Title: CEREBRAL CIRCULATORY AND METABOLIC RESPONSES TO INTRAVENOUSLY ADMINISTERED LORAZEPAM


Affiliation: Department of Anesthesia, Veterans Administration Hospital, San Diego, University of California, San Diego, La Jolla, California, 92093, University of Lund, Lund, Sweden

Introduction. Lorazepam, a recently introduced benzodiazepine, is structurally similar to diazepam but is a more potent sedative, has greater anesthetic properties, and increased duration of action. Diazepam is known to moderately lower cerebral blood flow (CBF) and metabolism (CMR), and this study was performed to determine the effect of Lorazepam on these variables in monkeys.

Methods. Ten macaca fascicularis (3.5-5.0 kg) were evenly divided into two groups. One group was premedicated with ketamine (10 mg/kg IM), otherwise both groups were treated the same. Under halothane anesthesia, surgery was performed to permit vascular sampling and pressure monitoring from the following locations: femoral artery and vein, a peripheral vein, and the posterior portion of the sagittal sinus. Auffed tracheal tube was introduced via tracheostomy and electroencephalographic and EKG leads attached. Following this, the animal was awakened in a primate restraining chair situated in a lead-lined isolation box for determination of CBF using a modification of the Kety-Schmidt technique. Control CBF and CMR determinations were made at least 2 hours after halothane was discontinued, and, in the ketamine group, between 5-8 hours following ketamine administration. All animals appeared fully alert within 30 minutes after discontinuation of halothane and then were allowed an additional 2 hours to acclimate to the restraining chair before control CBF determinations were made. Following this, Lorazepam, 4 mg/kg, was administered intravenously and cerebral blood flow and metabolic measurements made one hour later. Students T-test was used to determine statistical significance (p<0.05 as significant).

Results. Lorazepam induced sleep in 8 animals although they maintained intact corneal reflexes and were arousable to painful stimulation. Another animal remained awake and calm while the tenth remained unresponsive to all stimuli. No significant changes in arterial blood gas status or blood pressure were caused by the administration of Lorazepam. Most importantly, PaCO2 remained unchanged at 33 mmHg.

Table 1 summarizes the cerebral circulatory and metabolic effects of Lorazepam. Monkeys premedicated with ketamine had significantly greater control cerebral blood flow and metabolic rates. However, the administration of Lorazepam to the ketamine premedicated group and to the non-ketamine premedicated group resulted in significant reductions in CBF and CMR glucose of about 25%. CMR oxygen was not significantly lowered.

Discussion. These data indicate that Lorazepam produces a reduction in CBF and CMR which is similar in magnitude (17-30%) to results reported by others in dogs and rats given diazepam. In our study, as in that reported by Carlsson in rats, CMRO2 was not significantly reduced (1). However, we found a significant reduction in CMR glucose, while Maekawa found CMR glucose to remain unchanged (2). The reasons for this discrepancy are not evident but most likely relate to minor CMR depressive effects of benzodiazepine drugs. Benzodiazepines reduce consciousness with cerebral hemodynamic effects that are different from barbiturates which cause a clearcut dose-dependent parallel decrease in both CBF and CMR.

References: