EFFECTS OF PROPOFOL ON CEREBRAL AND SPINAL CORD BLOOD FLOW AUTOREGULATION IN RATS

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The present study investigates the effects of propofol on cerebral and spinal cord blood flow and autoregulation in rats.

Methods: This study was approved by the Institutional Animal Care Committee. Twenty-two male Sprague Dawley rats (320-470 g) were anesthetized, intubated and ventilated with 2% isoflurane in O_2 air. Catheters were inserted into both femoral arteries and veins and the left ventricle via the right carotid artery. At completion of surgery the isoflurane was removed from the inspiratory gas mixture and the animals were equilibrated for 30 minutes according to their respective group treatment: Rats in group 1 (n=12, control) received a bolus of fentanyl (10 µg/kg iv), 70 % N_2O in O_2 and a continuous infusion of fentanyl (25 µg/kg/h iv). Group 2-animals (n=10) received a continuous infusion of propofol (2 mg/kg/min iv) and 30 % O_2 in air. Cerebral and spinal cord blood flows were measured using 4 radioactive microsphere species. The homogeneous distribution of microspheres was tested by comparison of kidney blood flows. MAP was increased using phenylephrine infusion and decreased using arfonad infusion combined with hemorrhage. MAP-levels were maintained constant for 5 minutes before each cerebral and spinal cord blood flow measurement. Arterial blood gas tensions and pH were maintained constant over the investigation period. Blood flow was calculated for cortical, subcortical and midbrain sections and the spinal cord. Autoregulation curves were plotted using a least squares fit. Differences between groups were calculated using analysis of co-variance.

Results: Cerebral and spinal cord blood flow autoregulation was present within a blood pressure range of 60-150 mmHg in both N_2O/fentanyl and propofol treated animals. Table 1 gives tissue blood flows (mean±SEM) within the autoregulatory range for groups 1 (N_2O/fentanyl) and 2 (propofol) (*=$p<0.05$ compared to group 1). Propofol significantly decreases cerebral blood flow in supratentorial brain regions within the autoregulatory range. Midbrain and spinal cord blood flows did not change.

	cortex	subcortex	midbrain	spinal cord
	$ml \cdot 100g^{-1} \cdot min^{-1}$			
N_2O/fentanyl	127±8	93±8	96±5	63±3
propofol	60±5 *	60±5 *	85±6	56±4

Discussion: These results show that propofol decreases CBF but does not impair or abolish cerebral or spinal cord blood flow autoregulation in doses that produce brain electrical silence. The use of propofol therefore seems to be of advantage in situations where adequate anesthesia is required in patients with critical cerebral perfusion pressures.

THE ANGIOTENSIN CONVERTING ENZYME INHIBITOR CAPTOPRIL IMPROVES NEUROLOGIC OUTCOME FROM INCOMPLETE ISCHEMIA IN RATS

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Introduction: Recent studies suggest that the angiotensin converting enzyme complex (ACE) is involved in the modulation of ischemic brain damage. Here we investigated whether the lipophilic ACE inhibitor captopril improves neurologic outcome from incomplete ischemia in rats.

Methods: This study was approved by the Institutional Animal Care Committee. Male Sprague-Dawley rats (330-420 g) were anesthetized with isoflurane and 30 % O_2 in air. Saline filled catheters were inserted into the right femoral artery and both femoral veins and the right jugular vein. At completion of surgery the isoflurane was removed from the inspiratory gas mixture and the animals received a bolus of fentanyl (10 µg/kg iv) followed by an equilibration period of 30 minutes at 70 % N_2O in O_2 and a continuous infusion of fentanyl (25 µg/kg/h). Ischemia was produced by combined unilateral carotid artery ligation and hemorrhagic hypotension to 30 mmHg for 30 minutes. Temperature, arterial blood gases and pH were maintained constant over time. Group 1-rats (n=10) received 70 % N_2O in O_2 as a control treatment. Animals in group 2 (n=10) received 70 % N_2O in O_2 plus a bolus injection of 10 mg/kg captopril 30 minutes prior to induction of ischemia. Neurologic outcome (NO) was evaluated for 3 days after ischemia using an 18 point performance scale with 0 = normal and 18 = stroke related death.

Results: Arterial blood pressure was significantly lower before and after ischemia in captopril treated animals (group 2) compared to controls (group 1). Post-ischemic blood glucose levels were significantly higher in captopril treated animals. Figure 1 shows neurologic outcome for both groups over the 3 days examination period. Treatment with captopril improved NO significantly compared to animals without ACE inhibition (control).

Discussion: The improvement in neurologic outcome following treatment with the ACE inhibitor captopril suggests direct involvement of reduced angiotensin II or increased tissue kinins in the modulation of ischemia. Possible mechanisms are decreases in excitatory neurotransmitter release and improvement of intra- and post-ischemic cerebral perfusion.