risks associated with induced hypotension. It is critical to monitor arterial blood pressure at the circle of Willis, which is reflective of cerebral circulation. In the patient with cardiac compromise, a pulmonary artery catheter may be advantageous in optimizing cardiac function and ultimately, cerebral circulation. The benefits and risks of this complex scenario must be calculated with appropriate steps taken to maintain cellular function.

Induced hypotension is often accomplished with a combination of pharmaceuticals. This can be achieved with isoflurane while preserving cardiac output and providing some cerebral protection. Other potential choices include nitroprusside, nitroglycerin, trimethaphan, hydralazine, beta-blocking agents, or combination sympathetic blockers, such as labetalol. Many peripheral vasodilators may be accompanied by reflex tachycardia that may be attenuated with small doses of beta blockers. Shorter acting agents are beneficial for intermittent induced hypotension. Each selection must be based on a thorough evaluation of the patient's condition to determine a plan to optimize the situation.

Cerebral protection from ischemia must be at the forefront of any anesthetic plan. Factors that may precipitate ischemia include induced hypotension, cerebral edema, occlusion of arterial supply, massive blood loss, and hematoma. Ischemia results when the vasculature is unable to meet the metabolic demands of cerebral tissue. Relative to other organs in the body, the brain consumes a significant amount of oxygen. This high oxygen consumption is necessary for signal transmission and cellular integrity. The brain's initial protective response to hypoxia is to vasodilate in an attempt to improve oxygenation. This may be futile if the vasculature is already maximally dilated. Neuronal cells deprived of oxygen become unexcitable when adenosine triphosphate (ATP) is not available for ionic pumps. This can be reversible unless ionic pump failure leads to loss of cellular membrane integrity. The brain begins anaerobic metabolism and depletes limited phosphocreatine stores to increase the ATP supply. This process results in the accumulation of lactic acid and free fatty acids. Free fatty acids, in turn, produce damaging effects on neuronal cells during hypoxic periods and upon restoration of blood flow, they are metabolized to free radicals that further damage cell membranes. It is therefore imperative to maintain a balance in the consumption and delivery of oxygen in the brain to avoid cellular death.

Several interventions can facilitate achieving this balance. These are directed toward reducing neuronal electrical activity, generally reducing overall metabolic function, and/or blocking mediators of hypoxic injury. It can be assumed that maintenance of sufficient oxygenation of the blood should be provided and that further interventions are necessary when flow may be insufficient to maintain neuronal function and cellular integrity. Hypothermia remains at the forefront of methods to reduce the cerebral metabolic rate of oxygen (CMRO₂). Research has demonstrated that mild hypothermia attenuates detrimental consequences associated with ischemia. Profound hypothermia, on the other hand, results in the same ionic pump problems that are associated with ischemia and can also precipitate dysrhythmias and coagulopathies. Hypothermia produces an exponential decline in CMRO₂, such that during hypoxia, a reduction of 1°C in temperature produces a 50% reduction in ATP utilization, and a reduction of 3°C in temperature more than doubles the preservation of phosphocreatine stores. It is assumed that less metabolism results in less accumulation of the toxic products of anaerobic metabolism and thus may reduce the degree of reperfusion hyperemia.

In addition to hypothermia, CMRO₂ can be pharmacologically reduced. Doses of barbiturates sufficient to cause EEG burst suppression are widely accepted as a modality to provide cerebral protection from certain ischemic events. Several mechanisms for the protective effects of barbiturates have been proposed. Barbiturates produce suppression of electrical activity and therefore are capable of reducing CMRO₂. One proposed mechanism is the ability to block sodium and calcium...
channels. Barbiturates are known to reduce intracranial hypertension not ameliorated by other means, such as diuretics, hyperventilation, and cerebrospinal fluid drainage, and subsequently improve blood flow. They may also improve blood flow by shunting blood from well-perfused areas to ischemic areas.

