Title: EFFECT OF A HYPERTONIC LACTATED RINGERS SOLUTION ON CEREBRAL EDEMA AND INTRACRANIAL PRESSURE FOLLOWING CRYOGENIC BRAIN INJURY

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Introduction: Uncontrollable cerebral edema and intracranial hypertension are the most common causes of death for head-injured patients who reach a hospital alive. Many of these patients require the administration of large volumes of crystalloid solutions to treat or prevent hypovolemia. Previous studies have suggested that the osmolality (OSM) of the infused solution may play a crucial role in the development of cerebral edema and intracranial hypertension.[1] We therefore compared the cerebral effects of lactated Ringers (LR, measured OSM=254 mOsm/kg) with those of a hypertonic lactated Ringers solution (HTLR, measured OSM=469 mOsm/kg) in a freeze-lesion model of traumatic brain injury.

Methods: 8 New Zealand white rabbits weighing 3.1-3.7 kg were anesthetized with 4% halothane in oxygen, paralyzed with pancuronium, intubated, and ventilated with 66% N_2O in O_2 and 0.5%-0.7% halothane. The $PaCO_2$ was maintained between 36-40 mmHg. Esophageal temperature was monitored and maintained at 37° C through the use of servo-controlled heat lamps. Following infiltration with 0.25% bupivicaine, the scalp was incised in the midline and reflected laterally to expose the skull. A transducer-tipped, fiberoptic catheter (Camino Labs) was inserted into the right parietal lobe for continuous monitoring of intracranial pressure (ICP). A funnel with a neck diameter of 1 cm was epoxied to the skull overlying the left hemisphere. Simultaneously, bilateral groin incisions were made for the placement of femoral arterial and central venous catheters. An arterial blood sample was obtained for measurement of pH, PaO_2, $PaCO_2$ OSM, colloid oncotic pressure (COP), and hematocrit (HCT). Baseline values of mean arterial pressure (MAP), central venous pressure (CVP), and ICP were recorded. Evans blue dye (1 cc, 3% solution) was administered intravenously and a cryogenic lesion was created by pouring liquid nitrogen into the funnel over the left hemisphere for 70 seconds. Over the ensuing 45 minutes, blood was withdrawn and either LR or HTLR was administered at a rate sufficient to decrease the HCT to 20-25% while maintaining MAP and CVP at baseline values. At the end of the 45 minutes of hemodilution, a second blood sample was obtained, MAP, CVP, and ICP were recorded, and the animals sacrificed with an intravenous bolus of KCL. The brains were rapidly removed and samples obtained from each hemisphere for wet/dry weight measurement of water content. The remainder of the brain tissue was placed in cold (4° C) kerosene for 15 minutes. $2mm^3$ samples of the left cortex were then obtained from the lesion, in the perilesional area, and remote from the lesion as well as corresponding samples from the right hemisphere. These were placed on a kerosene/bromobenzene density gradient for determination of their specific gravities (SpGr). Data comparing the two groups were analyzed using unpaired t-tests. Significance was assumed for p values <0.05.

Results: There were no significant differences between the two groups prior to the hemodilution. Following hemodilution there were no differences between the two groups for MAP, CVP, HCT, COP, pH, PaO_2, or $PaCO_2$. Over the course of the experiment the LR group required significantly more fluid than the HTLR group (245 ± 5 ml vs. 132 ± 20 ml, $p < 0.0001$) to maintain a stable CVP and MAP. There was no difference in the mean volume of blood withdrawn during hemodilution (84 ml in the LR group vs. 82 ml in the HTLR group). OSM increased in the HTLR group by 13.5 ± 3.3 mOsm/kg whereas it decreased in the LR group by 5.5 ± 2.6 mOsm/kg ($p<0.0001$). ICP increased in both groups over the course of the experiment but the change in ICP was greater in the LR group than the HTLR animals (Δ ICP = 9.5 ± 2.4 vs. 1.7 ± 1.5 mmHg, Figure 1). Brain water content was significantly increased in the lesioned hemisphere as assayed by both the wet/dry weight method and the cortical SpGr but there was no difference between the two groups (Table 1). Water content of the non-lesioned hemisphere was significantly less in the HTLR animals as compared with the LR group (SpGr 1.0448 ± 0.0004 vs. 1.0436 ± 0.0004, $p<0.005$. Note: As SpGr increases, water content decreases).

Discussion: This study examined the acute cerebral effects of hemodilution with LR and HTLR in a model of traumatic brain injury. The sharp increase in ICP seen in the LR group was markedly attenuated in those animals receiving HTLR. This was accompanied by a modest increase in serum osmolality and evidence of dehydration of the normal, non-lesioned hemisphere. These preliminary results suggest that HTLR may be useful for the resuscitation of hypovolemic patients with localized brain injury. Further studies examining the chronic effects of administration of HTLR are in progress.

References: 1) Zornow MH, Todd MM, Ward DM, Moore SS: The acute cerebral effects of changes in plasma osmolality and oncotic pressure. Anesthesiology 65:A584, 1986.

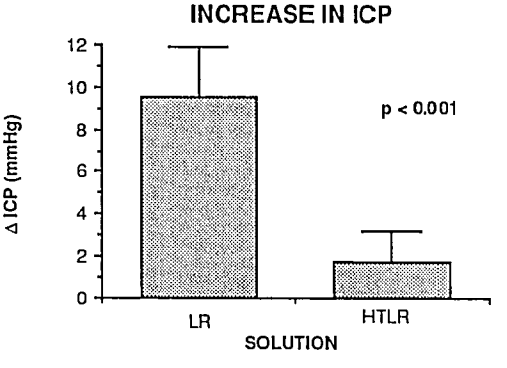

Figure 1: Change in ICP over the course of the experiment in the LR and HTLR groups.

	LR	HTLR
CORTICAL SPECIFIC GRAVITY		
LESIONED	1.0373 ± 0.0007	1.0376 ± 0.0013
NON-LESIONED	1.0436 ± 0.0004	1.0448 ± 0.0004 *
% WATER CONTENT		
LESIONED	79.73 ± 0.25%	79.53 ± 0.51%
NON-LESIONED	78.12 ± 0.13%	77.99 ± 0.32%

Table 1: Cortical specific gravities and per cent water content for the left (lesioned) and right (non-lesioned) hemispheres of the LR and HTLR groups. Note: As specific gravity increases, water content decreases. * = $p<0.01$, LR vs. HTLR.