The osmolality of subdural hematoma fluid

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In 23 patients with subdural hematomas the osmolality of the hematoma fluid was compared with that of venous blood and in 11 of these cases with lumbar cerebrospinal fluid. There was no significant difference in the osmolalities of these fluids. The electrophoretic pattern of the subdural hematoma fluid resembles that of serum in that it usually does not contain prealbumins. The hemoglobin breakdown products migrate with the alpha 1I and beta globulins and include methemoglobin, oxyhemoglobin, and bilirubin. It is suggested that the late onset of symptoms, which often occurs, is due to either progressive bleeding from the neovascular outer membrane, effusion through it of albumin and fluid, or recurrent bleeding from a venous stump. It is also possible that very little expansion in the size of the subdural hematoma occurs following the initial formation and that late decompensation results from dynamic changes in the compressed brain. This work provides no evidence either to support or refute the concept of an osmotic mechanism for hematoma expansion.

KEY WORDS • osmolality • subdural hematoma • cerebrospinal fluid • serum • electrophoresis

In 1932, Gardner published a hypothesis that sought to explain the latent interval between injury and the development of symptoms in subdural hematomas. He stated that there was a gradual increase in the size of the hematoma following the initial formation due to the accession of tissue fluid, particularly spinal fluid. He hypothesized that this fluid was drawn into the hemorrhagic cyst through the semipermeable arachnoid membrane and adjacent cyst wall by the osmotic tension of the blood proteins contained in the cyst. Zollinger and Gross published a similar explanation of the late onset of pressure symptoms. They presented evidence that the wall of the subdural hematoma acts as a semipermeable membrane, that blood within it breaks down slowly over a period of months, that disintegration of the blood produces a great rise in effective osmotic pressure, and that blood within the hematoma is progressively diluted. They felt that it is more likely that fluid drawn into the hematoma comes from the plasma of circulating blood rather than the cerebrospinal fluid.

On the basis of their study of the protein content of hematoma fluid, Munro and Merritt believed that blood within the hematoma dissolves and that fluid diffuses across the pia arachnoid, which acts as a dialyzing membrane. The dissolution of blood was thought to cause a high protein content of the solution, and the diffusion of fluid to cause an increase in its volume. In the classic clinical study of subdural hematoma in infancy by Ingraham and Matson, it was accepted as well established fact that the quantity of fluid within the hematoma sac could increase without further bleeding because the encapsulated high protein fluid acts by osmosis to draw in fluid from the outside
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through the wall of the sac. The views above have come to be generally accepted and are adopted by Zülch in a recent scholarly review of the neuropathology of intracranial hemorrhage.

These hypotheses, however, are based mainly upon deductions, and relatively little evidence supports the existence of an osmotic mechanism of hematoma expansion. Since it is now possible to measure osmolality directly, it was decided to test the concept by carrying out simultaneous measurements of osmolality from hematoma fluid, venous blood, and cerebrospinal fluid.

Materials and Methods

Twenty-three patients with subdural hematomas were randomly selected from patients with this condition admitted to the University of Alberta Hospital and the Royal Alexandra Hospital during 1968 and 1969. The osmolality of hematoma fluid and of venous blood drawn at the same time as the hematoma fluid was determined. The hematoma specimens were obtained via burr holes. The dura was punctured with a sharp No. 18 needle and hematoma fluid aspirated. Irrigating fluid was not used. Although an intravenous drip was started routinely on all these patients, the amount of fluid administered was purposely limited prior to obtaining the specimens. Venous blood was drawn from the arm not being used for the intravenous drip. The total amount of intravenous drip usually did not exceed 50 cc and was isotonic saline and glucose/water solution. The spinal fluid samples were obtained within 20 to 30 min following the removal of the other specimens. This was done in 11 of the 23 patients by a lumbar puncture immediately following burr holes. Following removal of 5 to 6 cc of spinal fluid through a No. 22 needle, a volume of 20 to 30 cc of normal saline was injected into the subarachnoid space. Three patients in the series died. Two of them had acute subdural hematomas with massive brain injury, and the third also had massive brain destruction associated with the subdural hematoma from which he died several months following the operation; in none of these patients was the spinal fluid examined.

The specimens obtained were spun down in an ordinary centrifuge and supernatant fluid was examined for osmolality using the freezing point depression method with an Osmometer (Advanced Instruments Company). One milliosmol (mOsm) will cause a change of 0.001858°C in the freezing point. It is possible to measure concentrations very precisely since repeated measurements of the freezing point can be made within ± .001°C. The results of the osmolality determinations were correlated with the interval between trauma and operation. In three patients in whom there was no definite history of trauma and in whom no external evidence of trauma to the head was found, it was assumed for purposes of the calculations that the trauma had occurred more than 2 weeks prior to operation.

The electrophoretic pattern of the fluids was determined using clear cellulose acetate membranes in a Gelscan scanner. To determine the hemoglobin breakdown products, starched gel and spectrophotometric scans using a DK2 Beckman instrument were carried out.

Twelve patients admitted to hospital with a provisional diagnosis of protruded intervertebral disc, who had myelograms performed, comprised the control group. Osmolality measurements and electrophoretic patterns were determined in specimens of spinal fluid and simultaneously drawn venous blood.

Results

The mean osmolalities in mOsm/kg of subdural hematoma fluid, venous blood, and lumbar cerebrospinal fluid are listed in Table 1. The comparable value for the control group is also shown. There was no signif-

<table>
<thead>
<tr>
<th>Fluid</th>
<th>Mean (mOsm)</th>
<th>Mean Deviation (mOsm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>venous blood</td>
<td>287</td>
<td>8</td>
</tr>
<tr>
<td>hematoma fluid</td>
<td>285</td>
<td>7</td>
</tr>
<tr>
<td>CSF</td>
<td>287</td>
<td>5</td>
</tr>
<tr>
<td>venous blood (control)</td>
<td>295</td>
<td>5</td>
</tr>
<tr>
<td>CSF (control)</td>
<td>293</td>
<td>7</td>
</tr>
</tbody>
</table>

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TABLE 2
Analysis of fluid osmolalities in hematomas under 2 wks old and over 2 wks old

<table>
<thead>
<tr>
<th>Fluid</th>
<th>No. of Patients</th>
<th>Mean (mOsm)</th>
<th>Mean Deviation (mOsm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>venous blood under 2 wks old</td>
<td>10</td>
<td>288</td>
<td>7</td>
</tr>
<tr>
<td>venous blood over 2 wks old</td>
<td>13</td>
<td>285</td>
<td>9</td>
</tr>
<tr>
<td>hematoma fluid under 2 wks old</td>
<td>10</td>
<td>286</td>
<td>5</td>
</tr>
<tr>
<td>hematoma fluid over 2 wks old</td>
<td>13</td>
<td>284</td>
<td>9</td>
</tr>
<tr>
<td>CSF under 2 wks old</td>
<td>4</td>
<td>290</td>
<td>4</td>
</tr>
<tr>
<td>CSF over 2 wks old</td>
<td>7</td>
<td>285</td>
<td>7</td>
</tr>
</tbody>
</table>

Significant difference in the osmolalities, and it is obvious that the hematoma fluid is not hyperosmolar with reference to either the spinal fluid or venous blood.

Since it was possible that the earlier hematomas might be hyperosmolar with a change occurring in the hematoma fluid with the passage of time toward isosmolality, the samples were divided into those coming from hematomas under 2 weeks old and those over 2 weeks. The results of this analysis are shown in Table 2; there was no significant change in osmolality with increasing age of the hematoma.

The grand mean of all classes of osmolalities was 288 ± 13mOsm. When the means of the samples above were tested on an x² distribution, it was found that all means were distributed normally (p > 0.99). It was noted that all four "red" subdural hematomas were less than 1 week old. All the "brown" hematomas were older than this.

A composite diagram of the electrophoretic patterns of the various fluids is illustrated in Fig. 1. The various patterns were arbitrarily aligned according to the albumin peak. It can be seen in the pattern for the hematoma fluids that hemoglobin breakdown products migrated with the alpha II and beta globulins. Only one spinal fluid specimen contained hemoglobin breakdown products. This was a very atypical case in that the subdural hematoma was actually straw-colored, and the spinal fluid obtained by lumbar puncture was dark brown. This patient had been comatose preoperatively, and bilateral angiography had shown a unilateral subdural collection; he made an uneventful recovery.

Eight of the 11 spinal fluid specimens showed a prealbumin peak which was just to the left of the albumin peak in Fig. 1. Only one of the hematoma fluid specimens contained prealbumin. Further analysis of the hemoglobin breakdown products showed...
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them to include bilirubin, methemoglobin, and oxyhemoglobin. The mean total protein in the hematoma fluid was 6.7 gm/100 ml, in the venous blood 6.7 gm/100 ml, and in the spinal fluid 77 mg/100 ml. In the control group the mean total protein was 7.5 gm/100 ml in the venous blood and 56 mg/100 ml in the spinal fluid. The mean percent gamma globulin in the hematoma group spinal fluid was 11.2%.

Six patients had 99-technetium per-technetate brain scans carried out. Four of these were positive, with the youngest hematoma being 3 weeks. Two negative scans were found in patients with well-documented histories of head trauma 3 weeks prior to the scan. There were abnormalities in the plain skull films in only two cases that showed fracture lines. Angiography was diagnostic in all cases in which it was performed (21 of the 23 cases). The mean shift of the anterior cerebral artery was 1.5 cm. The mean shift of the anterior cerebral artery in five patients who had postoperative angiograms on an average of 10 days following initial drainage of the hematoma was 0.9 cm. The mean maximum thickness of the subdural was 1.9 cm.