Study of ionic channel blockers, such as nimodipine, lidocaine, and magnesium, has led to mixed conclusions as to their efficacy in cerebral protection. Propofol has been touted as providing effects similar to barbiturates on EEG activity, cerebral blood flow (CBF), CMRO₂, and ICP, while preserving autoregulation, although cerebral protective effects remain disputed. As mentioned previously, ischemia alters energy production pathways, which in turn results in the release of excitatory molecules and free radicals that can produce neuronal membrane damage. Research is ongoing to identify means to scavenge these molecules.

Preparation for anesthesia begins with a thorough preanesthetic assessment. Unless life-threatening bleeding or a significant hematoma is present, there is little reason to rush to the operating room with an unstable patient. Arteriovenous malformations have a low incidence of rebleeding (6% in the first year and 2% per year thereafter), although, large AVMs are most prone to recurrent bleeding. Neurologic studies, such as angiograms, CT scans, and magnetic resonance imaging, should be evaluated to gain a complete perspective of intracranial pathology and compensatory changes that might influence the anesthetic and surgical course. The physical assessment should include the usual systems review and neurological examination to determine baseline function and deficits that could affect the patient's likely response to surgical and anesthetic interventions. Laboratory values and the medication regimen should be evaluated for potential fluid and electrolyte disturbances that may result from the initial insult or may be related to current therapies, such as steroids, calcium channel blockers, beta blockers, diuretics, or fluid restrictions. The patient's record should be reviewed for ECG changes and any evidence of ischemia. The history should be thoroughly investigated to elicit any coexisting diseases, activity tolerance, allergies, prior surgical and anesthetic experiences, significant social history such as alcohol or tobacco use, and initial symptoms of the AVM.

The patient and perhaps family should be apprised of the expected course of events, associated risks of proceeding, and alternative options. Premedication should be tailored to the patient's needs with consideration to the risks of respiratory depression, hypercarbia, and increased ICP. Of course, the patient should not be unduly anxious either. Other precautions include preparation for a long operative procedure, the ability to induce hypotension, and the ability to provide cerebral protection, if needed.

Induction should follow application of monitors and baseline measurements of vital signs and arterial blood gases. Monitoring should minimally include ECG, pulse oximetry, end-tidal carbon dioxide, direct arterial blood pressure, temperature, nerve stimulator (to assess the level of neuromuscular blockade), and urinary output. Optional monitors, such as central venous pressure, pulmonary artery pressure, and EEG, should be used if the patient's condition warrants. Induction should include measures to avoid intracranial hypertension or systemic hypertension as these could result in neurologic compromise. Both sodium thiopental and propofol are good choices for induction, and the addition of narcotics, beta blockers, or lidocaine can attenuate sympathetic responses to intubation. Nondepolarizing neuromuscular blockers are selected according to the status of the patient. Succinylcholine remains controversial in the patient at risk for elevated ICP, and the risks and benefits of its use should be carefully evaluated.

