NEUROCRITICAL CARE OF SUBARACHNOID HEMORRHAGE

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Aneurysmal subarachnoid hemorrhage (SAH) typically presents as an apoplectic event triggered by rupture of an intracranial aneurysm. This rupture results in the release of a jet of blood under arterial pressure squirting into the subarachnoid space causing an abrupt rise in intracranial pressure. Cerebral perfusion falls precipitously, causing temporary intracranial circulatory arrest and syncope in many cases, and severe headache. Failure of the aneurysm to seal results in sustained arrest of the intracranial circulation and death in 15 % or more of patients. On presentation, the majority of SAH patients have altered sensorium and many are in coma. The jet of arterial blood can also produce mechanical injury to the brain; this combined with the toxic effect of extravascular blood initiate as cascade of events, referred to as early brain injury (EBI).

Aneurysm rupture can further damage the brain (secondary injury) through rebleeding, acute hydrocephalus, cerebral ischemia, seizures, cerebral edema, tissue shifts and herniation syndromes. In addition, sympathetic activation can produce a variety of systemic complications including arrhythmias, hypertension, stunned myocardium, neurogenic pulmonary edema, hyperglycemia, fever, impaired regulation of body sodium, water and systemic inflammatory response syndrome (SIRS). The major cause of secondary injury is delayed cerebral ischemia (DCI). While no interventions currently exist to address EBI, monitoring for and management of secondary injuries is the focus of patient care.

Rebleeding

Rebleeding following SAH is most frequent in the 24 hours following the initial hemorrhage and occurs in up to 10 % of patients in the first 3 days who do not undergo aneurysmal ablation. It dramatically worsens prognosis, and often results in death. Aneurysm obliteration by surgical or endovascular means is effective at preventing rebleeding. In the window between presentation and aneurysm repair potential strategies for reducing the risk of rebleeding involve control of hypertension and a short course of antifibrinolytic therapy.

The selection of the best method to repair the aneurysm is complex involving a variety of technical factors with distinct advantages and disadvantages to each technique. In patients whose aneurysms are appropriate for either surgical or endovascular repair availability of the necessary infrastructure and technical expertise of the operator are important considerations. Finally, brain injury associated with the procedure appears to be more common after surgical repair.

Evidence to support the use of blood pressure control and antifibrinolytic therapy to prevent rebleeding is equivocal. Early studies of long-term use of antifibrinolytic therapy suggested harm, however, more recent studies of short-term use found it to be effective. Some centers initiate antifibrinolytic therapy in patients in whom aneurysm repair is delayed. The effect of blood pressure levels on the risk of rebleeding has not been systematically studied.

Seizures

Seizure-like movement are often reported to occur at the onset of SAH, but it is unclear whether they are in fact seizures or represents posturing at the time of aneurysm rupture. Early clinical seizures after the initial rupture are uncommon (1–7% of patients) and are often the manifestation of aneurysmal re-rupture. Risk factors for seizures include surgical aneurysm repair in patients >65 years of age, thick subarachnoid clot, intraparenchymal hematoma and infarction. For many years, prophylactic treatment with anticonvulsants in SAH patients without seizures was commonplace, despite a lack of randomized trials addressing this issue. Recent retrospective studies suggested that the use phenytoin is associated with worsened long-term outcome although little is known about other anticonvulsants. Presently SAH patients who undergo surgical repair of the aneurysm are usually treated with a short (3-7 day) course of an anticonvulsant other than phenytoin.

Cardiopulmonary Complications

Sympathetic activation is the likely cause of myocardial injury following SAH. Markers of myocardial injury are frequently elevated and troponin I levels are abnormal in approximately 35% of patients. Arrhythmias, mostly atrial and benign, occur in about 35%, and wall motion abnormalities are present on echocardiography in up to 25% of SAH patients. A clinical syndrome referred to as ‘‘Neurogenic Stress Cardiomyopathy’’ or ‘‘Stunned Myocardium’’ is manifest with hypoxemia, cardiogenic shock and pulmonary edema may develop, usually within hours of SAH. The manifestations are usually transient and after 2–3 days myocardial function returns to normal. Management focuses on support of cardiopulmonary function with inotropes, vasopressors and diuretics while balancing that with the need to preserve cerebral perfusion.

Blood pressure management varies as the course of the illness. Prior to aneurysm repair, targeting a normal blood pressure seems most prudent, balancing the theoretical risk of rebleeding with avoiding cerebral hypoperfusion. Once the aneurysm is secured and the risk of rebleeding eliminated, the balance favors maintaining cerebral perfusion, especially since the patient is moving into the phase were delayed cerebral ischemia (DCI) may develop. During this period antihypertensive use is reduced and “permissive hypertension” is allowed. In patients who develop DCI, vasopressors and inotropes are frequently used to elevate blood pressure (see below).

