

Brain Edema and Neurologic Status Following Head Trauma in the Rat

*No Effect from Large Volumes of Isotonic or Hypertonic Intravenous Fluids,
With or Without Glucose*

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Disagreement exists regarding the need to restrict the administration of fluid and glucose following head injury to prevent cerebral edema and neurologic deterioration. We examined whether blood osmolality and glucose, neurologic outcome, and the development of brain edema following head trauma were altered by intravenous infusion of large volumes of isotonic or hypertonic fluids that contained or did not contain glucose. Fifty-five rats that survived ether anesthesia and closed head trauma (delivered using a weight drop device) were assigned to one of five groups. In the first group no fluid was infused. In the second group minimal volumes of saline were infused during placement of a jugular vein catheter. In the three remaining groups 10 ml · kg⁻¹ · h⁻¹ of either total parenteral nutrition (TPN) (glucose 25%, amino acids 4.25%, 40 mEq/l sodium and 40 mEq/l potassium, 1935 mOsm/kg), dextrose 5% in 0.45% saline (495 mOsm/kg), or Haemaccel (isotonic plasma expander, 298 mOsm/kg) was infused *via* the jugular vein. Following head trauma and cannula placement, ether was discontinued. Neurologic severity score at 1 and 18 h after head trauma was used to assess neurologic outcome. A score between 0 and 6 was assigned by an observer who was blinded as to the experimental groups, with 0 representing no neurologic damage and 6 representing severe damage. Specific gravity of brain tissue samples containing gray matter and subcortical white matter from the traumatized and contralateral hemispheres was measured at 18 h after head trauma to determine the development of brain edema. There were no statistically significant differences in neurologic outcome and brain edema between the groups. Blood osmolality (318 ± 8 mOsm/kg, mean ± SD) and glucose (17.5 ± 4.2 mM) were increased in the group receiving total

parenteral nutrition but not in the groups receiving dextrose 5% in 0.45% saline or Haemaccel. It is concluded that giving large volumes of isotonic or hypertonic intravenous solutions, with or without glucose, for 18 h after head trauma does not significantly alter neurologic outcome or formation of brain edema in rats. (Key words: Blood; glucose. Brain: edema; head injury. Fluid balance: crystalloid; Haemaccel; osmolality. Nutrition: parenteral.)

PATIENTS suffering severe head trauma traditionally are treated by restriction of fluid and glucose intake. The stated reason for fluid restriction is to reduce brain water content and to prevent cerebral edema and increased intracranial pressure.¹ Collins *et al.*² advocated that fluid be restricted to 75 ml/h for adults. McComish and Bodley³ suggested that no more than 60 ml/h should be administered. However, the efficacy of fluid restriction has been questioned. Thomas and Gurdjian⁴ recommended moderate fluid restriction during the first 24 h only. Safar and Bircher⁵ and Becker and Garner⁶ suggested 125 ml/h of 5% dextrose in 0.45% saline solution for adults. They claimed that overhydration, *per se*, will not cause brain edema if the serum sodium concentration remains normal. Studies by others indicated that vigorous fluid resuscitation following head injury,⁷ cold injury,^{**} or brain ischemia,⁸ regardless of the fluid used, did not have major adverse effects on either the injured or noninjured brain in the posttrauma period. Isotonic as well as hypertonic solutions were advocated and used in those studies.

The effect of hyperglycemia on focal cerebral ischemia remains controversial. Several studies reported that hyperglycemia worsens the injury,^{9,10,††} whereas others found that hyperglycemia either decreases^{11,12,‡‡} or has no effect on¹³ the extent of cerebral injury. Moreover, total parenteral nutrition (TPN), which improved out-

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** Tommasino C, Todd MM, Shapiro HM: The effects of fluid resuscitation on brain water content (abstract). ANESTHESIOLOGY 57: A109, 1982.

†† Brint S, Kraig R, Kiessling M, Pulsinelli W: Hyperglycemia augments infarct size in focal experimental brain ischemia (abstract). Ann Neurol 18:127, 1985.

‡‡ Jernigan J, Evans OB, Kirshner HS: Hyperglycemia and diabetes improve outcome in a rat model of anoxia/ischemia (abstract). Neurology 34(suppl 1):262, 1984.

come in critically ill patients,^{14,§§} has been reported¹⁵ to improve survival rates and neurologic status in patients following head trauma.

The present study was designed to determine whether administration of glucose and large volumes of intravenous (iv) fluid (three times the calculated daily requirement) after head injury in rats significantly altered blood composition or neurologic outcome. The solutions studied were either isotonic or hypertonic and either contained or did not contain glucose. The blood values we examined were osmolality and concentrations of glucose, sodium, and urea. The neurologic values we examined were brain edema and severity of neurologic deficit.

Materials and Methods

EFFECTS OF EXPERIMENTAL TREATMENTS

The methodology used for the three parts of this study conformed to the Guiding Principles in the Care and Use of Animals by the Council of the American Physiologic Society and was approved by the institutional Animal Care Committee. Sixty-two adult male Sabra rats (Hebrew University strain) weighing 328 ± 37 g (mean \pm SD) were anesthetized in a bell jar containing ether-drenched cotton. Rats breathed spontaneously, and their tracheas were not intubated. Corneal reflexes were assessed at intervals, and anesthesia was considered sufficient for surgery once corneal reflexes were abolished. A midline scalp incision was made; the scalp and underlying muscles were reflected laterally; and closed head injury was delivered to the skull over the frontal portion of the left cerebral hemisphere by a special weight drop device.¹⁶ The weight drop device was designed to deliver a standard blow to the cranium resulting in a controlled head injury. Impact is delivered by a silicone-coated metal tip that extrudes from a platform falling down a frame. Settings on the frame control the distance of the fall of the platform.¹⁶ The reproducibility of the impact was determined previously by measuring the velocity developed during the free fall of the platform and the change in the velocity of the tip on collision with the target.¹⁶

Following head trauma, 7 rats became apneic and died. The 55 rats that survived and continued to breathe spontaneously were randomized into five experimental groups of 8–14 animals each. In group 1 ($n = 14$), the jugular vein was not cannulated, and no fluids were infused. Groups 2–5 underwent jugular vein cannulation with a 22-G medical-grade silicone tubing attached to a swivel

mechanism enabling continuous infusion while rats moved freely in metabolic cages. In group 2 ($n = 12$), minimal volumes of saline were infused only as needed for placement of the catheter. In groups 3–5, large volumes of solution (three times the calculated daily requirement) were infused through the jugular catheter at a rate of $10 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ for 18 h. Group 3 ($n = 11$) received a TPN formula containing amino acids 4.25% (Travasol-Baxter), glucose 25%, (for a total of 0.77 g protein and 18 cal per 100 g body weight per 18 h), Na^+ 40 mEq/l, K^+ 40 mEq/l, MVI_{12} 5 ml/l, vitamin C 250 mg, Cl^- 50 mM, acetate 70 mM, P^{5+} 15 mM, Zn^{2+} 10 mg, Cu^{2+} 1 mg, Mg^{2+} 5 mM, and Ca^{2+} 2.25 mM with an osmolality of 1,935 mOsm/kg. The infusion rate was 3.4 ml/h, providing an 18-h cumulative volume of 61.8 ± 3.3 ml (mean \pm SD). Group 4 ($n = 10$) received 5% dextrose in 0.45% saline solution (495 mOsm/kg) at a rate of 3.5 ml/h, providing an 18-h cumulative volume of 63.4 ± 2.7 ml. Group 5 ($n = 8$) received Haemaccel (Hoechst Pharmaceuticals, Middlesex, U.K.), a polypeptide manufactured from bovine gelatin with molecules of an average molecular weight of 35,000 D and osmolality of 298 mOsm/kg. The infusion rate was 3.1 ml/h, providing an 18-h cumulative volume of 56.5 ± 3.1 ml. In all groups, anesthesia was discontinued after head injury was delivered, and animals were returned to their cages, where unlimited food and water were supplied.

