Committee News

Inotropes and Vasopressor Effect on Cerebral Blood Flow

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Anesthesiologists are responsible for managing blood pressure during surgery. This task is particularly important during neurosurgical procedures, as brain cells are uniquely vulnerable to hypoxia, which may occur if hypotension is left untreated. The presence of a brain tumor may increase intracranial pressure and impair auto regulation, making the task of maintaining cerebral oxygenation more difficult. It's worth remembering that adequate oxygenation of brain cells is the goal. We can't measure tissue oxygenation under normal circumstances, so we use blood pressure as a surrogate. If blood pressure is adequate, we assume perfusion and oxygenation are adequate.

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The administration of anesthesia very often decreases arterial blood pressure below a patient's baseline blood pressure. Vasopressors and inotropes are necessary to maintain mean arterial pressure within predetermined parameters during surgery. These agents reliably raise blood pressure, but it's not clear what effect vasopressors have on the cerebral circulation. Normal brain function necessitates a narrow regulated parenchymal environment different in composition and strictly separated from the peripheral circulation (*J Neurosurg Anesthesiol* 2020;32:18-28). Arterioles within the brain parenchyma have intrinsic

innervation from cerebral neurons, rather than the usual sympathetic and parasympathetic innervation. Additionally, the cerebral circulation exhibits a relative nonreactivity to blood-borne catecholamines. This nonreactivity is attributed partly to the relative impermeability of the endothelial lining to polar, lipid-insoluble substances and partly to the endothelial enzymatic apparatus capable of degrading monoamines (*J Neurosurg Anesthesiol* 2020;32:18-28). Although these agents may not directly affect the cerebral circulation under normal circumstances, they do effect cardiac output, which may alter cerebral blood flow.

There are a number of vasopressor/inotrope agents available for use in the OR, and most practitioners have a favorite. Anesthesiologists assume these medications are equally effective in raising blood pressure and improving perfusion. Is that assumption correct? The relevant studies comparing vasopressor use and patient outcomes in the OR have not been done. However, recent work comparing vasopressors/inotropes in anesthetized patients suggests there may be subtle differences between the effects these agents have on cerebral circulation.

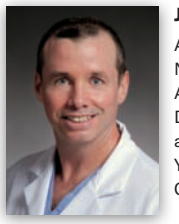
Vasopressors/inotropes work by activating alpha-adrenergic and beta-adrenergic receptors in vascular smooth muscle throughout the body. Some vasopressors are naturally occurring compounds like epinephrine and norepinephrine, produced by the adrenal glands. These substances act directly on receptors to produce their effect.

Ephedrine and phenylephrine are vasopressors frequently used by anesthesiologists in bolus form to raise blood pressure quickly. Ephedrine has a direct effect on alpha and beta receptors, but it also acts indirectly by causing the release of norepinephrine. Phenylephrine is a pure alpha 1 receptor agonist. Norepinephrine and dopamine activate both alpha and beta receptors and are used as infusions.

It is possible to measure the effect of vasopressors on cerebral circulation using cerebral oximetry. One study published a few years ago demonstrated a decrease in cerebral saturation with a bolus administration of phenylephrine (*Br J Anaesth* 2011;107:209-17). The decrease in cerebral saturation occurred despite an increase in mean arterial pressure. In this study, a bolus of ephedrine maintained cardiac output and cerebral oxygenation. It is not clear if the decreased cerebral saturation with phenylephrine represents a clinically significant decrease in oxygen delivery to brain cells or is an artifact from blood in the skin below the sensor. This study and others like it demonstrate how achieving adequate mean arterial blood pressure may not guarantee adequate cerebral oxygenation (*J Neurosurg Anesthesiol* 2023;35:31-40). Maintaining cardiac output may be more important than maintaining mean arterial pressure.

A more recent article by Koch et al. compared the effect of ephedrine and phenylephrine infusions on cerebral perfusion and oxygenation in patients with brain tumors (*Anesthesiology* 2021;135:788-803). The authors used dynamic susceptibility contrast MRI to measure cerebral capillary transit time heterogeneity in patients with brain tumors. This emerging imaging technology gives insight into how vasopressors/inotropes affect blood flow at a capillary level.

Measurements were made at baseline, and then compared to measurements made during phenylephrine or ephedrine infusions in these tumor patients. They also measured cerebral blood flow, brain tissue oxygenation, and estimated oxygen extraction fraction. Ephedrine improved cerebral microcirculation by decreasing capillary transit time heterogeneity. Phenylephrine conversely increased capillary transit time heterogeneity. Ephedrine also improved cerebral macro circulation with increased cerebral blood flow and higher brain tissue oxygen tension compared to phenylephrine. The increased cerebral blood flow with ephedrine was also demonstrated in a study using positron emission in brain tumor patients (*Anesthesiology* 2020;133:304-17). Phenylephrine reliably raises blood pressure, but it may not increase cerebral blood flow or improve brain tissue oxygenation.



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The Koch study involved only 24 patients, and it's not clear that the measured differences between vasopressors are clinically significant. Additionally, most American anesthesiologists have no experience administering ephedrine as an infusion.

As of now it is uncertain if one vasopressor/inotrope is superior to another in maintaining cerebral perfusion and oxygenation during brain tumor surgery. Most of the studies available for review involve trauma patients in the intensive care unit or patients having a surgery other than brain tumor surgery. Studies on tumor patients in the OR setting are few in number. The articles by Koch are interesting, as are the cerebral oximetry studies, but they do not definitively answer the question of which vasopressor/inotrope is superior for maintaining cerebral blood flow and oxygenation during brain tumor surgery. Further studies of brain tumor patients performed in the OR, and focused on clinical outcome, will be necessary to answer the question. ■

Roadmap to Becoming an Anesthesiologist

Anesthesiologists are detail-oriented, vigilant, hands-on, skillful with procedures, calm in stressful scenarios, and communicate well with patients, surgeons, nurses, and multidisciplinary health care teams. Becoming an anesthesiologist is challenging but rewarding. See how you can build a successful career in this exciting field. Learn more at **asahq.org/education-and-career/roadmap-to-anesthesiologist**.