Title : THE EFFECT OF DIAZOXIDE ON INTRACRANIAL PRESSURE IN CATS WITH INTRACRANIAL MASS LESIONS

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Introduction. Increases in intracranial pressure (ICP) occur with systemic vasodilators such as nitroprusside and hydralazine. Diazoxide is a direct acting systemic vasodilator which to our knowledge has not been evaluated for its effect on ICP. This study evaluates the effect of diazoxide on ICP in cats with intracranial hypertension.

Methods. Twelve pentobarbital anesthetized cats were paralyzed and ventilated with an air/oxygen mixture to a $PaCO_2$ of 30-34 torr and a PaO_2 of 90-100 torr. Arterial pressure (BP) and ICP (epidural bolt) were continuously monitored. Temperature was servo-controlled to 37°C. An epidural balloon was gradually inflated to elevate ICP. Only animals exhibiting a 5 torr increase in ICP within 90 seconds of inhalation of a mixture of 5% CO_2 in oxygen were studied. A bolus of diazoxide 5 mg/kg was given twice, the second dose 30 minutes after the first. Observations were continued 15 minutes after the second dose.

Results. The effects of diazoxide on ICP, BP, and cerebral perfusion pressure (CPP) on two groups of cats, those with ICP < 20, group 1, and those with ICP ≥ 20, group 11, are compared in table 1. Uniform blood pressure reductions occurred in each group within 30 seconds after injection of diazoxide. Elevations in ICP occurred after injection of diazoxide in all groups. The highest elevations were seen in group 11. The ICP elevation after the second dose in group 1 was not significant from the first dose response at $p < .05$. The elevation after the second dose in group 11 was similar to that seen after the first. The lowest CPP occurred at approximately the time of the lowest blood pressure in group 1. In group 11, lowest CPP occurs when blood pressure was increasing. No cats demonstrated slowing or flattening of EEG. One cat in group 11 dilated a pupil ipsilateral to the epidural balloon following the second dose.

Discussion. Based on the results of this study, diazoxide is either a direct acting cerebral vasodilator and/or causes cerebral vasodilation secondary to cerebral blood flow autoregulation in response to reduction in systemic BP. The lack of a statistically significant response after the second dose in group 1 may be due to alterations in compliance that occurred after the first dose. This study shows small, significant, transient increases in ICP occur with diazoxide which might be clinically significant when given to patients with intracranial hypertension. We suggest that attempts be made to control ICP prior to administration of diazoxide in this circumstance.

TABLE 1
MEAN BLOOD PRESSURE, INTRACRANIAL PRESSURE AND CEREBRAL PERFUSION PRESSURE BEFORE AND AFTER DIAZOXIDE (ALL VALUES TORR ±1 SEM)

		INITIAL VALUES	LOWEST BP	HIGHEST ICP
GROUP I ICP < 20				
Dose I	BP	110 ± 6	*74 ± 7.7	86 ± 8
	ICP	17 ± 0.7	16.7 ± 0.6	*22.8 ± 1.7
	CPP	93 ± 6.7	*59 ± 6.9	*62.8 ± 8.6
Dose II	BP	99.2 ± 6.3	*73.3 ± 4.2	*78.3 ± 5.4
	ICP	17.2 ± 1.3	16.7 ± 1.5	18.7 ± 1.9
	CPP	82 ± 5.6	*56.7 ± 4.1	*58.2 ± 3
GROUP II ICP ≥ 20				
Dose I	BP	104.2 ± 3.3	*72.3 ± 4.8	*81 ± 3.1
	ICP	25.8 ± 1	27 ± 1.9	*36.8 ± 2.9
	CPP	78.3 ± 3	*46.5 ± 4.8	*44.2 ± 4.2
Dose II	BP	92.5 ± 4.2	*71.7 ± 4.6	*75 ± 3.6
	ICP	24.3 ± 1.6	32 ± 0.9	*41 ± 3.4
	CPP	63.2 ± 4.7	*46.5 ± 4.8	*35.3 ± 1.7

(* indicates significant difference from initial at $p < .05$)