At both 1 and 18 h following head trauma, a neurologic severity score (NSS) was determined. This NSS assesses the clinical condition of the rats (mobility, reflexes, seeking behavior, and focal neurologic deficits) following head trauma, with a score of 0 indicating no neurologic impairment and a score of 6 indicating severe impairment (table 1). NSS was determined at 1 h to assess the severity of damage caused by the cranial impact and to provide a post-head trauma "baseline" for comparison with later evaluations. NSS at 18 h assessed the effects of the experimental treatments. The examination was carried out in a light room by an observer who was blinded as to the experimental groups.

TABLE 1. Neurologic Severity Score for Evaluation of Clinical Condition at 1 and 18 h after Head Trauma

	Points
Inability to exit from a circle 50 cm in diameter.	
For 30 min	1
For 60 min	1
Loss of righting reflex	
For 30 min	1
For 60 min or more	1
Loss of seeking behavior	1
Hemiparesis or hemiplegia	0.5 or 1
Maximum score (worst deficit)	6

§§ Loirat PH, Rohan JE, Chapman A, Beaufils F, David R, Nedey R: Positive nitrogen balance in hypercatabolic states: Results obtained with parenteral feeding after major surgical procedures. *Eur J Intens Care Med* 1:11–17, 1975.

With this model of closed cranial impact, we previously reported that cerebral edema is maximal at about 18 h after injury and gradually resolves within the next several days.¹⁶ Accordingly, in the present study, rats were decapitated at 18 h after head trauma and their brains rapidly removed (42 ± 5 s, mean \pm SD). For the traumatized hemisphere, a tissue sample was taken from an area adjacent to the traumatic lesion, and for the nontraumatized hemisphere, a sample was taken from a corresponding contralateral site. Samples of up to 0.5 g that contained portions of the temporal and frontal cortices from each hemisphere (gray and subcortical white matter) were hand-cut on an ice-cooled glass plate and placed into gradient columns for determination of specific gravity.¹⁶ Specific gravity of brain tissue was determined by the method of Marmarou *et al.* using linear gradient columns of kerosene and bromobenzene.¹⁷ A calibration curve was generated for each column using anhydrous K_2SO_4 solution of known specific gravity (1.045, 1.040, 1.035, and 1.025).

Urine was collected over 18 h and analyzed for urea, sodium, and glucose. Blood was sampled from the carotid arteries into heparinized vials during decapitation. Samples were analyzed for concentration of urea, sodium, and glucose using a Technician SMAC II System (Technician Instruments Corp., Tarrytown, NY). Plasma osmolality was analyzed by the freezing-point-depression method using a Fiske Osmometer (Fiske Associates, Needham Heights, MA).

EFFECTS OF ANESTHESIA

To ensure that residual effects of ether would not impair neurologic assessment at 1 h after discontinuing anesthesia, an additional group of eight rats (weighing 379 ± 34 g) was studied. Anesthesia was induced with ether; the scalp was incised; no cranial impact was delivered; and anesthesia was discontinued. Because the site for surgical preparation was located immediately adjacent to the weight drop device, the time required to place rats in the device and deliver a cranial impact following scalp incision was only several seconds. Thus, the duration of anesthesia in this additional group was virtually identical to that in groups 1–5.

DETECTION OF CEREBRAL EDEMA

To ensure that the present model was suitable to detect an increase of brain edema following head trauma, a second set of additional studies was performed. In six rats (weighing 392 ± 21 g), anesthesia was induced with ether; the scalp was incised; and a cannula was inserted into a femoral artery for blood sampling and determination of arterial blood pressure and heart rate. Cranial impact was delivered; 20 ml distilled water was infused iv; and anes-

thesia was discontinued. Blood was sampled at 10 min and 1 h after completing the infusion of distilled water, and blood sodium concentration and hematocrit and plasma osmolality were determined. Rats then were decapitated, their brains rapidly removed, and brain tissue samples taken for determination of specific gravity as described above.

