Resuscitation from Hemorrhagic Shock

Alterations of the Intracranial Pressure After Normal Saline, 3% Saline and Dextran-40

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Resuscitation from hemorrhagic shock by infusion of isotonic (normal) saline (NS) is accompanied by a transient elevation in intracranial pressure (ICP), although cerebral edema, as measued by brain weights at 24 hours, is prevented by adequate volume resuscitation. The transient increase in ICP is not observed during hypertonic saline (HS) resuscitation. The effect of colloid resuscitation on ICP is unknown. Beagles were anesthetized, intubated, and ventilated, maintaining pCO_2 between 30–45 torr. Femoral artery, pulmonary artery, and urethral catheters were positioned. ICP was measured with a subarachnoid bolt. Forty per cent of the dog's blood volume was shed and the shock state maintained for 1 hour. Resuscitation was done with shed blood and a volume of either NS (n = 5), 3% HS (n = 5), or 10% dextran-40 (D-40, n = 5) equal to the amount of shed blood. Intravascular volume was then maintained with NS. ICP fell from baseline values (4.7 ± 3.13 mmHg) during the shock state and increased greatly during initial fluid resuscitation in NS and D-40 groups, to 16.0 ± 5.83 mmHg and 16.2 ± 2.68 mmHg, respectively. ICP returned to baseline values of 3.0 ± 1.73 mmHg in the HS group with initial resuscitation and remained at baseline values throughout resuscitation. NS and D-40 ICP were greater than HS ICP at 1 hour ($p < .001$) and 2 hours ($p < .05$) after resuscitation. These results demonstrate that NS or colloid resuscitation from hemorrhagic shock elevates ICP and that HS prevents elevated ICP.

THE OBSERVATION THAT successful resuscitation from hemorrhagic shock demands the administration of saline in addition to reinfusion of blood was first made by Wiggers.[1] The electrophysiologic basis for this requirement was established by Shires and associates.[2–5] To restore cell membrane potential differences and repair the sodium-potassium pump after shock, a volume of crystalloid approximately four times the volume of hemorrhage is needed. Inadequate resuscitation is associated with the development of cerebral edema,[6] a process that is prevented by adequate restoration of intravascular volume.[7] Recently, however, increased ICP has been noted despite adequate resuscitation from hemorrhagic shock as well.[8]

The massive amounts of isotonic crystalloid solution required for adequate resuscitation of severely injured patients has prompted the evaluation of smaller volumes of either hypertonic saline (HS) or colloid solutions as a substitute. In a number of studies, HS solutions were as effective in resuscitation as isotonic electrolyte solutions of three times the volume.[9–11] Likewise, colloid resuscitation effectively expands plasma volume and also maintains this volume for a greater time than that observed with crystalloid resuscitation.[12,13]

We compared the effect of ICP of normal saline (NS), HS, and colloid (Dextran-40 [D-40]) during resuscitation from experimental hemorrhagic shock.

Materials and Methods

Beagles weighing 8.5–14.5 kg were splenectomized. After an overnight fast, each dog was anesthetized with 4 mL of 5% thiamylal sodium, placed in a supine position, intubated endotracheally, and ventilated at a tidal volume of 15 mL/kg and a fraction of inspired oxygen (FiO_2) of 1.00. Ventilation was adjusted to maintain pCO_2 between 30–45 torr. Additional intravenous doses of sodium pentobarbital, 2.5–5.0 mg/kg, were given as needed for anesthesia. Bilateral femoral vessel cutdowns were performed and 16-gauge 2-inch catheters placed in both femoral arteries. A flow-directed thermodilution pulmonary artery catheter was positioned via a femoral vein.

Each dog was then turned on its left side. A burr hole was made in the right hemicranium with a 0.25-inch twist drill, and ICP was measured with a pediatric subarachnoid

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Submitted for publication: May 29, 1986.

bolt attached to a transducer. ICP was calibrated against a mercury column and zeroed at the level of the right orbit. Right femoral arterial and pulmonary catheters were attached to pressure transducers zeroed at the level of the atria and calibrated against a mercury column. ICP, right atrial pressure (RAP), pulmonary capillary wedge pressure (PCWP), and pulmonary artery pressure (PAP) were recorded simultaneously on a Beckman polygraph, and values for each were documented in 15-minute intervals from baseline values. Cardiac output (CO) and core temperature were also recorded at each interval. Pulmonary vascular resistance (PVR) was calculated using the following equation: PVR = PAP − PWP/CO. A urethral catheter was used to measure urine output every 15 minutes. The bladder was emptied just before the shock period.

