TITLE: USE OF MAGNESIUM TO PROTECT AGAINST SPINAL CORD ISCHEMIA

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Paraplegia is a disastrous complication following cross-clamping of the thoracic aorta. Katz[1] showed that with an occlusion time greater than 30 min, paraplegia occurred in 1/3 of patients. N-Methyl-D-Aspartate (NMDA) receptors have been shown to mediate some of the pathological events in the spinal cord following cross-clamping. We investigated the use of Magnesium (Mg), a competitive antagonist of the NMDA system, in an attempt to protect the spinal cord from ischemic damage. Mg was administered intrathecally (IT) or intravenously (IV)

METHODS: Spinal cord ischemia (SCI) was produced in 5 kg rabbits using the method described by Drummond[2] They were intubated and ventilated with 1-2% halothane/O_2 to maintain normal $PaCO_2$ and pH. Halothane was discontinued when Mg was administered. Normal body temperature was maintained and fluids (0.5 N saline) given at 15 ml/kg/hr. A 4 Fr balloon-tipped catheter was advanced into the abdominal aorta and the tip positioned distal to the L renal artery. Heparin was given and SCI induced by inflating the balloon for 30 min. Treated rabbits were divided into 2 groups. IT Group $MgSO_4$ (100 mg), was injected at L4-5 interspace 30 min prior to balloon inflation. IV Group $MgSO_4$ (800 mg/kg/hr) was infused 1 hr before, during and ½ hr post induced SCI. Following cessation of the IV infusion, furosemide, 5 mg IV, was given to expedite excretion of Mg. A phenylephrine infusion was used to offset the hypotensive effect of Mg and maintain arterial BP at baseline values. Following recovery, two blinded observers did daily neurologic assessments for 3 days.

RESULTS: Neurologic outcome is based on day 3 evaluations. Balloon inflation for 30 min resulted in paraplegia in all controls (N=6). All IT Mg controls (N=3) recovered and were assessed normal on day 1. All rabbits receiving IT Mg prior to SCI were paralyzed on days 1-3. Of the 5 rabbits receiving IV Mg, 2 were normal on days 1-3, 1 was paretic and 2 were paralyzed. In most animals, neurologic assessments between day 1 and 3 did not differ. No therapy was required to treat the moderate metabolic acidosis post SCI. IV Mg rabbits required 2-4 hrs of ventilatory support after stopping the Mg infusion.

CONCLUSION: These preliminary results suggests that the NMDA antagonist Mg, when given IV, may be useful in reducing the ischemic damage to the spinal cord.

Neurological Outcome Following Induced Spinal Cord Ischemia

Treatment	N	Normal	Paretic	Paralyzed
None	6	0	0	6
$MgSO_4$ IT	6	0	0	6
$MgSO_4$ IV	5	2	1	2

REFERENCES:
1. J Thorac Cardiovas Surg 81:669-674, 1981
2. Anesthesiology 70:64-70, 1989

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TITLE: L-644,711 DECREASES FOCAL CEREBRAL ISCHEMIC INJURY

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Introduction: L-644,711, an anion transport inhibitor, has decreased brain injury and edema in animal models of traumatic-hypoxic cerebral injury.[1] We evaluated the effect of L-644,711 on brain injury and edema in a rat model of ischemia (middle cerebral artery occlusion [MCAo]).

Methods: During 1.2 MAC isoflurane anesthesia, rats (n=21) with chronically implanted subarachnoid catheters received one of the following doses of intrathecal L-644,711 immediately prior to 180 minutes of MCAo: Control-vehicle only; Dose I-200 $\mu g \cdot kg^{-1}$; or Dose II-320 $\mu g \cdot kg^{-1}$. The 180 minute period of MCAo was followed by 120 minutes of reperfusion. The brains were assessed for injury with TTC stain and edema with microgravimetry. The data were analyzed using a two-way analysis of variance, and Dunnett's t-test when appropriate.

Results: There were no differences in the physiologic or microgravimetric data. Brain injury was less in rats which received the higher dose of L-644,711 (320 $\mu g \cdot kg^{-1}$) versus the Control group ($p<0.05$, see Table 1). No other differences were present.

Discussion: L-644,711 is hypothesized to effect brain injury by improving the neuronal acid-base state, inhibiting astroglial swelling, or decreasing neutrophil aggregation.[2] The absence of a difference in the microgravimetric data would argue against astroglial swelling as the mechanism of improved brain injury in the present study. Further studies are necessary in order to define the mechanism of L-644,711's beneficial effect on ischemic brain injury.

	Control	Dose I	Dose II
Section 1	43±5	38±6	34±5*
Section 2	46±5	44±6	36±6*

Table 1-injury differences (% of the cross-sectional area that failed to stain with TTC in the hemisphere ipsilateral to MCAo [mean±SD]). *$p<0.05$ versus Control.

References:
1. Central Nervous System Trauma 4:3-14, 1987
2. Cerebrovascular Diseases. New York:Raven Press, 1989:247-250.