Effects of Nicardipine on Cerebral Vascular Responses to Hypocapnia and Blood Flow Velocity in the Middle Cerebral Artery

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We noninvasively evaluated the effects of nicardipine on cerebral vascular responses to hypocapnia and blood flow velocity in the middle cerebral artery of 10 patients aged 17–60 (mean ± SD 46.1 ± 11.8) years. During fentanyl/diazepam/nitrous oxide anesthesia, mean blood flow velocity in the middle cerebral artery was measured and cerebral vascular reactivity to hypocapnia induced by hyperventilation was assessed before and during the administration of nicardipine. Mean blood flow velocity was measured using transcranial Doppler ultrasonography, and the cerebral vascular reactivity was expressed as the percentage change in mean blood flow velocity per unit change in end-tidal PCO₂. During the administration of 5.1 ± 1.3 μg/kg/min nicardipine, which caused a 26% reduction in mean arterial blood pressure, mean blood flow velocity increased significantly from 57.2 ± 19.2 to 64.2 ± 21.6 cm/sec (p < 0.01, paired t test), whereas cerebral vascular reactivity showed no significant change (4.0 ± 1.2% and 4.9 ± 2.5%, respectively). In conclusion, during fentanyl/diazepam/nitrous oxide anesthesia in patients, cerebral vascular reactivity to hypocapnia was maintained and nicardipine-induced hypotension resulted in increased middle cerebral artery blood flow velocity with maintenance of carbon dioxide reactivity to hypocapnia. (Stroke 1991;22:1170–1172)
A 2-MHz pulsed-Doppler instrument with an external probe diameter of 22 mm (TC2-64, EME, Uberlingen, FRG) was used for transcranial Doppler examination. Focal depth of the Doppler signal varied in 5-mm increments from 25 to 150 mm. Pulse repetition frequencies included 5, 8, or 10 kHz, depending on depth. Bidirectional signals were recorded with a 10-kHz low-pass filter and a 150-Hz high-pass filter. Spectral analysis was accomplished with fast Fourier transformation and 64-point resolution. The average time-mean velocity from 10 consecutive cardiac cycles was calculated for each patient. Doppler signals from the MCA were obtained by placing the probe against the side of the skull just above the zygomatic arch and adjusting its position for a maximal reflected signal at a depth of 45–55 mm.

An hour or more after the operation began, we measured mean blood flow velocity during normocapnia and during hypocapnia induced by hyperventilation. Mean blood flow velocity was measured 10 minutes after the end-tidal Pco₂ had changed. While maintaining end-tidal Pco₂ during normocapnia, we administered nicardipine until mean arterial blood pressure decreased to about 75% of the initial value. Mean blood flow velocity was then measured. Hypocapnia was again induced, and cerebral vascular reactivity was examined during hypotension. The cerebral vascular reactivity was defined as the percentage change in mean blood flow velocity per unit change in end-tidal Pco₂.

Mean arterial blood pressure was measured by noninvasive automatic devices employing slow cuff deflation (78354A, Hewlett-Packard Co., Waltham, Mass.). End-tidal Pco₂ was monitored with capnometry (78354A, Hewlett-Packard Co.).

Statistical comparisons were made using the paired t test, and p<0.05 was considered significant. Data are expressed as mean±SD.

Results

Table 1 shows the changes of mean arterial blood pressure, heart rate, end-tidal Pco₂, mean blood flow velocity, and cerebral vascular reactivity. During the administration of 5.1 ±1.3 μg/kg/min nicardipine, which caused a 26.3% reduction of mean arterial blood pressure, mean blood flow velocity increased significantly from 57.2 ±19.2 to 64.2 ±21.6 cm/sec (p<0.01) (Figure 1). Heart rate also increased significantly (p<0.01). Cerebral vascular reactivity to hypocapnia showed no significant change before and after the administration of nicardipine (4.0±1.2% and 4.9±2.5%, respectively) (Figure 2).

Discussion

Cerebral vascular reactivity to hypocapnia has been noninvasively evaluated using transcranial Doppler ultrasonography and capnometry. Markwalder et al⁷ reported that the end-tidal Pco₂ response curves for
blood flow velocity in the MCA strongly resembled the Paco2 response curves for CBF. Bishop et al8 showed that changes in MCA blood flow velocity reliably correlated with changes in CBF measured with intravenous xenon-133 when hypercapnia was induced; these authors expressed the carbon dioxide reactivity as the percentage change in MCA peak blood flow velocity per unit change in end-tidal Paco2. According to the results of linear correlation in our preliminary study, cerebral vascular reactivity was assumed to be the percentage change in mean blood flow velocity per unit change in end-tidal Paco2.

Previous studies3-6 have reported that CBF responses to hypocapnia are lost during hypotension to a mean arterial blood pressure of ≤50 mm Hg achieved with sodium nitroprusside, trimethaphan, nitroglycerin, nimodipine, and halothane in animals. Oishi et al9 reported that nicardipine decreased cerebrovascular reactivity to hypercapnia in cats. Nicardipine did not significantly change cerebral vascular reactivity to hypocapnia in our study. However, the effects of vasodilators on cerebral vascular responses differ at different levels of mean arterial blood pressure or Paco2. We induced moderate hypotension by administering nicardipine to examine the effects of moderate hypocapnia on cerebral vascular responses. Further study might be needed in situations such as lower arterial blood pressures or severe hypocapnia or hypercapnia.

Mean blood flow velocity increased significantly during the administration of nicardipine, which is compatible with previous studies. Nicardipine has been reported to produce a potent vasodilation with selective actions on the cerebral and coronary vascular beds in anesthetized dogs.10 Takenaka and Handa11 reported that the intravenous injection of nicardipine significantly increased CBF in patients. Kuriyama et al12 also showed that nicardipine produced a significant increase of CBF in patients when mean arterial blood pressure was significantly decreased. However, since we did not specifically measure CBF, the effects of nicardipine on CBF are not clear.

Our study involved a rather young cohort of patients, all of whom received anesthesia. Older or unanesthetized subjects may be affected differently by nicardipine infusion.

It should be noted that there are several problems in studying intracranial hemodynamics by using transcranial Doppler ultrasonography. If the patients have intracranial or extracranial artery stenosis, MCA territory or collateral blood flows might change during hypotension induced by vasodilators. Therefore, strict selection of patients is necessary. We selected patients without a clinical history of cerebrovascular disease; however, the patients were not examined using computed tomography or angiography. It is possible for patients to have cerebral artery disease without clinical symptoms or for the MCA territory to change when hypotension is induced by vasodilators. Lindegaard et al13 reported that the relation between internal carotid artery blood flow volume and blood flow velocity in the MCA was nearly linear when systemic blood pressure changed moderately, suggesting that the MCA territory changes relatively little during moderate changes of systemic blood pressure. However, because the use of blood flow velocity to study intracranial hemodynamics is still in a developmental stage, caution is required.

In summary, during fentanyl/diazepam/nitrous oxide anesthesia in patients, cerebral vascular reactivity to hypocapnia was maintained and nicardipine-induced hypotension increased MCA blood flow velocity with maintenance of carbon dioxide reactivity to hypocapnia.

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