Data from the principal experimental groups in this study ($n = 55$) were tabulated as the mean \pm SD. The data for the treatment groups *versus* time (1 and 18 h) and the treatment groups and specific gravity (left and right) were evaluated using a two-way analysis of variance. Data measured at only one time period were evaluated using one-way analysis of variance. Where the calculated F value exceeded the critical value for the 0.05 probability level, the Student-Newman-Keuls test was used to determine which differences were significant at $P < 0.05$. Data for NSS were evaluated using the Kruskal-Wallis test with *post hoc* evaluation using the Mann-Whitney U-test. NSS data were tabulated as median and range. Two-tailed Spearman's rank correlation test was used to examine for a correlation between NSS and specific gravity. A P value < 0.05 was considered significant.

Results

EFFECTS OF EXPERIMENTAL TREATMENTS

Rats in groups 1 and 2 drank 3–4 ml water during 18 h, while rats in groups 3–5 drank no water. Groups 3–5 were infused with 60.8 ± 1.8 ml/18 h and urinated 45.5 ± 8.3 ml/18 h as compared to 5.5 ± 1.5 ml/18 h of urine in groups 1 and 2.

Neurologic Severity Score

There was no significant difference in the NSS between the experimental groups prior to head trauma or at 1 or 18 h after injury (fig. 1). The combined median NSS at 1 h posttrauma for all groups was 3 (range 0–6). At 18 h the combined median NSS for all groups was 1 (range 0–4) ($P < 0.05$).

Specific Gravity

Figure 2 summarizes brain tissue specific gravity of the ipsi- and contralateral hemispheres in the five experimental groups 18 h after trauma. The left, contused hemisphere showed a statistically significant ($P < 0.01$) decrease in specific gravity as compared to the noncontused hemisphere, indicating brain edema in all groups. There was no statistically significant difference in brain tissue specific gravity between the experimental groups. There was a negative linear correlation between the NSS at 1 and 18 h posttrauma and the specific gravity of the

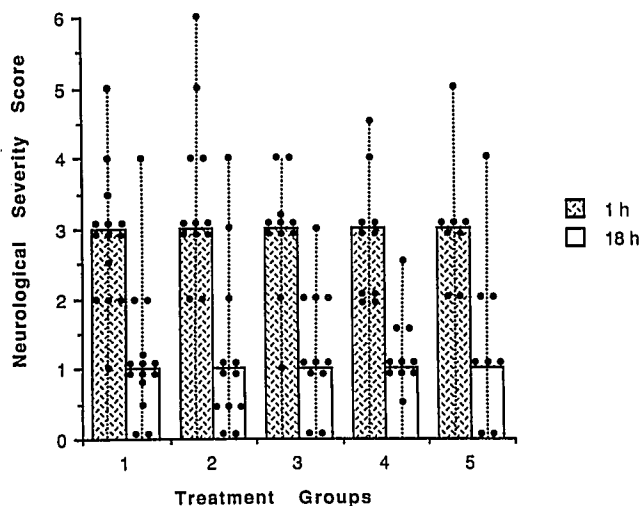


FIG. 1. Median values for neurologic severity score (NSS) are shown for the five treatment groups at 1 h (stippled bars) and 18 h (open bars) after head trauma. A nonpenetrating cranial impact was delivered to all rats by a stereotactically guided weight drop device. All rats had free access to food and water. In group 1 the jugular vein was not cannulated and no fluids were infused. In groups 2–5 the jugular vein was cannulated and the following fluids were infused: group 2 received minimal volumes of saline only as needed for placement of the catheter; group 3 received total parenteral nutrition at $10 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$; group 4 received 5% dextrose in 0.45% saline solution at $10 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$; and group 5 received Haemaccel at $10 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$. NSS did not differ between groups at either 1 or 18 h following head trauma. The filled circles represent the data for each group at both 1 and 18 h. Combined median NSS for all groups at 18 h was significantly decreased ($P < 0.05$) compared to combined median NSS at 1 h.

contused brain hemisphere (at 1 h $r = 0.41$, $n = 42$, $P < 0.01$; at 18 h, $r = 0.28$, $n = 55$, $P < 0.05$; fig. 3).