Maintenance of anesthesia can be accomplished by both narcotic-based and inhalation agent techniques. Because halogenated agents can increase cerebral blood flow, they have advantages and disadvantages. Isoflurane is probably the best choice, as it is known to provide cerebral protection by reducing CMRO₂, and it increases CBF and ICP less than other agents. Desflurane is gaining acceptance, as it is reputed to have similar properties to isoflurane and a low blood:gas partition coefficient. This translates to faster induction and recovery times and tighter blood pressure control if used for its hypotensive effects. Faster neurologic evaluation at the conclusion of surgery may be appealing to the surgeon. Desflurane needs further study to determine if it can provide cerebral protection from ischemic events. Narcotics provide no cerebral protection but do reduce CMRO₂ and cerebral blood flow. They also provide hemodynamic stability with little effect on intracranial pressure. The use of sufentanil is debated, as reports vary regarding its effect on ICP. Desflurane needs further study to determine if it can provide cerebral protection from ischemic events. Narcotics provide no cerebral protection but do reduce CMRO₂ and cerebral blood flow. They also provide hemodynamic stability with little effect on intracranial pressure. The use of sufentanil is debated, as reports vary regarding its effect on ICP. Desflurane needs further study to determine if it can provide cerebral protection from ischemic events. Narcotics provide no cerebral protection but do reduce CMRO₂ and cerebral blood flow. They also provide hemodynamic stability with little effect on intracranial pressure. The use of sufentanil is debated, as reports vary regarding its effect on ICP. Desflurane needs further study to determine if it can provide cerebral protection from ischemic events. Narcotics provide no cerebral protection but do reduce CMRO₂ and cerebral blood flow. They also provide hemodynamic stability with little effect on intracranial pressure. The use of sufentanil is debated, as reports vary regarding its effect on ICP.
effect of hypocarbia and hypotension. The goal of fluid therapy is to avoid cerebral edema from too much “free water” and to optimize hemodynamics. Glucose solutions are avoided, as hyperglycemia may precipitate neuronal injury during an ischemic event. Mannitol may be given to reduce intracranial volume and ease brain retraction. Furosemide therapy can have an additive effect by decreasing total body water volume, cerebrospinal fluid production, and intracranial astroglial swelling. Electrolyte disturbances that may result from diuretic therapy should be monitored and corrected as needed. Fluid replacement with crystalloid solutions is limited to avoid cerebral edema and may necessitate the use of colloid solutions to maintain intravascular volume. Adequate venous access and blood products must be available to replace large blood losses.

Prevention of normal perfusion pressure breakthrough is the goal once the AVM is ligated. The blood pressure is maintained at the low end of autoregulatory range to avoid exceeding the upper limits of the previously ischemic vessels. Exceeding this limit may result in severe malignant brain swelling. The same medications used to induce hypotension are appropriate with consideration of side effects and the desired length of action. Emergence should be smooth and atraumatic. Coughing and bucking will precipitate increases in cerebral perfusion pressure and ICP. As anesthesia is lightened during closure, hypertensive responses to stimulation must be blunted. When substantial intraoperative brain edema occurs, it may be prudent to avoid emergence trauma and keep the patient sedated and ventilated, allowing a period for recovery from the insult.

Manipulation of an AVM is a challenge for the neurosurgeon and the anesthetist. A complex array of cerebral hemodynamics and compensatory changes can occur in the presence of an AVM. As mentioned previously, an AVM that presents after hemorrhage has occurred may be prone to rebleeding. The constant threat of vasospasm, intracranial hypertension, and systemic responses following SAH complicate the scenario. Seizures must also be managed, if present. Once the AVM has been reduced, the patient is prone to normal perfusion pressure breakthrough, which can lead to profound cerebral edema or hemorrhage.

REFERENCES


AUTHOR

Karen Roth Tasman, CRNA, MSN, is currently employed as a CRNA with Medical Anesthesia Garrett and Associates at Lee Memorial Hospital, Fort Myers, Florida. Ms Tasman received an MSN from Case Western University/Cleveland Clinic Foundation, Cleveland, Ohio. She has received a BSN from the University of Kentucky, Lexington, Kentucky, and an ASN from Eastern Kentucky University, Richmond, Kentucky.

ACKNOWLEDGMENT

The author would like to extend many thanks to Peggy Contrera, CRNA, MSN, for her inspiration, encouragement, and expertise. Further acknowledgments are extended to the faculty and Anesthesia Department staff at the Cleveland Clinic Foundation.
In life-threatening VT or VF refractory to other therapy

A clear choice when the risk is high

INTRODUCING

Cordarone®
(amiodarone HCl)

150 mg/3 mL

New from Wyeth-Ayerst Laboratories

Please see brief summary on last page of this ad.
In life-threatening VT or VF refractory to other therapy

Cordarone® (amiodarone HCl)
The Power of Cordarone The Speed of I.V.

150 mg/3 mL

Reduces the frequency of and increases the time between arrhythmic events during the critical first 24 hours\textsuperscript{1,2}
Cordarone I.V. is indicated for initiation of treatment and prophylaxis of frequently recurring ventricular fibrillation and hemodynamically unstable ventricular tachycardia in patients refractory to other therapy.