Baseline hemodynamic measurements were obtained. Forty per cent of the total blood volume (79 mL/kg) was shed via the left femoral artery catheter over 5 minutes and collected in a citrate-phosphate-dextrose blood bag. After 1 hour of shock (end shock period), one half of the shed blood was transfused over 15 minutes. Hemodynamic measurements were obtained and then an amount of NS (Group I [GrI], n = 5) or 3% HS (Group II [GrII], n = 5) equal to the amount of shed blood was given. Group III (GrIII) comprised five dogs from GrI and GrII that had recovered from the first experiment for at least 2 weeks and had a normal hematocrit and neurologic status. GrIII received 10% D-40 in NS in an amount equal to the crystalloid solutions given to GrI and GrII. All groups were then given 1500 mL of NS over the subsequent 75 minutes. The remaining shed blood was transfused in the final 15 minutes. At the completion of each experiment the subarachnoid bolt and vascular catheters were removed. The burr hole was filled with bone wax and the incision was closed. Femoral arteries were repaired and the groin incision was closed. All dogs were breathing spontaneously at this time and regained consciousness. Baseline arterial samples were obtained and taken hourly for the duration of the experiment. From each sample, hematocrit (Hct), sodium (Na), potassium (K), osmolarity (osm), and base deficit (BD) determinations were made.

Data were analyzed using the Statistical Analysis System (SAS) at the University of Illinois, Chicago, Illinois. Unpaired t-tests were performed between group values for each time point. Values of $p < 0.05$ were considered significant.

Results

Mean weight and volume of blood shed for GrI, GrII, and GrIII are listed in Table 1. Mean weight for all dogs was 11.2 ± 1.72 kg and the mean volume of blood loss was 351 ± 54.1 mL. Baseline mean arterial blood pressures (MAP) of the three groups shown in Figure 1 were not different. After hemorrhage, MAP dropped to between 31 ± 16.2 and 52 ± 23.6 mmHg. During shock, MAP spontaneously increased to between 51 ± 19.2 and 74 ± 20.1 mmHg. The addition of one-half shed blood volume increased MAP to 75% of baseline values. MAP reached near baseline values after infusion of either NS, HS, or D-40. For the duration of resuscitation, MAP was at or near baseline values and was not statistically different among the groups at any time. Systolic and diastolic blood pressures followed a pattern similar to MAP. Heart rate (Fig. 2) remained at essentially baseline values for the duration of the experiment (all dogs had tachycardia most likely due to light anesthesia). Baseline cardiac outputs ranged from 1.53 ± 0.44 to 2.07 ± 0.66 L/min (Fig. 3). Hemorrhage decreased CO to 20% of baseline values. During shock, CO increased spontaneously to 40% of baseline values. Reinfusion of one-half shed blood volume increased CO to 75% of baseline values. The addition of NS, HS, and D-40 increased CO above baseline values. A hyperdynamic state continued during infusion of 1500 mL of NS although CO was not statistically different among the groups. Mean measurements of RAP, PAP, and PCWP are shown in Figures 4, 5, and 6, respectively.

TABLE 1. *Mean Weight of Dogs and Volume of Blood Loss*

	GR I	Gr II	Gr III
Baseline weight	11.6 ± 1.96 Kg	11.1 ± 1.39 Kg	10.8 ± 1.82 Kg
Amount bleed (40% blood volume)	358 ± 69.6 mL	351 ± 44.1 mL	343 ± 57.6 mL

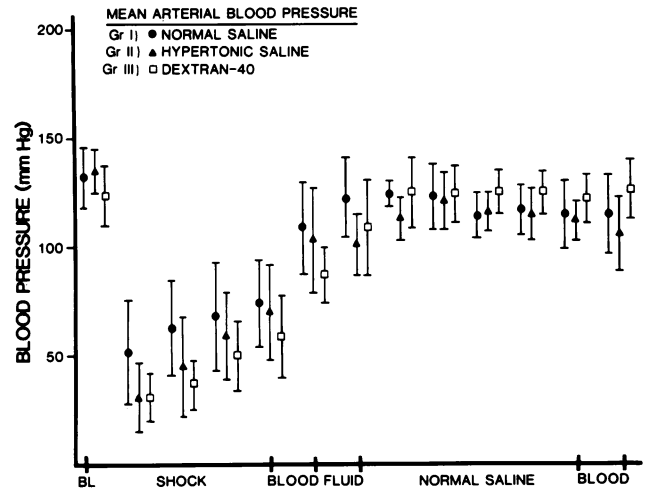

FIG. 1. Mean arterial blood pressure measurements at baseline (BL), through shock (1 hour) and resuscitation. Resuscitation was initiated with one-half shed blood volume followed 15 minutes later by a volume of test fluid, either NS (GrI), HS (GrII), or D-40 (GrIII) equal to the amount of shed blood. Infusion of 1500 mL of NS and the remaining shed blood over 90 minutes completed the study period. Values are mean ± SD.

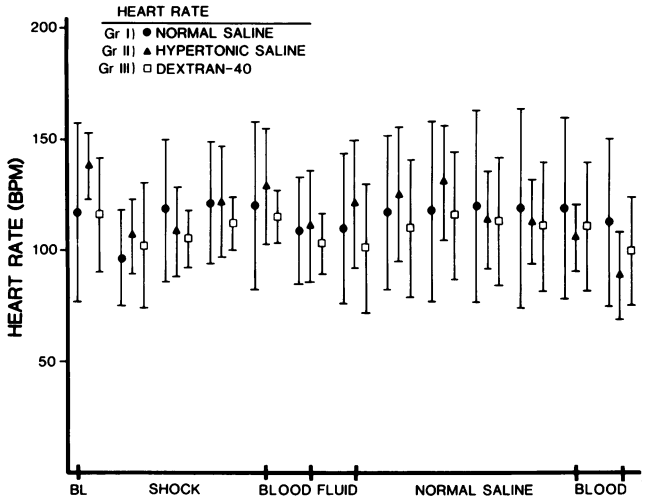

FIG. 2. Heart rate measurements at baseline (BL), through shock (1 hour) and resuscitation. Resuscitation was initiated with one-half shed blood volume followed 15 minutes later by a volume of test fluid, either NS (GrI), HS (GrII), or D-40 (GrIII) equal to the amount of shed blood. Infusion of 1500 mL of NS and the remaining shed blood over 90 minutes completed the study period. Values are mean ± SD.