Laboratory Results

In the TPN group, blood osmolality ($318 \pm 8 \text{ mOsm/kg}$) was significantly increased compared to that in the instrumented controls (group 2, $301 \pm 3 \text{ mOsm/kg}$), and blood glucose ($17.5 \pm 4.2 \text{ mM}$) and urine glucose ($27.5 \pm 2.5 \text{ mM}$) were significantly increased compared to the other treatment groups (table 2). In the group receiving 5% dextrose in 0.45% saline, blood urea ($3.80 \pm 0.42 \text{ mg/100 ml}$) was decreased compared to the other treatment groups, and urine urea ($113.5 \pm 35.4 \text{ mg/100 ml}$) was decreased compared to that in the instrumented controls (group 2, $478.0 \pm 103.2 \text{ mg/100 ml}$).

EFFECTS OF ANESTHESIA

In the same examination setting as that used for rats receiving head trauma, the NSS of nontraumatized rats was 0 (no neurologic impairment) within 5 min of removal from the anesthetic chamber.

DETECTION OF CEREBRAL EDEMA

Plasma osmolality, initially $301 \pm 10 \text{ mOsm/kg}$, decreased by $20 \pm 5 \text{ mOsm/kg}$. Blood sodium concentration and hematocrit, initially $144.6 \pm 1.2 \text{ mEq/l}$ and $32 \pm 1\%$ respectively, decreased by $12.8 \pm 5.6 \text{ mEq/l}$ and $11 \pm 5\%$. Specific gravity of the contused (left) hemisphere was 1.0375 ± 0.0021 , significantly decreased compared to the noncontused (right) hemisphere in this study (1.0430 ± 0.0020) and to the mean specific gravity of the contused hemispheres from groups 1–5 (1.0391 ± 0.0021). The median NSS at 1 h was 4 (range 3–5).

Discussion

EFFECTS OF EXPERIMENTAL TREATMENTS

This study evaluated the impact of fluid loading and glucose administration on brain edema and neurologic status following head trauma in rats. During 18 h following head trauma, rats received iv fluids at $10 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$, which is about three times more than the normal oral intake of the rat. Three types of fluids were used: Haemaccel, which is an isotonic plasma expander; dextrose 5% in 0.45% saline, which is mildly hypertonic;

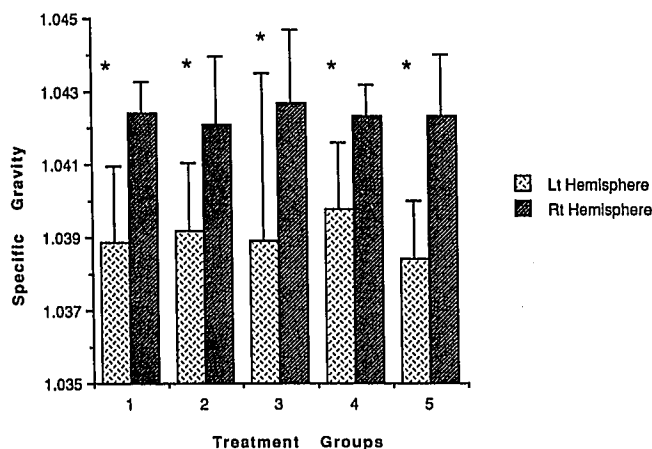


FIG. 2. Values for specific gravity are shown for the five treatment groups at 18 h after head trauma. Stippled bars represent values from the contused (left) hemisphere, and filled bars represent values from the noncontused (right) hemisphere. Values are mean \pm SD. A nonpenetrating cranial impact was delivered to all rats by a stereotactically guided weight drop device. All rats had free access to food and water. In group 1 the jugular vein was not cannulated and no fluids were infused. In groups 2–5 the jugular vein was cannulated and the following fluids were infused: group 2 received minimal volumes of saline only as needed for placement of the catheter; group 3 received total parenteral nutrition at $10 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$; group 4 received 5% dextrose in 0.45% saline solution at $10 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$; and group 5 received Haemaccel at $10 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$. Specific gravity did not differ between groups for either the left or right hemisphere. Asterisks indicate that in all groups specific gravity of the left hemisphere was significantly decreased ($P < 0.05$) compared to that of the right hemisphere.

