

Title: EFFECT OF A Ca⁺⁺ CHANNEL BLOCKER ON CEREBRAL REFLOW PHENOMENON IN THE DOG

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Introduction. The no reflow phenomenon has been described by Ames et al. Though this phenomenon was initially thought to be due to capillary endothelial edema, Hart and Sokoll demonstrated evidence of arterial spasm. Vasodilators therefore could be helpful in management of patients following cerebrovascular accidents. As Ca⁺⁺ channel blockers produce vasodilation this study was set up to evaluate the effect of one Ca⁺⁺ channel blocker (Verapamil) on cerebral blood flow following ischemic insult in the dog.

Materials and Methods. 27 dogs 15-25 kg were studied. They were anesthetized with halothane, intubated and ventilated to maintain normal blood pH and gas tensions. Temperature was measured with a thermistor and kept normal with a heating blanket.

I. Catheters were placed in 1) femoral artery for blood pressure and blood flow measurement and for blood gas tension and pH determination, 2) femoral vein for fluid and drug administration, 3) left ventricle for administration of radio active microspheres labeled with 5 different isotopes for blood flow measurement.

II. A thoracotomy was performed and slings placed around innominate and brachiocephalic arteries.

III. The sagittal sinus was cannulated for blood gas tension and pH measurement and a catheter was placed in the cisterna magna.

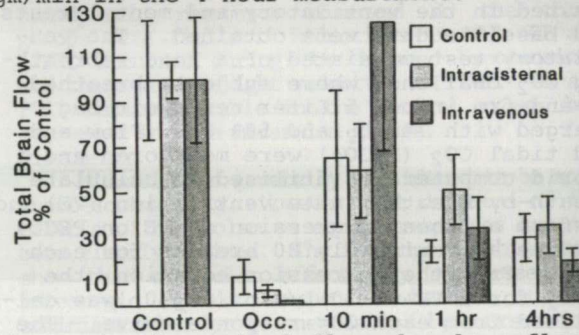
IV. Pediatric orthopedic cuff placed around the animal's neck.

V. A bipolar EEG was constantly recorded. After a stabilization period of one hour a control cerebral blood flow was measured. Ischemia was established by simultaneously pulling the intrathoracic slings tight and inflating the tourniquet to 1500 mmHg. Ischemia was maintained for 20 minutes. After 10 minutes of inflow occlusion blood flow was measured. Blood flow measurements were repeated 10 minutes after releasing the tourniquet, one and 4 hours later. Blood samples were collected for gas tension and pH determination during all the blood flow measurements.

9 animals were used as control. Two groups of 9 animals received Verapamil 0.1 mg/kg either intravenously or intracisternally immediately following the ischemic episode. At the end of the experiment, tissue samples were obtained from the brain and other organs to evaluate regional blood flow. Statistical analysis of the data collected was done with student's t-test for paired comparisons.

Results. Control cerebral blood flow in

all animals was 144.32 ml/100 gm/min. There was no physiologically significant flow at the 10 min measurement during the occlusion. 10 minutes after the ischemic period flow was not significantly different from control in all animals. At 1 hour post ischemia the total brain flow was significantly less than control (47.9±16 ml/100 gm/min) and remained at that level in the intracisternally treated group at the 4 hour measurement. The intravenously treated group showed a further decrease to 23.5±7 ml/100 gm/min in the 4 hour measurement.



The regional cerebral flow closely reflected the tissue composition with the more cellular grey matter having higher blood flow than the white matter. However, with the intracisternally treated group at 1 hour post ischemia the caudate nucleus and the thalamus had significantly higher flows than the rest of the specimens studied. Flows were also higher than in the intravenously treated animals. By 4 hours post ischemia the flows had decreased to approximately the same extent as in the whole brain blood flows and were similar in the control and treated groups.

There were no significant changes in the arterial blood gas tension or pH. The sagittal sinus blood samples as expected showed an elevation of pCO₂ and a decrease in pO₂ and pH during ischemia. There was no change in ionized Ca⁺⁺ level in CSF or blood in the treated animals. All animals died within 24 hours.

Conclusion. There was no apparent protection of the brain or improvement in cerebral blood flow with either modality of Verapamil administration.

References.

1. Ames A III, Wright RL, Konada J: Cerebral ischemia II the no reflow phenomenon. *Am J Pathol* 52:437-453, 1968.
2. Hart MN and Sokoll MD: Vascular spasm in cat cerebral cortex following ischemia. *Stroke* 9:52-57, 1978.

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