Title: ACUTE CEREBRAL EFFECTS OF HEMODILUTION WITH ISOTONIC CRYSTALLOID AND COLLOID SOLUTIONS FOLLOWING CRYOGENIC BRAIN INJURY

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Introduction: Although the intravenous administration of large volumes of isotonic crystalloid solutions may result in peripheral edema, a recent study demonstrated that a 65% decrease in colloid oncotic pressure (COP) failed to have an acute effect on brain water content or intracranial pressure (ICP) of neurologically normal New Zealand white rabbits.[1] What effect such a hypo-oncotic state may have on cerebral edema formation following head injury is unknown. Therefore, using a cryogenic lesion as a model of traumatic brain injury, we measured COP, ICP, and regional brain water content in 32 rabbits following hemodilution with saline (S), 5% albumin (A), or 6% hetastarch (H).

Methods: 32 New Zealand white rabbits (3.0-3.6 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 32-36 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 ventriculostomy needle was stereotacticly inserted into the right lateral ventricle for continuous monitoring of 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. 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 60 seconds. The animals were then randomized to the type of fluid (S, H, or A) they would receive during hemodilution. Control (C) animals were not hemodiluted. The measured osmolality (OSM) and COP of the three hemodilution fluids were as follows:

	COP (mmHg)	OSM (mOsm/kg)
Control (C)	not hemodiluted	
Saline (S)	0	282
Hetastarch (H)	23	304
Albumin (A)	22	265

Baseline values for mean arterial pressure (MAP), central venous pressure (CVP), and ICP were recorded and a blood sample was obtained for determination of pH, PaO_2, $PaCO_2$, OSM, COP, and HCT. Over a 45 minute period, blood was withdrawn and the selected replacement fluid administered at rates sufficient to decrease the HCT to 20-25% while maintaining MAP and CVP at baseline values. MAP, CVP, and ICP were again recorded, a second blood sample was obtained, and the animals sacrificed by an intravenous bolus of KCL. The brains were rapidly removed and placed in cold (4° C) kerosene. 2 mm^3 samples of the left cortex were obtained from the lesion, in the perilesional area, and remote from the lesion as well as corresponding samples from the right hemisphere (Figure 1). These were placed in a kerosene/bromobenzene density gradient for determination of their specific gravities (SpGr). Data was analyzed using ANOVA and multiple comparison tests when appropriate. Significance was assumed for $p<0.05$.

Results: There were no differences between the 4 groups prior to hemodilution. Following hemodilution, no intergroup differences existed for MAP, CVP, ICP, pH, $PaCO_2$, or PaO_2. As intended, COP fell in the S group (Δ COP=9.5 mmHg, $p<0.001$). Changes in OSM were not significantly different between the 4 groups. Left hemispheric cortical samples showed decreasing SpGr (ie. increasing water content) as they approached the lesion. There were no differences in cortical SpGr between the various hemodilution groups at any of the sites (Figure 2).

Discussion: This study suggests that a decrease in plasma COP does not acutely exacerbate the cerebral edema produced by a model of traumatic brain injury. Disruption of the blood-brain barrier may be so extensive that macromolecules are able to extravasate into the interstitium and are therefore unable to produce an oncotic gradient favoring the retention of water within the vasculature.

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.

CORTICAL SAMPLING SITES FOR SPECIFIC GRAVITY DETERMINATIONS

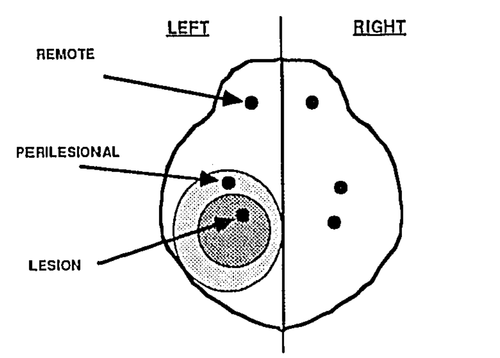

Figure 1: Location of cortical sampling sites for specific gravity determinations.

LESIONED HEMISPHERE

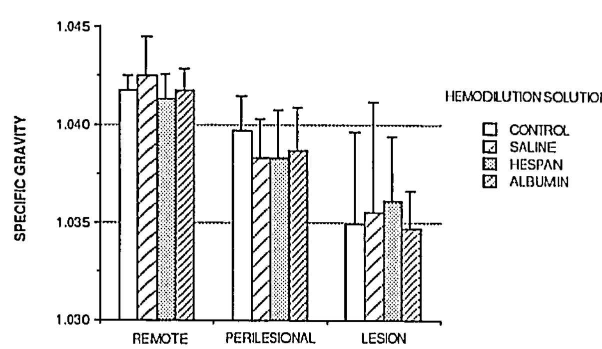

Figure 2: Cortical specific gravities at each sampling site (remote, perilesional, and lesion) for the 4 hemodilution groups. Tissue water content increases (specific gravity decreases) as the sampling site approaches the lesion.