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Points of View

Controlled Hypotension for Cerebral Aneurysm Surgery: Are the Risks Worth the Benefits?

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Neurosurgeons frequently ask the anesthetist to provide controlled hypotension during cerebral aneurysm surgery. The benefits of hypotension include reduced operative bleeding and a reduction in aneurysm wall tension, thereby facilitating surgical clipping of the aneurysm. Despite these benefits, there exists a significant risk of damage to the brain and other vital organs as a result of potentially ischemic blood flow encountered during the hypotensive period (1). In contrast, an acceptable alternative to facilitate cerebral aneurysm clipping is a focal reduction in blood flow by using temporary proximal vessel occlusion. This method of managing aneurysms eliminates many of the possibly serious complications associated with controlled hypotension.

Why should we denigrate controlled hypotension when the literature is replete with both human and animal studies that support the use and safety of controlled hypotension to mean blood pressures as low as 40 mm Hg (2–4)? This is well below the lower limit of autoregulation in normotensive humans (normal of 50 mm Hg). Animal studies examining the effects of controlled hypotension use normal animals without any cerebrovascular pathology. Therefore, it is difficult to draw any comparisons to the clinical situation of a ruptured cerebral aneurysm. Human studies examining the effects of aneurysm repairs done under hypotensive anesthesia following a recent subarachnoid hemorrhage are limited by small sample size, measurements of global cerebral blood flow (CBF) or measurements of CBF involving the contralateral hemisphere, varying time intervals between hemorrhage and surgery, lack of patient outcome data, and lack of comparative control groups. Therefore, the encouraging intraoperative results seen in these clinical studies may not accurately represent the incidence of ischemic complications that occur as a consequence of controlled hypotension.

We feel the major concern of hypotensive anesthesia following subarachnoid hemorrhage is the risk of focal cerebral ischemia. Angiographic evidence of cerebral vasospasm may be present in as many as 45% of patients within 3 days of aneurysm rupture (5). Although clinical evidence of focal ischemia due to vasospasm usually occurs 4 to 9 days after hemorrhage, it would appear that some patients undergoing early surgery may be at risk of ischemia during periods of hypotension. Together with reduced flow through vasospastic arteries, autoregulation is impaired in unanesthetized patients (6,7). The degree of impairment of autoregulation is closely correlated to the presence of arterial vasospasm as well as the severity of the patient's clinical condition (6). Intraoperatively, human studies examining the effects of hypotension on cerebral blood flow during surgical aneurysm repair have demonstrated impaired autoregulation in some patients (8,9). Farrar et al. (9) studied CBF in patients who were clinically low grade while undergoing aneurysm clipping with either halothane or halothane and nitroprusside-controlled hypotension. They demonstrated that patients without any preopera-

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tive angiographic evidence of cerebral vasospasm did not have any significant change in CBF when mean arterial blood pressure was reduced to 40–50 mm Hg. In contrast, all patients with preoperative angiographic evidence of vasospasm had a significant reduction in CBF during controlled hypotension (9). In addition, impaired autoregulation can occur globally as well as focally (6,7). Thus, controlled hypotension may place focal areas as well as the entire brain at risk of ischemia.

Animal models of focal cerebral ischemia have dramatically demonstrated the impact of hypotension on CBF, histopathology, and outcome. Monkeys subjected to middle cerebral artery occlusion during normotension have little or no evidence of ischemic damage after 2 h of arterial occlusion (10). This model may be similar to the clinical situation where temporary vessel occlusion is employed for aneurysm repair. In contrast, Boisvert et al. have demonstrated in halothane-anesthetized monkeys with a middle cerebral artery occlusion that nitroprusside-induced hypotension to a mean blood pressure of 45–50 mm Hg were associated with significant histopathologic damage and neurologic impairment after only 30 min of hypotension (11). Cole et al. (12) have demonstrated in rats with middle cerebral artery occlusion a significant increase in the area of brain with zero blood flow in isoflurane, nitroprusside, and hemorrhagic hypotension compared to normotensive animals. There were no significant differences between hypotensive regimens (12). In contrast, artificial elevation of blood pressure has been shown to increase CBF and reduce neurologic deficits in patients with vasospasm (13,14). These studies help demonstrate the importance of perfusion pressure on collateral blood flow during focal cerebral ischemia. Therefore, it would appear that patients at risk of focal cerebral ischemia due to vasospasm and undergoing operative aneurysm repair may be at lower risk of developing cerebral ischemic complications during temporary vessel occlusion at normal or elevated blood pressures compared to controlled hypotension.