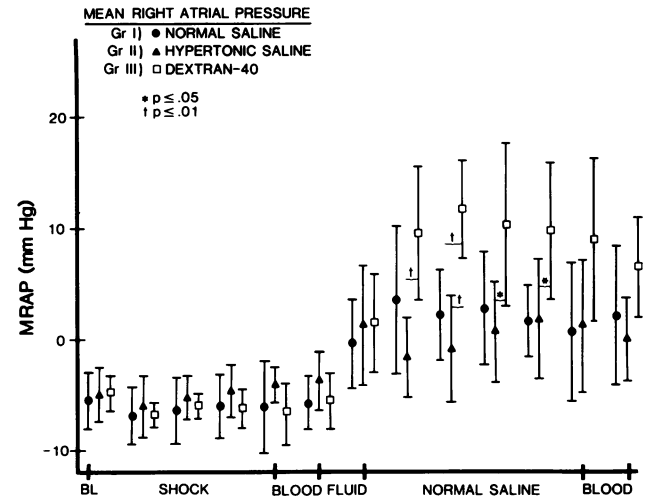

FIG. 4. Mean RAP measurements at baseline (BL), through shock (1 hour) and resuscitation. Resuscitation was initiated with one-half shed blood volume followed 15 minutes later by a volume of test fluid, either NS (GrI), HS (GrII), or D-40 (GrIII) equal to the amount of shed blood. Infusion of shed blood over 90 minutes completed the study period. Values are mean ± SD.

Filling pressures fell with hemorrhage and, like MAP, increased during the shock period. Infusion of one-half shed blood volume brought filling pressures to near baseline values in all groups. Filling pressures remained near or above baseline values for the duration of fluid resuscitation. GrIII (D-40) sustained filling pressures statistically greater than GrI or GrII during resuscitation. HS provided lower filling pressures than NS throughout fluid resuscitation although mean PAP measurements were statistically different between GrI and GrII only immediately after administration of the initial volume of shed blood and test fluid. GrIII filling pressures fell during late resuscitation.

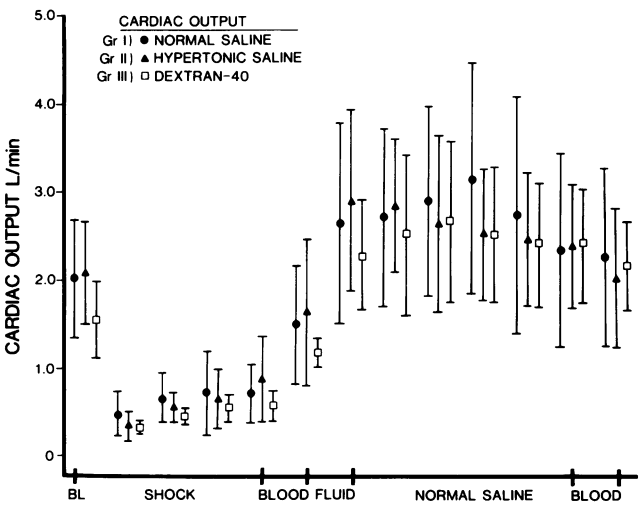

FIG. 3. Cardiac output measurements at baseline (BL), through shock (1 hour) and resuscitation. Resuscitation was initiated with one-half shed blood volume followed 15 minutes later by a volume of test fluid, either NS (GrI), HS (GrII), or D-40 (GrIII) equal to the amount of shed blood. Infusion of 1500 mL of NS and the remaining shed blood over 90 minutes completed the study period. Values are mean ± SD.

Urine outputs (mL/kg) for shock and resuscitation are listed in Table 2 and Figure 7. All dogs had no urine output during shock. Urine flow began early in resuscitation but diuresis was delayed in GrIII. Total urine output after 1 hour of resuscitation was highest in GrII (HS), intermediate in GrI (NS), and lowest in GrIII (D-40). These differences were significant. Although this trend persisted after 2 hours of resuscitation, the differences were not significant. The onset of diuresis in GrIII correlated with the fall in pulmonary and left ventricular filling pressures.

Baseline ICP values ranged from 3.8 ± 2.49 to 6.4 ± 3.21 mmHg (Fig. 8). ICP decreased during shock but then increased essentially to baseline values with the infusion of one-half shed blood volume. The addition of NS or D-40 significantly increased ICP. HS, however, maintained ICP at baseline values. GrI and GrIII showed greatly elevated ICP throughout resuscitation compared with GrII, which maintained baseline values throughout resuscitation with NS. ICP values in GrIII (D-40) decreased in late resuscitation coincidently with a fall in filling pressures and increased urine output.