Cordarone I.V. is contraindicated in patients with cardiogenic shock, marked sinus bradycardia, and second- or third-degree AV block in the absence of a functioning pacemaker.

The most important treatment-emergent adverse effects are hypotension (16%), bradycardia (4.9%), liver function test abnormalities (3.4%), cardiac arrest (2.9%), VT (2.4%), congestive heart failure (2.1%), cardiogenic shock (1.3%) and AV block (0.5%).

Hypotension is the most common adverse effect seen with Cordarone I.V. and may be related to the rate of infusion.

- 85% of patients in controlled studies survived the critical first 24 hours. Without a placebo comparison, a mortality benefit could not be established.²

- Stat administration of 150 mg over 10 minutes allows for immediate therapeutic intervention²

- Dosing guidelines designed to permit rapid loading in critically ill patients²

- Only 1.6% discontinuation due to hypotension, <1% incidence of proarrhythmia and <1% discontinuation due to CNS side effects²

Please see brief summary on last page of this ad.
A new treatment algorithm for life-threatening VT or VF

1. Diagnosis of life-threatening VT or VF with normal QT interval
2. Synchronized cardioversion or defibrillation
   - 100 J ▶ 360 J
3. Procainamide bolus + infusion for monomorphic VT
4. Cordarone I.V.
   - Loading infusion
   - Maintenance infusion
5. Lidocaine bolus plus infusion
6. Bretylium bolus + infusion for polymorphic VT/VF
7. Supplemental infusion of Cordarone I.V.
8. Consider addition of other pharmacologic agents
9. Consider emergency ablation or surgery

Arrows indicate recurrence

A clear choice when the risk is high

For more information about Cordarone I.V. call 1-800-934-5556 or contact your Wyeth-Ayerst/A.H. Robins representative.

Please see brief summary of prescribing information on adjacent page.

References:

INTRODUCING Cordarone® (amiodarone HCl)
The Power of Cordarone The Speed of I.V.
Cordarone® I.V. - Brief summary of prescribing information

Indications and Usage: Cordarone I.V. is indicated for 1) initiation of treatment and prophylaxis of frequently recurring VF and hemodynamically unstable VT in patients refractory to other therapy; 2) treatment of VT/VF in patients for whom oral Cordarone is indicated, but who are unable to take oral medication.

Contraindications: In patients with: 1) known hypersensitivity to any of its components; 2) cardiogenic shock; 3) marked sinus bradycardia; 4) 2nd- or 3rd-degree AV block unless a functioning pacemaker is available.

Warnings: Hypotension: Hypotension was the most common adverse effect seen with Cordarone I.V. in clinical trials (288 of 1836 patients; 16%). Clinically significant hypotension was seen in the first several hours of treatment and was dose related, but appeared to be related to rate of infusion. Hypotension necessitating alterations in therapy was reported in 3% of patients, with permanent discontinuation necessitated in 0.1% of patients. Hypotension immediately slowing the infusion; additional standard therapy may be needed including vasopressor drugs, positive inotropic agents, and volume expansion. The initial rate of infusion should be monitored closely and not exceed that prescribed in Dosage and Administration (see full prescribing information).

Bradycardia and AV Block: Drug-related bradycardia occurred in 90 (4.9%) of 1836 patients receiving Cordarone I.V. in clinical trials; it was not dose related. Treat bradycardia by slowing the infusion rate or discontinuing Cordarone I.V. in some patients, a pacemaker is required. Myocardial ischemia and hypotension has been seen during pregnancy, apprise the patient of the potential hazard to the fetus.

Precautions: Cordarone I.V. should be administered only by physicians who are experienced in the treatment of life-threatening arrhythmias, are thoroughly familiar with the risks and benefits of Cordarone, and have access to facilities adequate for monitoring the effectiveness and side effects of treatment.

