Anesthesiology
71:466, 1989

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

ZVI HERSCHMAN, M.D.
Instructor in Anesthesiology

DANIEL M. THYS, M.D.
Associate Professor of Anesthesiology

Department of Anesthesiology
The Mount Sinai Medical Center
One Gustave L. Levy Place
New York, New York 10029–6574

To the Editor:—We read with great interest the article by Smith *et al.* concerning the effects of phenylephrine on myocardial ischemia in patients undergoing carotid endarterectomy.[1] In their concluding statement, the authors made a broad clinical recommendation regarding the use of phenylephrine in patients at risk for myocardial ischemia. Since this recommendation may become accepted in the medical community, it is imperative that all concepts be clearly defined and agreed upon. While Smith *et al.* clearly defined the ECG criteria for ischemia, they unfortunately failed to do so for the echocardiographic measurements. Nevertheless, one gets the impression that decreases in regional myocardial function were equated with ischemia.

According to our understanding, regional myocardial function is determined by regional preload, regional afterload, and regional contractility. Ischemia can indeed decrease a segment's contractility (*i.e.*, its capacity to perform work) and, at equal loads, this would be manifested by reduced function. When loading conditions change, however, the effect of these changes must be evaluated before drawing conclusions about contractility or ischemia.

In normal subjects, a wide variability in quantitative regional function has been documented.[2] This variability increases after repeated ischemic insults. Since most of the patients in the study by Smith *et al.* were reported to suffer from angina or to have had previous myocardial infarctions, one would suspect that they exhibited considerable heterogeneity in regional function. It was, therefore, not surprising that as ventricular load was altered with the various pharmacologic regimens, a nonuniform response to the load alterations was observed and that some segments displayed a greater reduction in function than others.

Differentiating between ischemic changes in regional function and load-dependent changes in function is certainly not easy. However, the explanation by Smith *et al.* that some contraction was present at baseline and that, as a result, "the worsening of regional function was not due to changes in loading, *per se*," is inadequate. It ignores the growing body of evidence related to intraventricular mechanical interaction and the importance of regional loading in the determination of regional function.[3–5]

Since alterations in regional function are not necessarily manifestations of acute ischemia, it would be essential to confirm the presence of ischemia by independent techniques prior to recommending changes in medical management.

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(Accepted for publication May 9, 1989.)

Anesthesiology
71:466–467, 1989

In Reply:—The letter by Herschman and Thys raises a point about loading conditions and the diagnosis of myocardial ischemia by echocardiography. While we certainly appreciate their point, when regional wall motion abnormalities are accompanied by thickening abnormalities and EKG changes that indicate myocardial ischemia, myocardial ischemia may be present. In this effort, one should say, "Is the benefit of using the drug worth the probable risk that myocardial ischemia is occurring?" It is clear that all alterations in regional function are not necessarily manifestations of acute ischemia, but some undoubtedly are, and the occurrence of wall-thickening changes at the same time as a 2° change in wall motion, and at the same time as electrocardiographic changes indicating ischemia led us to believe the context of our statement, "The data do not support the routine use of phenylephrine to maintain blood pressure in patients at high risk for development of myocardial ischemia." We think a key word here is routine, as none of these patients demonstrated an indication for using phenylephrine that was other than routine, and in each patient there was an equally good alternative method of causing the same effect as that achieved by the use of phenylephrine.

MICHAEL F. ROIZEN, M.D.
Professor and Chairperson
Anesthesia and Critical Care
Professor Medicine
The University of Chicago

Department of Anesthesia and Critical Care
5841 South Maryland Avenue, Box 428
Chicago, Illinois 60637

Anesthesiology
71:467–468, 1989

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]