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The Hemodynamic Effects of Nimodipine in Patients Anesthetized for Cerebral Aneurysm Clipping

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Calcium entry blockers are used to manage several cardiovascular diseases, including angina pectoris, hypertension, hypertensive cardiomyopathy, myocardial infarction, and supraventricular tachydysrhythmias, and to preserve myocardial function during cardiopulmonary bypass.[1] Some calcium entry blockers alter the cardiovascular response to certain anesthetic drugs. Verapamil decreased systemic vascular resistance, arterial blood pressure, and left ventricular stroke work index when administered iv (0.075 $mg \cdot kg^{-1}$) during anesthesia with morphine, diazepam, and nitrous oxide.[2] Nifedipine also produced hypotension which given during halothane anesthesia; higher concentrations of halothane attenuated the nifedipine-induced compensatory increase in heart rate.[3]

Nimodipine is a calcium entry blocker that resembles nifedipine structurally but possesses selective cerebrovascular effects.[4–7] In a recent double-blind, randomized, placebo-controlled clinical trial, Allen *et al.*[8] administered nimodipine orally to patients with subarachnoid hemorrhage and minimal evidence of vasospasm: severe cerebral vasospasm occurred in eight of 60 control patients and in only one of 56 nimodipine-treated patients; three treated and seven control patients died. Guggiari *et al.*[9] found increased intracranial pressure, decreased mean arterial pressure, and increased cardiac output in head-injured patients given nimodipine iv during controlled passive hyperventilation.

Because neurosurgeons probably will employ nimodipine to control cerebral vasospasm in patients with subarachnoid hemorrhage who subsequently undergo surgical clipping of an aneurysm, we retrospectively evaluated the interaction between chronic oral nimodipine administration and general anesthesia in patients with intracranial aneurysms.

MATERIALS AND METHODS

Twenty-nine patients with acute subarachnoid hemorrhage seen between February 1, 1980, and April 30, 1983, randomly were selected to receive placebo or nimodipine (0.7 mg po as a loading dose followed by 0.35 mg every 4 hrs) as part of a prospective multicenter study of the ability of nimodipine to prevent vasospasm.[8] Twenty-six of these patients, while still under treatment with nimodipine, underwent aneurysm clipping under general anesthesia. Two anesthesiologists and two neurosurgeons provided the care of all 26 patients. All data in table 1 were reviewed.

Peak values manually recorded from an oscilloscope for systolic and diastolic arterial blood pressures, and heart rate, as well as calculated peak mean arterial pressure (MAP), were compared at six intervals: preinduction (and postinsertion of the arterial line), postendotracheal intubation, postincision, during emergence, in the recovery room, and in the intensive care unit; minimal values after tracheal intubation but before the incision also were recorded and calculated.

The data then were grouped according to whether patients received nimodipine (Group A, n = 14) or placebo (Group B, n = 12), and all variables were compared using the Student's two-tailed t test for paired data and multivariate analysis of variance of repeated measures. A probability level of $P < 0.05$ qualified as statistically significant.

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RESULTS

In all but one patient, anesthesia has been induced with thiopental iv; all patients received halothane or enflurane for maintenance of anesthesia; all but one had been paralyzed with pancuronium; and all had been treated with deliberate hypotension, usually with sodium nitroprusside.

All data in table 1 were similar for both groups of patients. MAC equivalents were 0.78 ± 0.08 for Group A patients, 0.77 ± 0.07 for Group B patients.

Table 2 compares hemodynamic measurements obtained just before induction of anesthesia and throughout the operation and the immediate postoperative course. Significant differences occurred only in the minimal systolic arterial blood pressure measured after endotracheal intubation and before the incision was made. In Group A patients, peak systolic arterial blood pressure was lower than in Group B patients after intubation of the trachea and after incision, but those differences failed to obtain statistical significance ($P = 0.071$ and 0.061, respectively).

TABLE 1. Data Studied to Assess the Hemodynamic Effects of Nimodipine

Preoperative	Intraoperative	Postoperative
Age	Monitoring	Time to extubation
Preoperative cardiovascular history	Anesthetic MAC equivalents*	Time spent in the ICU
Preoperative medical management	Neuromuscular blockers	Length of hospital stay
Admission laboratory data	Adjuvants	Cardiovascular complications
Aneurysm location	Hypotensive agents Type, duration of infusion	
	Fluid administration	
	Duration of surgery	
	Complications	

* Conversion of maintenance concentrations of potent inhalational agents to MAC equivalents by the following equation allowed a comparison of anesthetic requirements:

$$\text{MAC equivalents} = \frac{(C_{30\text{-}90} + C_{90\text{-}150} + C_{150\text{-}210}) \div 3}{\text{MAC}}$$

where C = average concentration of agent; subscript (*e.g.*, 30–90) = number of minutes postinduction; and MAC = minimal alveolar concentration for specific agent.

