But there are also unknown unknowns—the ones we don’t know we don’t know.

—Donald Rumsfeld, 2002

In the era of evidence-based medicine, case reports, presenting anecdotal experience of a practitioner, are a vanishing entity in medical journals. It is even more unusual to write an editorial on a case report. But 2 case reports in this issue of the Journal by Drummond et al. touch on the important issue of the role of intraoperative hypotension in the development of neurologic injury and, in doing so, raise a question about whether case reports can or should affect clinical practice.

The common theme for the 2 cases reported is that systemic hypotension resulted in devastating central nervous system (CNS) injury (spinal cord and brain, respectively). Systemic hypotension, as a cause of CNS injury, is not a novel concept. What is unusual is the apparent lack of major preoperative risk factors in these patients, other than the operating position (Trendelenburg position in the first case, and beach chair position [BCP] in the second case).

The authors propose that the presence of an anatomic variant in the vascular supply of the respective patient (no corroborative evidence of vascular anomaly in the spinal cord in the first case, but a common variant of the circle of Willis in the second case), in conjunction with the systemic hypotension, resulted in a devastating injury. Perhaps more importantly, the question is whether this represents a cause and effect or a simple association.

The first is a case report of a 19-year-old woman who developed a spinal cord infarction after an ileoanal pull-through performed under combined general and epidural anesthesia. The epidural catheter was inserted at L3-4 and the infarction involved T9 to conus, which was discovered on day 4 postoperatively, and the actual time of onset of injury was uncertain. Other than the initial test dose, the epidural infusate contained no epinephrine. The hypothesis was that the patient developed spinal cord infarction secondary to induced mild systemic hypotension to control blood loss, with the mean arterial blood pressure (MAP) maintained between 50 to 55 mm Hg for 2.5 hours. (There was some discrepancy between the systolic/diastolic blood pressure and MAP, with the former values lower than the recorded corresponding MAP.) The degree of hypotension was mild, and the authors speculated that the lumbar sacral segment of the spinal cord may experience a lower blood pressure than was indicated by the cuff because of the hydrostatic gradient due to the Trendelenburg position, that local pressure within the neuraxis was higher, and/or that the patient may have a “normal congenital” vascular anatomic variation that made her spinal cord vulnerable.

The second case involved an otherwise healthy 50-year-old man who underwent a shoulder procedure under general anesthesia in the BCP and subsequently developed a stroke within the distribution of the left middle cerebral artery. Risk factors included hyperlipidemia and history of smoking. Systolic blood pressure, as measured from the arm, was maintained between 95 to 100 mm Hg with a 10-minute period at 90 mm Hg. Total anesthesia duration was 137 minutes. Postoperatively, the patient remained unresponsive and a magnetic resonance angiography obtained 4.5 hours later showed ischemic changes in left anterior and middle cerebral artery distribution. Computed tomography angiogram did not reveal any stenosis or occlusion in any of the cerebral arteries. Subsequent magnetic resonance imaging confirmed infarctions in the left frontal, temporal, and parietal lobes. Time-of-flight magnetic resonance angiography demonstrated a predominantly fetal posterior cerebral artery in the right hemisphere with a small proximal segment, absent anterior communicating artery, and the left posterior communicating artery could not be visualized. The authors concluded that a combination of relative systemic hypotension due to the BCP and the anatomic variant of the circle of Willis caused the ischemic infarction.

The problem is this: despite a time-honored, tantalizing association between hypotension and adverse neurologic outcome, evidence linking hypotension of this degree and duration to infarction of the CNS is weak and reports of single cases do not make it stronger. In the spinal injury case, there is no indication of “anatomic variation” and the patient underwent a similar surgical procedure (colectomy) 3 months before, with a similar degree of hypotension (by MAP) of uncertain duration, with no neurologic sequelae. Furthermore, a cardiac echo revealed the presence of a patent foramen ovale, and there was evidence of a clot in...
one common femoral vein. We believe that a paradoxical embolus cannot be excluded from consideration as a cause for this unfortunate event. As such, we agree with the authors that “The etiology [of injury] cannot be defined with certainty.” The second case adds to the previous case series of strokes in the sitting position (cerebral infarction in 3, and spinal cord infarction in 1) reported by Pohl and Cullen, who also emphasized the importance of systemic hypotension as the etiologic factor. However, as with the cases presented by Drummond et al., Pohl and Cullen did not provide convincing evidence to support the contention that hypotension caused the infarctions.