Liver Enzyme Elevation: Elevations of blood hepatic enzyme values - ALT, AST, and GGT - are seen commonly in patients with immediately life-threatening VT/VF. Interpreting elevated AST activity can be difficult because values may be elevated in patients who have recent myocardial infarction, CHF, or multiple electrical defibrillations. In clinical studies, approximately 2% of patients had baseline liver enzyme elevations; 13% had clinically significant elevations. Liver enzymes can improve during therapy or remain at baseline levels. Baseline abnormalities in hepatic enzymes are not a contraindication to treatment.

Two cases of fatal hepatocellular necrosis have been reported after Cordarone I.V. treatment of atrial arrhythmias with an initial infusion rate of 1500 mg over 5 hours, a rate much higher than recommended. Both patients developed hepatic and renal failure within 24 hr of starting Cordarone I.V. and died of cardiac arrest respectively. Because these episodes of hepatic necrosis may have been due to rapid infusion rate with possible rate-related hypotension, the initial rate of infusion should be slowed. Monitor ALT, AST, and GGT (see full prescribing information). In patients with life-threatening arrhythmias, weigh the potential risk of hepatic injury against the potential benefit of Cordarone I.V., but carefully monitor patients for evidence of progressive weight gains. Weigh the risk of exposing the infant to amiodarone against the potential benefit of Cordarone IV., but carefully monitor patients for evidence of progressive weight gains.

Pulmonary Disorders: Two percent of patients were reported to have adult respiratory distress syndrome (ARDS) during clinical studies. ARDS is characterized by bilateral, diffuse pulmonary infiltrates with pulmonary edema and varying degrees of respiratory insufficiency. The clinical and radiographic picture can be rapidly progressive, such that respiratory distress, hypoxemia, shock, prolonged cardiopulmonary resuscitation, and aspersion pneumonia, conditions present in many of the patients enrolled in the clinical studies. It is not possible to determine what percent of patients I.V. played in causing or exacerbating the pulmonary disorder in those patients.

Pulmonary Fibrosis: Only 1 of more than 1000 patients treated with Cordarone I.V. in clinical studies developed pulmonary fibrosis. In that patient, the condition was diagnosed 3 months after Cordarone I.V. treatment, during which time she received oral amiodarone equivalent to about 600 mg daily. Pulmonary fibrosis is a well-recognized complication of long-term Cordarone use (see labeling for oral Cordarone).

Drug Interactions: Amiodarone can inhibit metabolism mediated by cytochrome P-450 enzymes, probably accounting for the significant effects of oral Cordarone (and presumably Cordarone I.V.) on the pharmacokinetics of other drugs, including digoxin, quinidine, procarbazine, warfarin, dextrothorphan, and cyclosporine. Hemodynamic and electrophysiologic interactions have also been observed with concomitant propranolol, diltiazem, and verapamil therapy. Agents producing a significant effect on amiodarone pharmacokinetics include warfarin, cyclosporine, and chlorothiazide. Because of the long half-life of amiodarone, drug interactions may persist long after its discontinuation. Few data are available on drug interactions with Cordarone I.V. Except as noted, the following summarizes important interactions between oral Cordarone and other therapeutic agents. Drugs Whose Effects May Be Increased (Inc.) By Cordarone: Warfarin (prothrombin time inc.), Digoxin, (serum concentration inc.), Quinidine, (serum concentration inc.), Procainamide, (serum concentration, NAPA concentration inc.), Disopyramide (QT prolongation inc., which could cause arrhythmia), Fentanyl (may cause hypotension, bradycardia, decreased cardiac output), Flecainide (reduces the flecainide dose needed to maintain therapeutic plasma concentrations), Lidocaine (oral dose bradycardia in 1 patient during local anesthesia; I.V. dose: seizure associated with inc. lidocaine concentration observed in 1 patient), Cyclosporine (produces persistently elevated plasma concentrations and requires increased oral dosing, reflected in decreased cyclosporine dose). Drugs That May Interfere With The Actions Of Cordarone: Cholestyramine (enterohepatic elimination of amiodarone inc., may reduce serum levels and half-life), Cimetidine (serum amiodarone levels inc.) - may decrease amiodarone serum levels.

