Title : THE EFFECT OF LORAZEPAM ON INTRACRANIAL PRESSURE AND CO_2 RETENTION IN CATS WITH INTRACRANIAL HYPERTENSION

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Introduction. An ideal premedicant for neurosurgery should reduce anxiety, not elevate $PaCO_2$ and reduce cerebral blood flow (CBF) or intracranial pressure (ICP). Diazepam has most of these attributes but is relatively short lived in its amnesic actions when compared to a new benzodiazapine, lorazepam (Wy 4036). We evaluated the effects of three dose levels of lorazepam on ICP in anesthetized cats and upon CO_2 retention in another group of awake cats.

Methods. ICP was measured during lorazepam administration in pentobarbital (40mg/kg IP) anesthetized cats. In these animals $PaCO_2$ was controlled to 30-34 mmHg and a PaO_2 of 90-110 mmHg. Arterial pressure (BP) and ICP (subdural catheter) were continuously monitored, with transducers zeroed to heart level and temperature servo-controlled to 37°C. The epidural balloon was gradually inflated within the sealed skull to elevate ICP and reduce intracranial compliance (ICC). ICC was evaluated by performing a volume-pressure response test using 0.05 cc of saline injected into the subdural catheter. The epidural balloon was inflated until ICP remained elevated by 5 mmHg one minute after subdural fluid injection. Three doses of lorazepam (0.25 mg/kg, 0.5 mg/kg, 1.C mg/kg were then given each animal approximately 20 minutes apart. In figure 1, ICP and BP (±SEM) data are shown at 6, 12, 18 and 36 seconds as well as 1,5,10, 15 and 20 minutes after each of the three doses.

In the awake group, CO_2 retention due to lorazepam was evaluated following a brief halothane anesthetic for intravascular catheter and epidural balloon placement. Movement artifact precluded reliable ICP measurement. The epidural balloon was inflated to between 0.8 and 1.0 cc, a volume similar to that used in anesthetized cats. Lorazepam was then given as in the anesthetized group. $PaCO_2$ was measured prior to and after each dose. Table 1 summarizes this data. Statistical analysis was performed using a paired-t analysis in both groups.

Results. As Fig. 1 illustrates, ICP showed a diphasic response with a small elevation in ICP occurring initially, followed by a reduction in ICP. The initial elevation in ICP occurred in two animals and was related to rapid bolus injection of lorazepam. Elevations were not seen when the drug was given slowly over 10-15 seconds. All animals showed reductions in ICP. Initial mean ICP prior to each dose of lorazepam was not significantly different but showed a downward trend from 22.7 to 20.9 mmHg between the first and third dose. ICP fell 4.3 mmHg after the first and third dose, 3.6 mmHg after the second dose. These decreases occurred within one minute. Recovery to levels insignificant from control at the $p < 0.05$ level occurred between 5 and 10 minutes after the first dose, 10 and 15 minutes after the second dose, and 15 and 20 minutes after the third dose. BP changes were not significant, but those cats given a a rapid bolus showed moderate initial reductions in blood pressure, particularly at the third dose level.

Table 1 summarizes mean $PaCO_2$ data collected on the awake animals. There is no significant difference at $p < 0.05$ between pre and post dose $PaCO_2$.

Discussion. We conclude that lorazepam does not cause significant CO_2 retention in the doses studied. Lorazepam also lowers ICP, and this effect is probably due to a decrease in CBF. Based on these results, we feel lorazepam shows promise as a safe pre-medicant in selected neurosurgical patients.

TABLE I

		$PaCO_2$ mmHg ± SEM	
		Pre-Dose	Post-Dose
Dose 1	0.25 mg/kg n=6	37.3 ± 2.19	35.2 ± 1.1
Dose 2	0.5 mg/kg n-5	34.6 ± 1.17	35.4 ± 5.42
Dose 3	1.0 mg/kg n=3	32.3 ± 2.6	37 ± 5.5

FIGURE 1