The pattern of PVR (Fig. 9) was similar in all groups regardless of the type of fluid resuscitation. PVR increased during shock when CO decreased and returned to values below baseline with resuscitation. The low PVR values were presumably due to the elevated CO observed in all groups.

Hct, osm, Na, and K values are listed in Table 2. Hct fell with hemorrhage and was lowest after 1 hour of resuscitation. After transfusion of the remaining blood vol-

ume in late resuscitation, Hct increased in all groups. After 1 hour of resuscitation, Hct of GrIII was significantly lower than that of GrI or GrII and remained significantly lower than that of GrII until the end of the study. Presumably the low Hct observed in GrIII was due to an increased intravascular volume and hemodilution.

Osm increased significantly in GrII after infusion of HS. The elevated osm correlated with a significantly elevated serum Na. Serum K values decreased equally in all groups with resuscitation from shock.

Temperature, arterial pH, BD are also shown in Table 2. All dogs had an increased BD and decreased arterial pH despite adequate fluid resuscitation. Temperature fell steadily throughout the study. Values were not statistically different among groups.

All dogs in GrI and GrII survived without neurologic sequelae. Two of five dogs in GrIII died after the study. One dog never regained consciousness but maintained respirations until death at 24 hours after the study. The second dog died 3 days after the study; this animal was lethargic but ambulatory. These two dogs had the lowest Hct after 2 hours of resuscitation, 15.5 and 14.5, respectively.

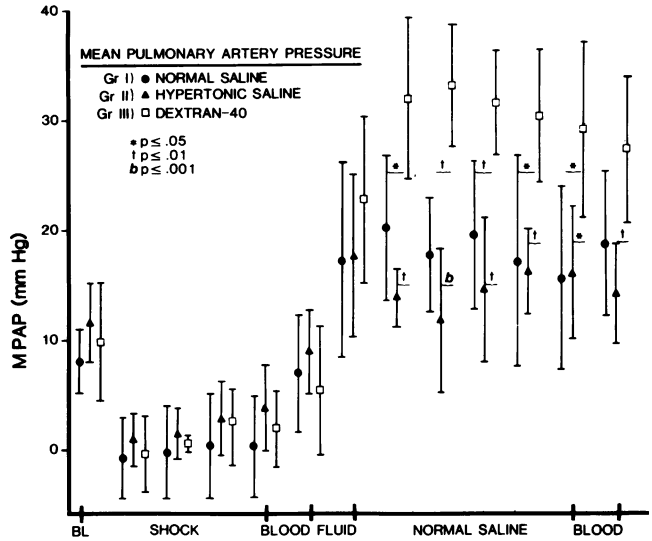

FIG. 5. Mean pulmonary artery pressure measurements at baseline (BL), through shock (1 hour) and resuscitation. Resuscitation was initiated with one-half shed blood volume followed 15 minutes later by a volume of test fluid, either NS (GrI), HS (GrII), or D-40 (GrIII) equal to the amount of shed blood. Infusion of 1500 mL of NS and the remaining shed blood over 90 minutes completed the study period. Values are mean ± SD.

Discussion

Hemorrhagic shock is associated with progressive deterioration of cellular function leading to death. As perfusion pressure falls, transmembrane potential decreases independent of pH, plasma potassium concentration, bicarbonate concentration, or CO_2 tension.[5,14,15] The adenosine-triphosphate (ATP)-dependent sodium-potassium pump fails, allowing Na flux into and K flux out of the cell. Interstitial water then enters the cell, causing intracellular edema. As shock continues, oxidative phosphorylation ceases and plasma membranes are disrupted. Lysosomal granules leak enzyme contents, and autodigestion of the cell begins.[16] Adequate resuscitation of cellular function requires restitution of blood volume and oxygen-carrying capacity. Whole blood is not entirely sufficient for resuscitation due to the extracellular losses of Na and water that require replacement with electrolyte solutions.[2,3,13] Resuscitation must begin before the condition of the "sick cell" is irreversible.

Relying on the studies of Lowe et al.,[17] we use isotonic crystalloid solutions for resuscitation of patients with depleted effective circulating plasma volume. Although the volumes of isotonic crystalloid required to resuscitate and maintain the severely ill or injured surgical patient are large, Lowe and associates[17] reported that no adverse effects on pulmonary parameters occurred, even when massive volumes of crystalloid were infused. The effects of crystalloid fluid resuscitation on intracranial pressures have not been well documented.