DISCUSSION

Investigators have employed many types of therapy to limit the occurrence and extent of vasospasm following subarachnoid hemorrhage.[10–12] Nimodipine is the first therapeutic intervention that appears to decrease the incidence of vasospasm without producing unacceptable side effects: it does not produce major decreases in arterial blood pressure as nifedipine does[10]; unlike isoproterenol,[11] it produces only minimal changes in heart rate; and unlike intravascular volume expansion,[12] it is unlikely to precipitate congestive heart failure. Consequently, nimodipine may become the preferred drug for the prophylaxis of vasospasm associated with subarachnoid hemorrhage, and possibly for its treatment as well.

Our data suggest that the preoperative administration of nimodipine exerts no clinically important effect other than a slight, albeit statistically significant, reduction in minimal arterial blood pressure at the postintubation, preincision phase. Perhaps the combined effects of nimodipine and general anesthesia generate systemic hypotension during a period of minimal sympathetic stimulation. Lower peak postintubation and lower peak postincision blood pressures, which were suggested by this study, would be desirable in this group of patients. However, because our review was retrospective, our findings should be considered as hypotheses for further study, rather than as conclusive evidence.

The tendency toward a higher intracranial pressure and a lower systemic arterial pressure, reported by

TABLE 2. Effects of Nimodipine on Direct Arterial Pressure and Heart Rate during General Anesthesia in Patients with Intracranial Aneurysm*

	Preinduction	Peak Postintubation	Minimal Postintubation	Peak Postincision	Peak Emergence	Peak in Recovery Room	Peak in ICU
Group A (nimodipine)							
Systolic (mmHg)	137 ± 6.5	128 ± 5.3	93 ± 3.3	119 ± 7.1	143 ± 4.0	158 ± 5.8	154 ± 5.2
Diastolic (mmHg)	80 ± 3.8	75 ± 3.1	61 ± 2.5	72 ± 4.8	80 ± 2.6	89 ± 4.0	84 ± 3.4
Heart Rate (beats/min)	67 ± 2.7	71 ± 3.3	66 ± 2.7	70 ± 4.8	68 ± 3.4	79 ± 5.7	85 ± 3.8
Group B (placebo)							
Systolic (mmHg)	137 ± 3.3	144 ± 6.4	103 ± 3.7†	138 ± 6.3	148 ± 4.3	145 ± 14	155 ± 7.9
Diastolic (mmHg)	75 ± 2.8	75 ± 4.3	61 ± 1.9	75 ± 3.2	77 ± 3.0	81 ± 7.9	87 ± 3.4
Heart rate (beats/min)	75 ± 3.5	74 ± 4.4	67 ± 2.8	71 ± 5.1	68 ± 3:7	66 ± 6.9	82 ± 5.6

* All values mean ± standard error.

† $P < 0.048$ placebo *versus* nimodipine.

Guggiari *et al.*[9] in a series of head-injury patients receiving nimodipine, should be of value by reducing transmural pressure within the aneurysm. However, nimodipine could compromise cerebral perfusion by reducing arterial blood pressure if vasospasm were present or by increasing intracranial pressure if it were already high. Since patients with subarachnoid hemorrhage may have intracranial hypertension because of mass effect, cerebral infarction, and edema or hydrocephalus, the potential additive effects on cerebral blood volume and intracranial pressure of nimodipine and vasodilator anesthetics cause concern and suggest the need for further prospective studies on the effects of nimodipine on cerebral blood flow and on the influence of nimodipine on the response of patients with subarachnoid hemorrhage to anesthetic drugs.

In conclusion, we reviewed our experience with the anesthetic management of patients who received nimodipine or placebo in a double-blind study on the effects of nimodipine prophylaxis on cerebral vasospasm. Nimodipine produced small, apparently desirable alterations in perioperative hemodynamic variables and did not otherwise appear to affect anesthetic management.

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Epidural Blockade for Cesarean Section Comparing Lidocaine Hydrocarbonate and Lidocaine Hydrochloride

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Lidocaine hydrocarbonate (Xylocaine CO_2®), when compared with lidocaine hydrochloride for regional analgesia, including labor and delivery, has been reported to have a faster onset and spread, while producing a more intense motor block.[1] The purpose of this study was to compare in a randomized, prospective, double-blind fashion, lidocaine–HCl and lidocaine–CO_2 in terms

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