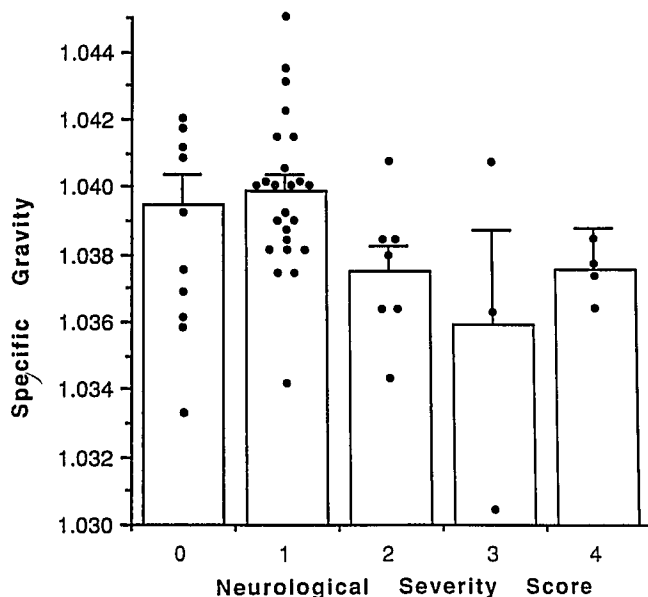


FIG. 3. The columns represent the correlation between specific gravity in the contused (left) hemisphere 18 h following head trauma and neurologic severity score (NSS) 18 h following head trauma. Values are mean \pm SD. The solid circles represent the data for each NSS set. There was a positive correlation between brain edema in the contused hemisphere (as estimated by decreased brain tissue specific gravity) and neurologic impairment (as indicated by increased NSS) with $R = 0.28$, $n = 55$, $P < 0.05$.

and a TPN formula containing 25% dextrose and 4.25% amino acids, which has an osmolality about seven times greater than that in blood. Although these three iv solutions differed significantly with respect to osmolality and glucose concentration, brain edema and neurologic status at 18 h following trauma was similar in all groups. It is possible that discrete samples of brain tissue from edematous, borderline, and nonedematous areas would provide additional information regarding regional brain tissue specific gravity values. Also, brain edema and neurologic status did not differ significantly among groups, despite the increase of blood osmolality and glucose in the TPN group. Moreover, there was a negative correlation between the NSS at 1 and 18 h after trauma and brain edema. The results are relevant to two aspects of care of patients following head trauma: selection of iv fluid and glucose administration.

EFFECTS OF ANESTHESIA

It was concluded from this additional set of studies that residual effects of ether did not impair neurologic assessment at 1 h after discontinuing anesthesia.

DETECTION OF CEREBRAL EDEMA

The finding of principal interest in this group was that greater brain edema was evident in rats receiving hypo-

tonic fluid iv to decrease plasma osmolality to 281 ± 5 mOsm/kg than in rats receiving iso- or hypertonic fluid iv and having plasma osmolalities in the range of 301 ± 3 to 318 ± 8 mOsm/kg (groups 1–5). It was previously reported in rabbits that withdrawal of blood (60 – 120 ml) and replacement with hypoosmolar crystalloid (273 mOsm/l) to decrease hematocrit from $41 \pm 1\%$ to $20 \pm 1\%$ or withdrawal of plasma (130 ± 14 ml) and replacement with hypoosmolar crystalloid (205 ± 20 ml of a 112 mOsm/l solution) decreased brain tissue specific gravity by 0.0009 – 0.0014 .^{18,19} Thus, in the present study, it was expected that water from the hypotonic fluid given iv would pass from blood into brain tissue, causing more edema in the contused hemisphere than that occurring following cranial impact in rats given iso- or hypertonic fluid iv. Our finding of decreased specific gravity in head-injured rats given hypotonic fluid as compared to head-injured rats given iso- or hypertonic fluid indicates that the present model is suitable to detect an increase of brain edema following head trauma. That brain tissue specific gravity was not decreased in the noncontused hemisphere of rats that received 20 ml hypotonic fluid and from which no blood or plasma was withdrawn (*i.e.*, the present additional group) presumably reflects adequate clearance of brain tissue water by the uninjured brain.

