Letters to the Editor

A Model of Bilateral Hemispheric Ischemia—Modified Four-Vessel Occlusion in Rats

To the Editor:

The four-vessel occlusion method developed by Drs. Pulsinelli and Brierley is widely used as an experimental model for bilateral hemispheric ischemia in the field of pathophysiology. However, this model has a major problem in the difficulty of confirming complete electrocauterization of the vertebral arteries at the level of the first cervical vertebra. We found that in Sprague-Dawley rats both the vertebral arteries at the level of the second cervical vertebra are visible and can be completely electrocauterized. We have established the occurrence of bilateral hemispheric ischemia after occlusion of both carotid arteries following electrocauterization of the vertebral arteries at the level of the second cervical vertebra. We compare our results obtained by this method with those in the original four-vessel occlusion model.

For these studies, we used male Sprague-Dawley rats weighing 320–380 g. Both of the vertebral arteries in anesthetized rats were permanently electrocauterized by insertion of an electrocautery needle into the right and left foramina of the cervical vertebra. Twenty-four hours after electrocauterization, both of the carotid arteries were occluded for 15 and 45 minutes, after which recirculation was allowed to occur. In the original method of Pulsinelli and Brierley, occlusion of the vertebral arteries without visualization at the level of the first cervical vertebra was often incomplete so that ischemic rats were selected based on the righting reflex and electroencephalograms. However, in our modification of the original model, we found that in rats without successful occlusion of both vertebral arteries, there was severe bleeding following the insertion of a 27-gauge needle into the right and left alar foramina of the cervical vertebra. Such bleeding was not observed in rats with permanent occlusion of both vertebral arteries. When the rats were treated using the four-vessel occlusion method of Pulsinelli and Brierley, six of 15 rats lost their righting reflex during 45 minutes of carotid artery occlusion (seven of 14 rats during 15 minutes of ischemia) and there was a relatively low mortality rate by Day 3. No rat with occlusion of one vertebral artery at the level of the second cervical vertebra lost its righting reflex during carotid artery occlusion. These rats also survived the experiments without any neurologic deficits (Table 1).

Our results suggest that if one vertebral artery in the original four-vessel occlusion method is accidentally not occluded, then severe ischemia will not be produced. On the other hand, in our modified method, all rats with 15 or 45 minutes of ischemia lost the righting reflex and the mortality was 30% and 70%, respectively. We agree that the four-vessel occlusion rat model described by Drs. Pulsinelli and Brierley produces severe cerebral ischemia only if both vertebral arteries are completely occluded.

In summary, bilateral hemispheric ischemia in rats was easily induced by the occlusion of both right and left carotid arteries after permanent electrocauterization of both the vertebral arteries at the level of the second cervical vertebra. This method gives a high level of success in producing severe forebrain ischemia.

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References

Oral Contraceptive Use and Risk of Stroke

To the Editor:

The association between oral contraceptive use and risk of stroke has been well documented over the last 20 years. The Collaborative Group for the Study of Stroke in Young Women showed that there is a ninefold increased risk of thrombotic stroke and a twofold increased risk of hemorrhagic stroke among oral contraceptive users compared with nonusers. Current oral contraceptive use emerged as a clear risk factor in the Oxford Family Planning Association Contraceptive Study. In the latter report, Vessey et al observed no strokes during 9,100 patient-years of observation in women using the modern birth control pill containing <50 μg estrogen.

A 23-year-old woman had been on a phase formulation containing 35 μg estrogen (Trinovum) for 11 months. She presented with a 6-week history of almost daily left occipital headaches radiating to the left periorbital region associated with...
nausea, vomiting, and dizziness. She also had a 1-hour episode of sudden loss of vision in her right eye 1 week before admission. She had recently noted unsteadiness of gait and a tendency to bump into objects on her left side. She gave a history of migraine.

Examination revealed a left lower quadrantanopia, a mild hemiparesis with brisk reflexes, and an equivocal plantar response on the left. She had a tendency to veer to the left on walking. Results of computed tomography and a lumbar puncture were normal.

A right hemisphere nonhemorrhagic stroke secondary to oral contraceptive use was diagnosed. The patient improved after stopping the oral contraceptive, but she had a residual field defect. From the patient's headaches a left-sided event would have seemed more likely, but this symptom was probably the nonspecific exacerbation of migraine described prior to stroke due to oral contraceptives. The transient loss of vision was interpreted as a transient retinal ischemic episode on the same side as the subsequent infarct.

While it would appear that the risk of stroke is extremely low in women on oral contraceptives containing <50 μg estrogen, continued vigilance is needed to exclude women with migraine or other factors predisposing to stroke even in users of this lower dosage.

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