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Phenylephrine and Myocardial Ischemia in Patients Undergoing Carotid Endarterectomy. III.

To the Editor:—Can we safely protect the brain from focal cerebral ischemia by using blood pressure support without it causing myocardial dysfunction? The implication by Smith *et al.*[1] is that, in the management of patients with systemic atherosclerotic disease in whom there exists a high risk of perioperative ischemia of both the coronary and cerebral circulations, the use of a vasopressor to augment cerebral perfusion pressure may be dangerous for the heart. It may, however, not be correct to assume that the use of light anesthesia *versus* slightly deeper anesthesia with supplemental vasopressor are similar means (to the heart) of achieving the same end (to the brain). Reading the Smith *et al.* article, we were prompted to retrospectively review our own experience in a similar clinical study population. Our data come from two completed studies[2,3] and one study in progress that examine the effects of anesthetic management on cerebral hemodynamics during elective carotid endarterectomy.

The pertinent observations from our studies are briefly summarized here. Preanesthetic medication consisted of atropine (0.4 mg/70 kg im) and diazepam (10 mg/70 kg po). All patients received 1–4 mg of midazolam iv during placement of catheters and monitoring devices that included a modified V5 EKG lead and a radial artery catheter. Anesthesia was induced with thiopental, 4 mg/kg, and tracheal intubation was facilitated with vecuronium 0.1 mg/kg. Patients received nitrous oxide in oxygen 1:1, and either isoflurane 0.75% (n = 26), or halothane 0.5% (n = 12). This corresponds to about 1.4 MAC, corrected for age and temperature.[4] A phenylephrine infusion was used to maintain mean arterial blood pressure (MBP) at or slightly above that measured on the ward, with an increase of up to 20% of that baseline pressure allowed in the period prior to carotid occlusion.

The pertinent demographic and cardiovascular data are shown in table 1. Only ten out of our 38 patients required phenylephrine support of their blood pressure at the equivalent time period (8/26 for isoflurane and 2/12 for halothane). In these ten patients, the mean ± SEM dose of drug infusion was 38 ± 7, μg/min. Three patients in the isoflurane group and one in the halothane group received nitroglycerin infusion (approximately 30 μg/min) for treatment of relative hypertension in the same period. Blood pressures were not significantly different from their counterparts who did not receive vasoactive drug. There were no overt instances of intraoperative cardiac ischemia and no patient suffered postoperative myocardial infarction.

In our experience, we find it surprising that adequate cardiovascular stability could be maintained by Smith *et al.* using "light anesthesia" with their dosage of either potent agent, unsupplemented with vasodilators, opioids, or perhaps other adjuvants. Other than thiopental for induction, there is no other mention of any other agents (premedication was not addressed) used for anesthesia. In contrast, it appears that our patients received a similar anesthetic regimen as their groups 2 and 4, yet fewer of our patients required vasopressor support. The reasons for the discrepancy are not clear to us, but perhaps if we knew the exact doses of potent agents, phenylephrine and/or vasodilators employed by Smith *et al.*, it would be easier to compare our patient groups with theirs.

TABLE 1. Demographic Profile and Physiological Variables (mean ± SEM) in the Period Just Prior to Carotid Occlusion.

	Isoflurane	Halothane
n	26	12
Age (yr)	66.9 ± 1.6	67.0 ± 2.8
Male/female	15/11	4/8
Hypertension	15	8
Coronary artery disease	6	6
Systolic blood pressure (mmHg)	132 ± 4	141 ± 6
Diastolic blood pressure (mmHg)	73 ± 2	76 ± 4
Mean blood pressure (mmHg)	93 ± 2	98 ± 5
Heart rate (bpm)	68 ± 3	65 ± 4
Pa_{CO_2} (mmHg)	33.4 ± 0.7	31.9 ± 1.0
Temperature (°C)	35.2 ± 0.2	35.4 ± 0.2
Phenylephrine infusion	8	2
Nitroglycerin infusion	3	1

Number of patients in each anesthetic group with essential hypertension or a history of coronary artery disease and those having received either phenylephrine or nitroglycerin are indicated.

It is difficult, at best, to extrapolate the results of their study into clinical practice. Many times during temporary carotid occlusion we have seen the EEG show signs of cerebral ischemia that promptly clears with an increase in blood pressure following phenylephrine infusion. To be sure, sometimes this may result in ST segment changes and a balance must be struck between the two extremes of coronary *versus* cardiac insufficiency. Nearly half of patients in the Smith *et al.* group 2 and 4 developed SWMA. Are we to infer that there is a nearly a 50% chance of developing myocardial ischemia if we treat an occurrence of cerebral ischemia with phenylephrine infusion? This notion is alarming, to say the least. EEG monitoring is a reliable and probably the most widely-used index of adequate cerebral perfusion. If blood pressure is controlled primarily by altering the anesthetic level, the sensitivity and selectivity of EEG monitoring is compromised.

Even if practitioners were not interested in maintaining a constant anesthetic depth to facilitate EEG monitoring, the patient undergoing carotid endarterectomy tends to have a hemodynamically labile intraoperative course for a variety of reasons, including baroreceptor dysfunction, advanced age and concomitant systemic hypertension. In our experience, use of light anesthesia as described by Smith *et al.* would invariably result in an increased use of vasodilators and/or autonomic blockers to smooth out what would be an otherwise extremely labile blood pressure course. From a practical standpoint, this practice carries with it an attendant risk of hypotensive swings. We feel that erring on the side of relative hypertension is probably safer during carotid endarterectomy, at least in the period before flow is reestablished through the reconstructed carotid artery.[5]

In conclusion, the Smith *et al.* study raises many interesting questions and potential directions for further investigations, as interest in blood pressure augmentation in the management of focal cerebral ischemia grows.[6-8] Rather than discouraging the intraoperative use of phenylephrine-induced blood pressure augmentation as a means of providing cerebral protection or as therapy for cerebral ischemia, their presentation is a call for improvements in monitoring of both the coronary and cerebral circulations to more effectively gauge the adequacy, or the potential harm, of our therapeutic maneuvers.

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In Reply:—Young and Ornstein state they did not find overt instances of intraoperative cardiac ischemia nor do they find patients suffering postoperative myocardial infarction; unfortunately, we do not know from their description how they looked for these outcomes. Naturally, if myocardial ischemia is not sought, it is often not found; the short stay of patients undergoing carotid artery surgery, at least in our institution, would preclude even the 3-day follow up were it not for the fact that we telephoned every patient and had the 4-week surgical outcome integrated with ours.

Young and Ornstein also ask, "Are we to infer that there is a nearly 50% chance of developing myocardial ischemia if we treat an occurrence of cerebral ischemia with phenylephrine infusion?" We suggest that the data would indicate that treating patients with severe atherosclerosis with phenylephrine may not be benign. Certainly the notion *is* alarming and perhaps that is one of the reasons why echocardiographic monitoring should or might be undertaken.

It is important to remember that the major cause of morbidity and mortality after surgery for carotid artery disease is not cerebral injury, nor is there evidence that flow-related changes are the major cause of cerebral dysfunction following carotid endarterectomy. The major cause of cerebral dysfunction after carotid artery surgery is from emboli, and the major cause of morbidity is from myocardial dysfunction. Thus, one's focus perhaps should be on the myocardium; in fact, we believe in using the EEG to indicate when blood pressure may be safely decreased and using the transesophageal echocardiograph to monitor myocardial well being.

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