SELECTION OF INTRAVENOUS FLUID FOLLOWING HEAD INJURY

In the present studies, brain edema in rats receiving colloid-containing solutions was not significantly different from that in rats receiving crystalloid solutions. Colloid-containing solutions have traditionally been used in neurosurgery, because of concern that reduction in colloid osmotic pressure will cause brain edema, as it causes peripheral edema. It was previously reported that, in the brain, water content following colloid administration is not significantly different from that following crystalloid administration.^{7,8,18–22} The key determinant of water movement across the intact blood–brain barrier is plasma osmolality, rather than colloid oncotic pressure.

In a study in rabbits with no brain injury, plasma was removed and replaced with solutions of differing osmolality or oncotic pressure, and then brain edema was determined by measuring tissue specific gravity.¹⁸ Decrease of plasma osmolality by 13 ± 6 mOsm/kg (from a baseline value of 295 ± 5 mOsm/kg) resulted in a significant increase in cortical water content ($\approx 0.5\%$), whereas a 65% reduction in oncotic pressure (from 20 ± 2 to 7 ± 1

¹⁹ Todd MM, Tomasino C, Moore S, Drummond JC: The effects of acute isovolemic hemodilution on the brain: A comparison of crystalloid and colloid solutions (abstract). ANESTHESIOLOGY 61:A122, 1984.

TABLE 2. Blood and Urine Values at 18 h after Head Trauma

Treatment Group	Blood				Urine		
	Urea (mg/100 ml)	Sodium (mEq/l)	Glucose (mM/l)	Osmolarity (mOsm/kg)	Urea (mg/100 ml)	Sodium (mEq/l)	Glucose (mM/l)
1	6.47 ± 0.15	153.0 ± 3.6	7.7 ± 1.4	306 ± 7	254.5 ± 86.3	64.5 ± 23.3	0
2	6.83 ± 0.69	150.5 ± 2.6	7.3 ± 2.1	301 ± 3*	478.0 ± 103.2†	158.5 ± 45.2	0
3	5.95 ± 0.35	151.2 ± 1.4	17.5 ± 4.2‡	318 ± 8*	294.2 ± 11.3	54.1 ± 4.2	27.5 ± 2.5‡
4	3.80 ± 0.42‡	152.0 ± 4.2	8.1 ± 1.7	307 ± 5	113.5 ± 35.4†	70.5 ± 2.1	0
5	6.35 ± 0.38	151.1 ± 2.8	7.8 ± 1.6	304 ± 4	307.1 ± 32.1	63.2 ± 7.1	0

Values are mean ± SD.

A nonpenetrating cranial impact was delivered to all rats by a stereotactically guided weight drop device. All rats had free access to food and water. In group 1 the jugular vein was not cannulated and no fluids were infused. In groups 2–5 the jugular vein was cannulated and the following fluids were infused: group 2 received minimal volumes of saline only as needed for placement of the catheter; group 3

received total parenteral nutrition at 10 ml · kg⁻¹ · h⁻¹; group 4 received 5% dextrose in 0.45% saline solution at 10 ml · kg⁻¹ · h⁻¹; and group 5 received Haemacell at 10 ml · kg⁻¹ · h⁻¹.

* Significant difference, group 2 compared to group 3, $P < 0.05$.

† Significant difference, group 2 compared to group 4, $P < 0.05$.