If ICP becomes elevated as a consequence of massive fluid resuscitation, adverse effects may be seen, especially in patients who have head injury complicating their trauma. Preservation of cerebral perfusion appears to be a determining factor in survival after hemorrhage.[18] Multiple mechanisms protect cerebral perfusion pressure. Autoregulation of cerebral blood flow over a wide range of systemic blood pressures maintains cerebral perfusion

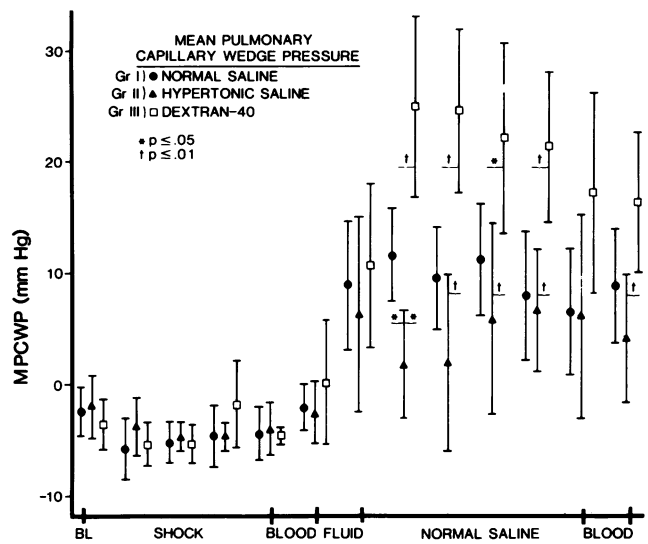

FIG. 6. Mean pulmonary capillary wedge pressure measurements at baseline (BL), through shock (1 hour) and resuscitation. Resuscitation was initiated with one-half shed blood volume followed 15 minutes later by a volume of test fluid, either NS (GrI), HS (GrII), or D-40 (GrIII) equal to the amount of shed blood. Infusion of 1500 mL of NS and the remaining shed blood over 90 minutes completed the study period. Values are mean ± SD.

TABLE 2.

	Baseline	End Shock	1 Hour of Resuscitation	2 Hours of Resuscitation
Na				
Gr I	141 ± 1.48	141 ± 1.48	144 ± 1.22	146 ± 1.92
Gr II	142 ± 1.64	140 ± 1.14	162 ± 3.03	157 ± 4.16
Gr III	140 ± 1.30	137 ± 3.21	141 ± 1.79*	146 ± 3.29*
K				
Gr I	3.6 ± 3.6	2.9 ± .56	3.0 ± .91	2.5 ± .41
Gr II	3.7 ± .29	2.9 ± .43	2.9 ± .34	2.5 ± .31
Gr III	3.9 ± .32	2.9 ± .24	3.0 ± .26	2.7 ± .18
Osm				
Gr I	301 ± 12.2	294 ± 12.9	295 ± 12.1	290 ± 34.0
Gr II	294 ± 17.3	292 ± 8.5	326 ± 3.8	317 ± 14.5
Gr III	289 ± 9.1	297 ± 6.0	299 ± 14.8†	309 ± 14.7
Hct				
Gr I	34.5 ± 4.76	26.3 ± 3.96	19.5 ± 3.08	27.5 ± 4.97
Gr II	35.3 ± 3.93	25.8 ± 3.56	21.0 ± 2.15	29.1 ± 4.01
Gr III	35.6 ± 4.77	26.0 ± 5.79	14.5 ± 3.79‡	21.4 ± 6.04‖
Urine Output	Bladder emptied			
Gr I		0.0	18.9 ± 5.84	80.3 ± 20.1
Gr II		0.0	34.9 ± 14.3	125.4 ± 55.8
Gr III		0.0	5.2 ± 7.94§	65.3 ± 42.0
Temp				
Gr I	33.2 ± 1.41	32.6 ± 1.44	31.6 ± 2.77	31.6 ± 3.66
Gr II	34.4 ± 1.37	33.7 ± 1.23	32.3 ± 1.25	29.9 ± 1.83
Gr III	34.1 ± 1.22	33.5 ± 1.49	31.4 ± 1.42	30.7 ± 1.64
Arterial pH				
Gr I	7.41 ± .14	7.42 ± .10	7.34 ± .12	7.32 ± .12
Gr II	7.46 ± .09	7.37 ± .06	7.30 ± .11	7.33 ± .11
Gr III	7.46 ± .09	7.35 ± .14	7.33 ± .10	7.28 ± .07
BD				
Gr I	−3.26 ± 2.34	−6.48 ± 3.36	−8.38 ± 2.49	−8.46 ± 1.61
Gr II	−2.28 ± .84	−8.70 ± 3.40	−10.58 ± 1.29	−9.46 ± 2.03
Gr III	−1.16 ± 1.17	−9.08 ± 5.42	−7.16 ± 4.14	−8.08 ± 3.21

* $p \leq .001$ (Gr I *vs.* Gr II); $p \leq .001$ (Gr II *vs.* Gr III)
† $p \leq .01$ (Gr I *vs.* Gr II); $p \leq .05$ (Gr II *vs.* Gr III)
‡ $p \leq .05$ (Gr I *vs.* Gr II); $p \leq .01$ (Gr II *vs.* Gr III)
§ $p \leq .05$, $p \leq .01$ (Gr I *vs.* Gr II); $p \leq .01$ (Gr II *vs.* Gr III)
‖ $p \leq .05$ (Gr II *vs.* Gr III)

with MAP as low as 50 mmHg.[19,20] Below this pressure, regionalization of cerebral blood flow occurs.[21] The diencephalon (thalamus and hypothalamus), brain stem, and cervical spinal cord then receive preferential flow. In severe shock most of the CO is directed to the brain due to elevated systemic vascular resistance.[20,22] Restoration of intravascular volume with crystalloid restores CO and cerebral perfusion pressure, although cerebral blood flow remains below preshock values for several hours.[23] If only the shed blood is returned, cerebral edema and cellular damage occur.[6,7]