It has become acceptable practice to repair aneurysms soon after subarachnoid hemorrhage in patients with minimal neurologic impairment. The advantage of early surgery includes avoiding the risk of rebleeding, blood evacuation from the basal cisterns that may reduce the risk of vasospasm postoperatively, and the ability to induce postoperative hypertension and hemodilution therapy for the treatment of clinically significant vasospasm without risk of aneurysm rupture. However, surgery done early may be technically difficult because the brain may have a "swollen, angry" appearance (15). Therefore, surgical exposure may necessitate more aggressive retraction of the brain. In animals, during controlled hypotension, the brain tolerance to increased retractor pressure is reduced (16,17). Evidence for this includes decreased regional CBF, altered somatosensory evoked potentials, and poor neurologic outcome compared to normotensive controls (16,17). Together with the technical difficulties of exposing the aneurysm and the fragility of the aneurysmal sac, the risk of hemorrhage is always present. There are data that demonstrate a significantly lower CBF and metabolic deterioration with hemorrhage-induced hypotension compared to drug-induced hypotension (18,19). Accordingly, intraoperative hemorrhage superimposed on controlled hypotension is an emergency that may necessitate more aggressive brain retraction for clipping or inadvertent clipping of major vessels, potentially resulting in disastrous consequences.

Many drugs have effectively been used to induce hypotension, including isoflurane, nitroprusside, adenosine, nitroglycerine, and trimethaphan. Isoflurane is perhaps the most frequently used hypotensive agent during aneurysm surgery. The advantages include easy titration, maximal metabolic depression at clinically attainable doses, maintenance of cerebral oxygenation compared to other hypotensive regimens, and no apparent central nervous system toxicity at high concentrations (20,21). Animal and human data suggest that isoflurane is a unique anesthetic that may protect the brain from ischemic injury (22,23). Yet, there are other studies that dispute this (24–27). A primate model of focal cerebral ischemia did not show any difference in the ischemic injury suffered by animals during controlled hypotension with either isoflurane or halothane and nitroprusside (27). At present, it would appear that controlled hypotension using isoflurane does not offer the advantage of cerebral protection compared to other commonly used hypotensive regimens.

Another potential problem that may occur during controlled hypotension is the risk of hyperglycemia. Animal data reveal significant increases in glucose during controlled hypotension (19,28). As well, iso-

flurane anesthesia is associated with significantly higher plasma glucose levels than other inhaled agents in both humans and animals (26,29,30). It is well established that hyperglycemia increases neurologic injury during central nervous system ischemia (31,32). Therefore, isoflurane anesthesia when used to promote hypotension may result in elevated plasma glucose levels, possibly jeopardizing ischemic brain further.

Subarachnoid hemorrhage is associated with electrocardiogram (ECG) changes in 42% of patients (33). There is a dispute as to whether these ECG changes are of clinical significance. The average age of patients with subarachnoid hemorrhage is 51 years (34). Therefore, some patients presenting to hospital with a ruptured cerebral aneurysm would be expected to have concurrent ischemic heart disease. Two-dimensional echocardiography, recognized as being a sensitive indicator of cardiac ischemia, has revealed significant wall motion abnormalities in patients with subarachnoid hemorrhage during the perioperative period (35). Therefore, there is a risk of cardiac ischemia in patients with a subarachnoid hemorrhage that may worsen with controlled hypotension.

Because of the potentially serious problems associated with controlled hypotension, it may be preferable to employ temporary vessel occlusion with normotension to facilitate aneurysm clipping. The advantages of this method are a more effective reduction in intramural pressure of the aneurysm, reduced intraoperative rupture, and elimination of the risks of controlled hypotension. A number of human studies to date support the safety of temporary vessel occlusion (36–38). Suzuki et al. demonstrated that temporary clipping of vessels was well tolerated up to 40 min.

The merits of the two methods used to decrease the risk of intraoperative aneurysmal rupture will continue to be debated until a study is done to compare them. Until then, deliberate hypotension for aneurysm surgery may potentially be hazardous to the brain and other vital organs. For the above-delineated reasons, we advocate the use of regional vessel clipping over controlled hypotension during aneurysm surgery. We believe that as neurosurgeons and neuroanesthetists gain more experience with regional vessel clipping, the use of controlled hypotension for cerebral aneursym surgery will be of historical interest only.

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