‡ Significant difference compared to other treatment groups, $P < 0.05$.

mmHg) failed to produce any change. In another study, administration of hypertonic saline solution (3%) without removal of plasma, which increased blood osmolality by 15 mOsm/kg (from a baseline valued of 270 ± 2 mOsm/kg), failed to produce any statistically significant decrease in brain water content by the wet/dry-weight method.²³ The difference in results, *i.e.*, increase in brain water content with decreased plasma osmolality¹⁸ but no change in brain water content with increased osmolality,²³ may relate to the removal of plasma in the first study, the lower baseline osmolality in the second study, or the methods used to determine brain water content (specific gravity¹⁸ as compared to wet/dry weight²³). The results of the aforementioned studies^{7,8,18–23} suggest that administration of isotonic colloids and crystalloids has similar effects on intracranial pressure and brain water content in normal brain.¹⁸ Reductions in oncotic pressure are inadequate to result in net water movement into the brain tissue, as colloid oncotic pressure forms only a small fraction of total osmolality.

In injured brain, where the blood–brain barrier is disrupted, oncotic and osmotic gradients cannot be maintained, and edema formation is dependent on hydrostatic forces. Therefore, administration of isotonic colloid and crystalloid solutions exert similar effects on edema formation and intracranial pressure in brain injury.^{7,8,21,22} Zornow *et al.*²⁴ examined brain water content and intracranial pressure when hypertonic lactated Ringer's solution (469 mOsm/kg) or isotonic lactated Ringer's solution was used for isovolemic hemodilution in rabbits with cryogenic brain injury. Although blood osmolality difference between the groups was 19 mOsm/kg, no decrease in water content was seen in the injured hemisphere as determined by the wet/dry-weight method. However, a small but statistically significant increase in specific gravity was found in the noninjured hemisphere. Zornow *et al.*²² acknowledged that the cryogenic lesion used in their studies is not identical to the brain lesion resulting from

cranial impact. The present studies examined the effects of iv infusion of solutions of differing osmolality following head trauma. Although the solutions used in the present studies differed from those used by Zornow *et al.*,²² our results are consistent with their data on brain water content as assessed by wet/dry weight; *i.e.*, in both studies, brain edema was not different between treatment groups.

GLUCOSE ADMINISTRATION FOLLOWING HEAD INJURY

Animal studies provide convincing evidence that dextrose administration, with or without marked hyperglycemia, augments neurologic damage in global cerebral ischemia^{25–27} and spinal cord ischemia.²⁸ An increased blood glucose concentration also correlates positively with more severe neurologic damage in humans following stroke²⁹ and cardiac arrest.³⁰ Administration of relatively small amounts of dextrose, which caused only modest increases in blood glucose, exacerbated neurologic damage in both types of injury.^{27,28} Results from studies using models of focal ischemia suggest that withholding glucose administration,^{9,10,***} or treatment with insulin^{31,32} protects neurologic status only in injuries where reperfusion occurs. Hyperglycemia improved neuronal damage,¹² infarct size,^{11,15} and neurologic outcome††† when animals experienced ischemia without reperfusion.

In summary, we found that neurologic outcome and formation of brain edema was not significantly influenced by administration of large volumes of isotonic or hypertonic iv solutions, with or without glucose, for 18 h following head trauma in rats. Blood osmolality and the con-

*** Brint S, Kraig R, Kiessling M, Pulsinelli W: Hyperglycemia augments infarct size in focal experimental brain ischemia (abstract). *Ann Neurol* 18:127, 1985.

††† Jernigan J, Evans OB, Kirshner HS: Hyperglycemia and diabetes improve outcome in a rat model of anoxia/ischemia (abstract). *Neurology* 34(suppl 1):262, 1984.

centration of glucose in blood was increased by administration of large volumes of TPN solution but not by a 5% decrease in 0.45% saline or by Haemaccel. Increase of blood osmolality and glucose did not significantly alter neurologic outcome or the formation of brain edema compared to the treatment given to other groups or to no treatment. These results do not support the proposal that glucose and iv fluid volumes should be restricted when planning fluid management of head injured patients.

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