Since 1951, isovolemic hemodilution models have shown that NS increases ICP, whereas HS prevents this rise.[24] Elevation in ICP correlates with increased brain water content.[25–27] Isovolemic colloid hemodilution does not affect the brain water content[26,28,29] and HS actually decreases ICP and brain water content.[25,27] Recently, NS resuscitation of experimental hemorrhagic shock was shown to increase ICP, and the addition of HS protected the brain from this increase in ICP,[8] although survival and neurologic sequelae were not documented. The effect on ICP of colloid resuscitation in a hemorrhagic shock model is not known.

We attempted to produce sufficient hemorrhage to overwhelm cerebral autoregulation, thereby causing cerebral cellular damage. Because ICP becomes elevated with cerebral swelling, any interstitial or cellular edema induced by NS, HS, or D-40 resuscitation would be reflected as an increase in ICP.

We demonstrated that ICP falls as MAP decreases below the level at which autoregulation maintains cerebral perfusion pressure. ICP remains below baseline values for the duration of the shock state, and increases as intravascular volume is restored. Marked differences are noted between dogs resuscitated with HS and those resuscitated with either NS or D-40. NS resuscitation elevates ICP to approximately 3–4 times baseline values, whereas HS resuscitation returns ICP to baseline values and maintains it there despite NS reinfusion. D-40 resuscitation initially elevates ICP to values similar to those observed with NS, but during the second hour of maintenance fluid replacement with NS, ICP returns to baseline values. These data

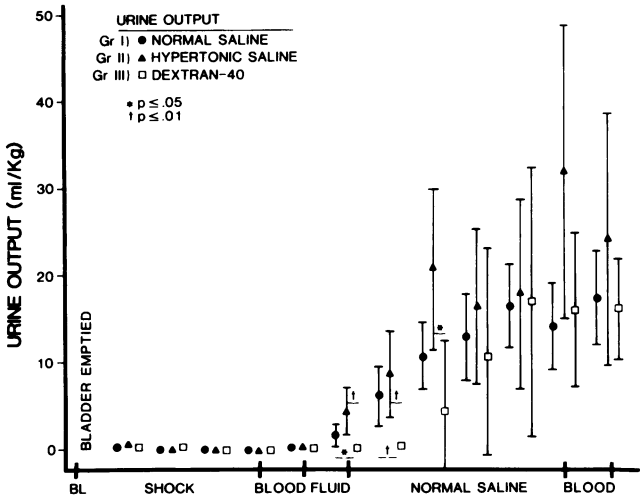

FIG. 7. Urine output measurements at baseline (BL), through shock (1 hour) and resuscitation. Resuscitation was initiated with one-half shed blood volume followed 15 minutes later by a volume of test fluid, either NS (GrI), HS (GrII), or D-40 (GrIII) equal to the amount of shed blood. Infusion of 1500 mL of NS and the remaining shed blood over 90 minutes completed the study period. Values are mean ± SD.

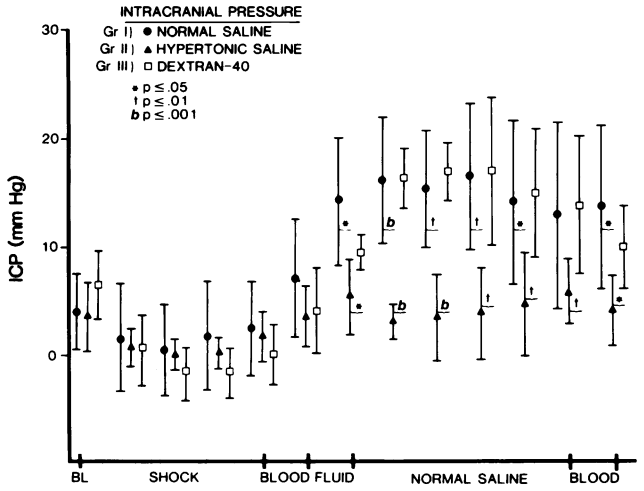

FIG. 8. Intracranial pressure measurements at baseline (BL), through shock (1 hour) and resuscitation. Resuscitation was initiated with one-half shed blood volume followed 15 minutes later by a volume of test fluid, either NS (GrI), HS (GrII), or D-40 (GrIII) equal to the amount of shed blood. Infusion of 1500 mL of NS and the remaining shed blood over 90 minutes completed the study period. Values are mean ± SD.

imply that cerebral edema occurs during NS and D-40 resuscitation of hemorrhagic shock. Administration of HS early in fluid resuscitation appears to prevent cerebral edema.