To put the issue in perspective, particularly as it applies to stroke in the BCP, one must take into account the following facts:

1. The incidence of perioperative stroke in noncardiac, non-neurosurgical procedures is low, and even lower, between 0.05% and 0.4%, when patients with apparent stroke risk factors are excluded. Most of these strokes are considered thromboembolic in origin. Even in patients with symptomatic carotid stenosis >70%, whereby hemodynamic impairment from hypotension could be detrimental, arterial-to-arterial emboli have been shown to be an important etiologic factor in watershed infarcts.

2. Approximately 200,000 shoulder surgery cases are performed in the BCP in the United States annually, yet the incidence of intraoperative cerebrovascular events is estimated to be only approximately 0.004%. Furthermore, based on the statistical analysis of the results of the survey, there is no apparent difference in the incidence of stroke between patients in the BCP and the lateral decubitus position.

3. Many shoulder procedures are performed in the BCP, and not infrequently hypotensive anesthesia is used to minimize blood loss and improve surgical conditions. Recently, YaDeau et al. observed no cerebrovascular complications in 4169 patients undergoing shoulder surgery using regional anesthesia in the BCP with deliberate hypotension, even though 47% of patients were hypotensive, as defined by a decrease of MAP by 30%, MAP <66 mm Hg, or systolic blood pressure <90 mm Hg. Because neurologic complication is a rare event, these numbers remain consistent with an incidence of a perioperative stroke rate of 0.07%. Even when deliberate hypotensive anesthesia is not used, it has been observed that patients on antihypertensive medications experience more hypotension in the BCP. Although we do not condone such practice of “benign neglect” or “permissible hypotension,” one can nevertheless surmise that a large cohort of patients undergoing shoulder surgery in the BCP indeed experience systemic hypotension without neurologic sequelae. Certainly, sustained hypotension in a susceptible patient can cause ischemia. Whether this ischemia would result in an infarction may be determined by the risk factors associated with the patient, both physiologic and genomic.

4. Cerebral autoregulation is the primary homeostatic mechanism that maintains blood flow to the brain despite changes in blood pressure, and is preserved in the sitting position. As Dr. Drummond previously observed, the lower limit of autoregulation varies with the individual and can range from 33 to 113 mm Hg. However, a decrease below the lower limit of autoregulation does not necessarily mean ischemia will occur, or that infarction will develop. Inadequate blood flow can be compensated with increased oxygen extraction, and there is a margin between ischemia and infarction (the ischemic penumbra). This consideration has prompted growing interest in using cerebral oximetry as a surrogate to monitor adequacy of blood flow to the brain. However, results of these studies raised questions about the importance of blood pressure management in these cases. Murphy et al. showed that cerebral desaturation occurred more frequently in the BCP compared with the lateral decubitus position, but the patients were managed in a similar manner, with no difference in blood pressure. Similarly, YaDeau et al. could not demonstrate a relationship between blood pressure and cerebral oximetry in patients undergoing shoulder surgery in the sitting position when hypotension occurred in 76% of the observations. Moreover, cerebral desaturation was present in only 0.77% of observations. Assuming that cerebral oximetry monitors the adequacy of blood flow to the brain, these observations suggest that blood pressure within the clinical range considered to be acceptable (within 25% of baseline) during anesthesia is well tolerated. Genomic factors may render an individual more susceptible to the effects of systemic hypotension, but are beyond the scope of this editorial.

5. The definition of “hypotension” under general anesthesia remains controversial. A study comparing the nadir during natural sleep to decrease in blood pressure after induction of general anesthesia suggests that a 30% decrease compared with normal blood pressure is acceptable, because this is comparable to what happens during the natural sleep cycle. Furthermore, hypotensive anesthesia continues to be practiced by some anesthesiologists, even in elderly patients, with apparently good results, and in one study, no cognitive deficits were demonstrated. Although these patients were not in the BCP, a decrease in cerebral perfusion pressure occurring from systemic hypotension should have placed them at similar risk of cerebral ischemia. Moreover, although the BCP will lead to a decrease in the blood pressure at the brain (when compared with cuff on the arm), this is partially offset by the decrease in intracranial pressure in this position, mitigating the overall decrease in cerebral perfusion pressure.