Potential drug class interactions with Cordarone: Beta Blockers: Since Cordarone has weak beta blocking activity, use with beta blocking agents could increase risk of hypotension and bradycardia. Calcium Channel Blockers: Cordarone inhibits AV conduction and decreases myocardial contractility. Give special attention to electrolyte and acid-base balance when using with verapamil or diltiazem or of hypotension with any calcium channel blocker. In addition to the interactions above, chronic (> 2 weeks) oral Cordarone administration increases metabolism of phenytoin, dextrothorphan, and methotrexate.

Electrolyte Disturbances: Corrects hypokalemia or hypomagnesemia whenever possible before treating with Cordarone, as these disorders can exaggerate the degree of QTc prolongation and increase the potential for torsades de pointes. Give special attention to electrolyte and acid-base balance in patients with severe oliguria. In a total of 288 patients in whom amiodarone was given intravenously to rabbits at dosages of about 0.1, 0.3, and 0.7 times the maximum recommended human dose (MRHD) on a body surface area basis, maternal deaths occurred in all groups, including controls. Embryotoxicity occurred at dosages of 0.3 x MRHD and above. No evidence of embryotoxicity was observed at 0.1 x MRHD and no teratogenicity was observed at any dosages. Administration of amiodarone to pregnant women is contraindicated, but who require therapy must be monitored closely for adverse effects. Preclinical studies in rodents have demonstrated reduced viability and reduced body weight gains. Weigh the risk of exposing the infant to amiodarone against the potential benefit of amiodarone suppression in the mother. Advise the mother to discontinue nursing. Pregnancy: Category D. See "Warnings, NEONATAL HYPO- OR HYPERTHYROIDISM." In addition to congenital goiter/hypo-thyroidism and hyperthyroidism, amiodarone has caused a variety of adverse effects in animals (see full prescribing information). In a reproductive study in which amiodarone was given intravenously to rabbits at dosages of about 0.1, 0.3, and 0.7 times the maximum recommended human dose in mg/m², no significant effects on fertility occurred at 30 mg/kg/day.

Labor and Delivery: It is not known whether use of Cordarone during labor or delivery has any immediate or delayed adverse effects. Preclinical studies in rodents have not shown any effect on duration of gestation or parturition.

Pediatric Usage: Safety and efficacy of Cordarone in the pediatric population have not been established. Use in children is not recommended.
IN A PERFECT WORLD, PATIENTS WOULD ALWAYS HAVE THE PERFECT TEMPERATURE. BUT SINCE THE WORLD ISN’T PERFECT, THERE’S MALLINCKRODT MEDICAL.

Fact: hypothermic patients are more at risk for myocardial ischemia, wound infections and blood loss. That’s what inspired the people at Mallinckrodt Medical to develop a comprehensive line of fully-integrated, state-of-the-art temperature management systems. Our portfolio now includes the Alton Dean Blood and Fluid Warmer that performs at high or low flow rates without water bath maintenance.

We also have the WarmTouch® Patient Warming System that delivers ultra-efficient convective heat to actively maintain patient normothermia. And to reduce heat loss due to respiration, the DAR Filter/HME traps the patients own heated moisture to warm each breath while filtering potentially contaminating bacteria and viruses. And finally, we carry a full line of Temperature Probes and Monitors to keep you aware of your patient’s temperature with the accuracy you demand. Our portfolio is better than ever ...

with the comprehensive Mallinckrodt Medical Temperature Management System, you can virtually eliminate hypothermia in the OR and PACU. For more information or for a risk-free trial, contact your Mallinckrodt Medical anesthesia representative, or call Mallinckrodt Medical at 1-800-833-8842.

Mallinckrodt Medical, Inc. P.O. Box 5840 St. Louis, MO 63134 1-800-833-8842 Customer Service 1-800-233-8969 Technical Representatives