Because brain weights and brain water content measurements were not done, we can only speculate that the elevated ICP observed in dogs given NS or D-40 develops secondary to fluid shifts into the extravascular space within the brain. In the absence of shock, colloid hemodilution with D-40 does not increase cerebral brain water or ICP. D-40 is of sufficient size (40,000 daltons) that it remains in the vascular space for up to 3 hours, after which it is degraded and excreted in the urine.[30] D-40 also creates a sufficient oncotic pressure to pull extravascular fluid into the vascular space. Since ICP increases with D-40 resuscitation from shock, we suspect that the shock state has caused a breakdown in the blood–brain barrier, permitting D-40 to enter the brain, drawing free water into the interstitium, and causing cerebral edema. A reversal of this process is noted during the second hour of resuscitation when ICP in GrIII (D-40) returns to baseline values. As ICP decreases, the urine output increases, suggesting that D-40 shifts back to the vascular space, bringing water with it. D-40 and water are then excreted in the urine as seen by a fall in the pulmonary artery and left ventricular filling pressures.

Restoration of adequate perfusion pressures during resuscitation from hemorrhage shock returns the cellular transmembrane potential to normal.[5] Since adequate perfusion pressures were obtained in all treatment groups during resuscitation, HS does not appear to exert its cerebral protective effect (lowering ICP) by stabilization of cell membranes through reestablishment of the transmembrane Na–K gradient. Instead, HS may act by replacing plasma Na deficits known to occur during shock.[31] Alternatively, HS may simply act osmotically, pulling water from the extravascular space into the intravascular space[9,11,12] and, indeed, serum osm and Na concentrations were significantly greater in the HS-treated group. Since plasma volume is expanded by HS only temporarily, losing 75% of its effectiveness within 30 minutes,[32] we propose that HS not only provides an osmotic gradient for water to enter the vascular space but also reestablishes

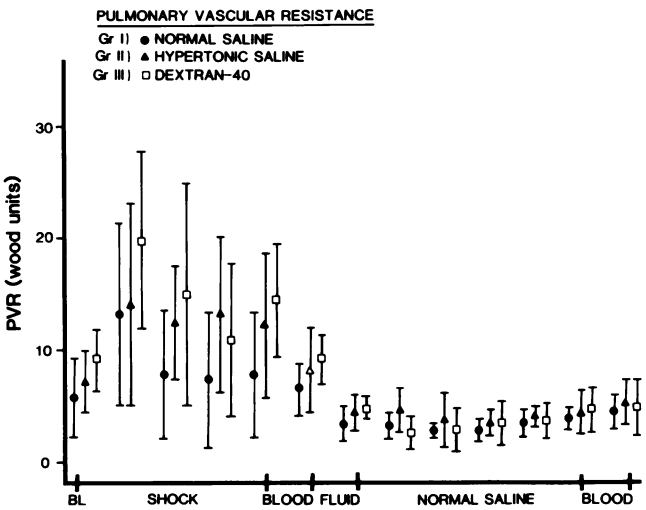

FIG. 9. Pulmonary vascular resistance calculated at baseline (BL), through shock (1 hour) and resuscitation. Resuscitation was initiated with one-half shed blood volume followed 15 minutes later by a volume of test fluid, either NS (GrI), HS (GrII), or D-40 (GrIII) equal to the amount of shed blood. Infusion of 1500 mL of NS and the remaining shed blood over 90 minutes completed the study period. Values are mean ± SD.

proper function of the cell membrane and the blood–brain barrier by another mechanism. Future studies will be directed toward identification of such mechanisms responsible for maintenance of the blood–brain barrier.

All dogs except two treated with D-40 survived the study neurologically intact. These two dogs sustained the greatest hemodiluton we observed, which led us to suspect they had neurologic damage resulting from inadequate replacement of the oxygen-carrying capacity of the blood. Red blood cell transfusion requirements may be greater when D-40 resuscitation is used.

Pulmonary artery and left ventricular filling pressures were significantly greater in dogs given D-40 (GrIII). The elevated filling pressures were not reflected in the systemic pressures. HS dilates the pulmonary vasculature,[33] and this is reflected in lower filling pressures; D-40 may exert an opposite effect. These differences in filling pressures among groups were not reflected by a change in PVR.

Resuscitation from hemorrhagic shock with either NS or D-40 is associated with significant elevations in ICP. HS (3%) prevents this increase in ICP. We believe that severe hemorrhagic shock with failure of autoregulation and cerebral perfusion compromises cell membrane integrity and blood–brain barrier function. Conventional resuscitation with NS or colloid solutions is not sufficient to restore these functions, and cerebral edema with elevating ICP occurs. The use of HS early in resuscitation may enhance the return of cell membrane and blood–brain barrier function, and may prove beneficial to the patient in hemorrhagic shock who has also sustained neurologic trauma.