6. The other potentially important factor cited by Drummond et al. is the anatomic variant in the circle of Willis. Although this undoubtedly can be a contributing factor, it must be noted that a complete circle of Willis is present in only 35% to 45% of the
population,\textsuperscript{17–19} and the anatomic variant as described probably occurred in approximately 20% of the population (Bart Keogh, MD, PhD, personal communication, Swedish Neuroscience Institute). Given the high frequency of mild hypotension during anesthesia, and the common use of induced hypotension, one might expect to see a higher incidence of stroke, yet the frequency of perioperative stroke remains low. According to a recent review of the American College of Surgeons National Surgical Quality Improvement Program, the incidence of perioperative stroke in noncardiac, non-neurologic patients is approximately 0.1%, and multivariate analysis fails to establish perioperative hypotension as a risk factor.\textsuperscript{20}

7. The collaterals in the circle of Willis are primarily useful when there is existing stenosis or occlusion. In the absence of hemodynamically significant lesions, collaterals are only potential conduits. Thus, all regions of the brain are potentially at risk during global hypotension, regardless of the presence or absence of collaterals, as the inflow artery into the collateral is subjected to the same driving pressure. Thus, the posterior circulation cannot supply blood flow to the right hemisphere via the small posterior communicating artery any more than it can to the left hemisphere, because the driving pressure is equally low in the anterior and posterior circulation. These considerations, and the distribution of the infarct, do not exclude systemic hypotension as the primary cause, but do suggest that embolic causes cannot be ruled out. Furthermore, venous air embolism during the BCP is a potential complication and fatality has been reported.\textsuperscript{21–24}

8. Finally, we must recognize that it is difficult to avoid hypotension, although it can and should be treated. The benefits of preventing hypotension, however, must be balanced against the risks of prophylactic vasopressor therapy. Additionally, there is debate on the appropriate vasopressor for blood pressure support to improve cerebral perfusion.\textsuperscript{25} However, there are simple maneuvers that we should adopt. Anesthesiologists do not routinely correct for the hydrostatic change in blood pressure between the cuff on the arm and perfusion to the brain in the sitting position, and we should. This would be particularly important if the cuff is placed on the lower limb (a practice that is best avoided).

So how do these case reports, or any others for that matter, help us understand terrible neurologic outcomes in otherwise reasonably healthy patients? Edward Huth, while editor of the Annals of Internal Medicine, listed the types of case report worth publishing: (1) the unique case presenting a totally new constellation of findings, (2) an unexpected association of 2 relatively uncommon diseases or disease manifestations in a single patient, and (3) an unexpected event such as an adverse drug reaction or recovery from an invariably fatal disease.\textsuperscript{26} To these we would like to include additional criteria: (4) if it increases awareness of a condition, (5) suggests the proper diagnostic strategy, (6) demonstrates a more cost-effective approach to management, or (7) delivers an important message or lesson.\textsuperscript{27} However, first and foremost, the “pathophysiology” or association reported should be built on an evidence-based argument for cause and effect. In other words, a case report must be both novel and credible.\textsuperscript{28} The case reports of Drummond et al. are not novel but they are credible and deliver an important cautionary message, but we disagree with Drummond et al. about the nature of that message. In our opinion, in neither case is there a frank breach of the clinical “standard.” Instead, we side with Rumsfeld and suggest it’s the things we don’t know we don’t know that humble us. In our view, the cause of these unfortunate events falls into that category.

As physicians, we like predictability and certainty so not knowing how to explain catastrophes such as these makes us justifiably uncomfortable. Hypotension, precisely because it is common, provides a ready explanation for a variety of adverse perioperative events. Strangely, when bad things happen, we find solace in hypotension, we know how to measure it, and are expert at treating it, because it’s theoretically controllable and gives us a sense of mastery. In day to day practice, however, things are seldom so straightforward. We are not always masters of our universe. If nothing else, the cases reported by Drummond et al. drive that disquieting fact home.

DISCLOSURES

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