Regulation of sodium and intravascular volume is perturbed following SAH with a tendency toward excessive diuresis and natriuresis leading to volume contraction and hypovolemia. Mineralocorticoids are ineffective in reversing the process and adjusting fluids to meet arbitrary central venous or pulmonary wedge pressure targets can lead to excessive complications. Current management focuses on monitoring fluid balance and body weight and adjusting fluid intake accordingly.

Glucose Management

Hyperglycemia is commonly following SAH and observational studies have linked associated hyperglycemia with poorer clinical grade and worsened outcome. However, there is little evidence to support tight glucose control. While very high glucose levels >220 mg/dl may be associated with increased infection risk, targeting a glucose level of 80–110 mg/dl leads to more episodes of hypoglycemia, which may be associated with more vasospasm and less favorable outcome. There have also been reports of cerebral microdialysis findings of cerebral metabolic crisis and low cerebral glucose in SAH patients being treated with insulin infusions, even in the absence of systemic hypoglycemia. Tolerating modest hyperglycemia (up to 200 mg/dl) and avoiding strict glucose control seems most prudent.

Management of Pyrexia

Fever occurs in up to 70% of patients following SAH and is more common in those who have a poor clinical grade, more subarachnoid blood and and intraventricular blood. The rise in body temperature appears to be part of a systemic inflammatory syndrome (SIRS) that is present in over 75% of SAH patients. SIRS is characterized by fever, tachypnea, tachycardia, and leukocytosis which may be related to elevated levels of inflammatory cytokines.

Retrospective studies have consistently found that fever is independently associated with poor outcome after SAH and infarcts are more common in febrile patients. While fever may develop concurrent with an infection, that is usually not the case in SAH patients. The impetus to suppress fever is based on extensive pre-clinical data indicating suppression of fever reduces cerebral ischemic injury and the high risk of SAH patients for delayed ischemia. Acetaminophen, ibuprofen, fanning, evaporative cooling, sponging, ice packs, and cooling blanket are often ineffective

Newer surface and intravascular devices are more effective at controlling fever. But their use does not come without a price. Aggressive means to control fever cause shivering which marked increases resting energy expenditure, carbon dioxide production, systemic oxygen consumption and a decrease in brain tissue oxygen tension. Measures to reduce shivering including counterwarming of extremities and the use of medications such as buspirone, magnesium, meperidine, propofol and other sedatives.

Suppression of infectious fever has additional risk. Fever is an adaptive host response to infection. In a number of different clinical settings treatment of fever results in a prolonged course of illness.

Statins

Statins have pleiotropic properties, and had been proposed as being beneficial in the context of vasospasm and DCI. Several retrospective and small prospective studies suggested benefit in SAH. However, large multicenter randomized controlled studies unequivocally found no benefit to simvastatin in SAH.

Magnesium

Magnesium is a non-competitive calcium antagonist with several important vascular and potentially neuroprotective effects. Phase II studies suggested the possibility of benefit. Most studies found magnesium to be safe, although in one study hypotension was identified as a problem. However, appropriately powered phase III studies failed to support its use.

Delayed cerebral ischemia (vasospasm, delayed neurologic deficit)

Three to five days after SAH patients enter a phase where they may deteriorate neurologically. While this may be a result of fever, over-sedation, metabolic disturbance, hydrocephalus or cerebral edema, it is often not the case. With the advent of cerebral angiography, it was noted that patients who developed delayed deteriorations often had associated narrowing or vasospasm of large cerebral vessels. While the exact nature of the relationship between vasospasm and neurologic deterioration is debated, patients developed regional or global hypoperfusion that may result in cerebral infarction and worse outcome. Additional processes that may contribute to DCI include small vessel autoregulatory dysfunction, spreading cortical ischemia, and microthrombi.

Diagnosis of DCI is made on clinical grounds. The process is often complicated by the limited ability to identify deterioration in patients who are poorly responsive or sedated. Prior to making a diagnosis of DCI it is critical to investigate other conditions that mimic DCI including fever, infection, electrolyte disturbances, hypoxia, sedative drugs, hydrocephalus or post-operative edema. Demonstrating large vessel vasospasm with transcranial Doppler or catheter angiography is supportive, but these studies are also often abnormal in asymptomatic patients. CT and MRI angiography and perfusion studies may also play role is assessing patients that cannot be adequately assessed clinically.

Treatment occurs in a stepwise fashion. Routine prophylactic measures used in all patients include oral nimodipine and avoiding hypovolemia. In those that develop DCI medical interventions focus on hemodynamic augmentation with fluids, inotropes and vasopressors. The specific combination chosen should be based evaluation of the patient's cardiovascular status and how it would be best augmented. Endovascular interventions are targeted at those who have vessel narrowing on angiography and include angioplasty of proximal vessels and infusion of intra-arterial vasodilators to treat distal vessel narrowing. The timing of medical and endovascular treatments is variable. Patients with poor cardiovascular reserve should be treated by endovascular means. In those with good cardiac function medical measures may be instituted first, followed by endovascular treatment if the patient does not improve with medical therapy or they may be applied concurrently with medical measures.

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