References

1. Wiggers CJ. Present status of the shock problem. Physiol Rev 1942; 22:74–123.
2. Crenshaw CA, Canizaro PC, Shires GT, et al. Changes in extracellular fluid during acute hemorrhagic shock in man. Surg Forum 1962; 13:6–7.
3. Shires T, Brown FT, Canizaro PC, et al. Distributional changes in extracellular fluid during acute hemorrhagic shock. Surg Forum 1960; 11:115–117.
4. Shires T, Coln D, Carrico J, et al. Fluid therapy in hemorrhagic shock. Arch Surg 1964; 88:688–693.
5. Shires GT, Cunningham JN, Baker CRF, et al. Alterations in cellular membrane function during hemorrhagic shock in primates. Ann Surg 1972; 176:288–295.
6. Smith SD, Cone JB, Bowser BH, et al. Cerebral edema following acute hemorrhage in a murine model: the role of crystalloid resuscitation. J Trauma 1982; 22:588–590.
7. Tamura H, Witoszka MM, Hopkins RW, et al. The nervous system in experimental hemorrhagic shock: morphology of the brain. J Trauma 1972; 12:869–875.
8. Prough DS, Johnson JC, Poole GV, et al. Effects on intracranial pressure of resuscitation from hemorrhagic shock with hypertonic saline *versus* lactated Ringer's solution. Crit Care Med 1985; 13: 407–411.
9. DeFilippe J Jr, Timoner J, Velasco IT, et al. Treatment of refractory hypovolemic shock by 7.5% sodium chloride injections. Lancet 1980; 2:1002–1004.
10. Lopes OU, Pontieri V, Rocha E, et al. Haemodynamic effects of hypertonic sodium chloride infusions during hemorrhagic shock in dogs. J Physiol 1980; 301:64–65.
11. Nakayama S, Sibley L, Gunther RA, et al. Small volume resuscitation with hypertonic saline (2,400 mOsm/liter) during hemorrhagic shock. Circ Shock 1984; 13:149–159.
12. Baue AE, Tragus ET, Parkins WM. A comparison of isotonic and hypertonic solutions and blood flow and oxygen consumption in the initial treatment of hemorrhagic shock. J Trauma 1967; 7:743–755.
13. Shoemaker WC. Comparison of the relative effectiveness of whole blood transfusions and various types of fluid therapy in resuscitation. Crit Car Med 1976; 4:71–78.
14. Campion DS, Lynch LJ, Rector FC Jr, et al. Effect of hemorrhagic shock on transmembrane potential. Surgery 1969; 66:1051–1059.
15. Jennishe E, Enger E, Medegard A, et al. Correlation between tissue pH, cellular transmembrane potentials and cellular energy metabolism during shock and during ischemia. Circ Shock 1978; 5: 251–260.
16. Bell ML, Herman AH, Egdahl RH, et al. Role of lysosomal disruption in the development of refractory shock. Surg Forum 1970; 21: 10–12.
17. Lowe RJ, Moss GS, Jilek J, et al. Crystalloid *vs* colloid in the etiology of pulmonary failure after trauma: a randomized trial in man. Surgery 1977; 81:676–683.
18. Golden PF, Jane JA. Experimental study of irreversible shock and the brain. J Neurosurg 1973; 39:434–441.
19. Fitch W, Ferguson GG, Sengupta D, et al. Autoregulation of cerebral blood flow during controlled hypotension in baboons. J Neurol Neurosurg Psychiatry 1976; 39:1014–1022.
20. Rittmann WW, Smith LL. Cerebral blood flow following severe hemorrhage. Surg Gynecol Obstet 1966; 123:67–72.
21. Chen RYZ, Fan F, Schuessler GB, et al. Regional cerebral blood flow and oxygen consumption of the canine brain during hemorrhagic hypotension. Stroke 1985; 15:343–350.
22. Weiss HR, Levy PJ, Kleinert HD, et al. Alterations in brain and muscle oxygenation during hypovolemia and replacement with plasma substitutes in rats. Circ Shock 1978; 5:115–124.
23. Prough DS, Johnson JC, Stump DA, et al. Effects of hypertonic saline *versus* lactated Ringer's solution on cerebral oxygen transport during resuscitation from hemorrhagic shock. J Neurosurg 1986; 64:627–632.
24. Wilson BJ, Jones RF, Coleman ST, et al. The effects of various hypertonic sodium salt solutions on cisternal pressure. Surgery 1951; 30:361–366.
25. Todd MM, Tommasino C, Moore S. Cerebral effects of isovolemic hemodilution with a hypertonic saline solution. J Neurosurg 1985; 63:944–948.
26. Todd MM, Tommasino C, Moore S, et al. The effects of acute isovolemic hemodilution on the brain: a comparison of crystalloid and colloid solutions. Anesthesiology 1984; 61:A122.
27. Todd MM, Tommasino C, Moore S, et al. The effect of hypertonic saline on intracranial pressure, cerebral blood flow and brain water content. Anesthesiology 1984; 61:A123.
28. Albright AL, Phillips JW. Oncotic therapy of experimental cerebral oedema. Acta Neurochir 1982; 60:257–264.
29. Tommasino C, Todd MM, Shapiro HM. The effects of fluid resuscitation on brain water content. Anesthesiology 1982; 57:A109.
30. Atik M. Dextran 40 and Dextran 70, a review. Arch Surg 1966; 94: 664–672.
31. Fulton RL. Absorption of sodium and water by collagen during hemorrhagic shock. Ann Surg 1970; 172:861–869.
32. Velasco IT, Pontieri V, Rocha E, et al. Hyperosmotic NaCl and severe hemorrhagic shock. Am J Physiol 1980; 239:H664–H673.
33. Bo G, Hauge A. Hyperosmolarity and pulmonary vascular resistance. Acta Physiol Scand Suppl 1969; 330:147.