All the patients were adults. The mean age of the patients was 48 years, with a range of 17 to 82 years. The mean age of the control group was 41 years, with a range of 21 to 72 years.

Discussion

It is generally assumed at present that uniformity of osmotic pressure prevails throughout the content of the various fluid spaces within the body. While precise equality of the osmotic pressures of intra- and extracellular fluids have not been proved directly, the bulk of evidence tends to indicate that osmotic equilibrium, while probably never attained, is always approached. A clinical study of a series of true body fluids, including cerebrospinal fluid, concluded that osmolality was identical to that of the corresponding serum within the limits of experimental error. It was felt that there was a "law" of constant osmotic pressure of all "true body fluids" (as distinct from "secretions") and that this was true whether the subject was biochemically normal or not. While the concept of instantaneous adjustment of osmotic equilibrium between body compartments by the movement of water is attractive in its simplicity, it probably should not be applied in all instances without an attempt at direct measurement. Since this study has shown virtually identical values for hematoma fluid and serum, it can be assumed that the hematoma fluid falls within the class of "true body fluids" rather than "secretions" which would result from the performance of osmotic work and the utilization of metabolic energy.

Hendry measured simultaneous spinal fluid and serum osmolalities in six cases and showed the mean of both to be approximately 289, with specimens from individual patients not differing by more than 2 mOsm. He concluded that the differences reported in the earlier study by Blegen on the total osmotic pressures of simultaneously collected specimens of serum and cerebrospinal fluid were within the limits of experimental error. Davson stated that in rabbits the osmolality of cerebrospinal fluid is significantly greater than that of plasma (p < 0.001). He also showed a similar difference for cats and dogs. In observations on six patients, Stueck and Fisher showed that the osmolality of cerebrospinal fluid was equal to the osmolality of serum.

Rabe, et al., measured the osmolality of bilateral subdural effusions in an infant and found them to be equal at 270 mOsm. Simultaneous serum osmolality and spinal fluid osmolalities were not determined. Suzuki, et al., gave repeated intravenous infusions of 20% mannitol to eight patients with subdural hematomas and, using serial angiography, demonstrated progressive decrease in thickness of the hematoma. Wise and Mathis showed that the administration of a hyperosmolar substance causes the serum to become transiently hyperosmolar with respect to spinal fluid. They documented this with serial measurements. It may be that if mannitol does not cross the neovascular external subdural membrane some shift of fluid out of the hematoma can take place. The so-called "nonbleeding" treatment for chronic subdural hematomas seemed much more hazardous than the generally satisfactory simple burr hole.

Gitlin in a study of subdural collections in 18 infants measured albumin and gamma
globulin by immunochemical procedures. He found that the albumin gamma globulin ratios and albumin total protein ratios in the subdural fluid were considerably higher than those ratios in the corresponding serum samples. He felt that the basic mechanism of fluid accumulation was an effusion through irritated or damaged capillary walls. He noted that it would be difficult to explain the source of additional albumin in the subdural fluid on the basis of oncotic pressure alone. The relatively high protein content of the subdural fluids precluded the simple entrance of protein from the cerebrospinal fluid across the pia arachnoid.

In the study by Rabe, et al., I labeled human serum albumin was given intravenously, and albumin specific activity in subdural and subarachnoid fluid and in plasma was determined over many days. They showed that radioactive albumin in subdural and subarachnoid spaces is derived from plasma and that the plasma, subdural, and lumbar subarachnoid spaces are not in direct continuity with one another with respect to content of albumin and absolute radioactivity. These authors also pointed out that the destruction of red blood cells does not lead to the release of albumin, which is the protein molecule in greatest concentration and the largest osmotic activity in the subdural space. They also noted that the amount of total protein available from red blood cells in the subdural space would only be one-hundredth of the amount of albumin available from transcapillary turnover.

It has always been accepted a priori that subdural hematomas undergo progressive augmentation in size subsequent to their initial formation. There does not appear to be any direct angiographic evidence of such a phenomenon although it may well occur. Trotter first proposed the obvious explanation of progressive enlargement as being a slow, continuous, or perhaps intermittent bleeding from the responsible vessel. Gardner rejected this hypothesis because injured blood vessels anywhere else in the body do not behave in this fashion. Actually, these large fragile sinusoidal capillaries have been shown in various pathological studies and can be observed grossly to be delicate and subject to easy rupture with hemorrhage. Additional evidence against the continuous or intermittent bleeding hypothesis was given by Gardner as being the fact that vascular disease did not constitute an etiological factor and the hemorrhagic diathesis was not demonstrated. We now know that anticoagulants are frequently associated with subdural hematomas and that they also occur in patients with bleeding tendencies much more commonly than in the normal population. Putnam and Cushing suggested that the granulation tissue of the outer wall of the hematoma could be the seat of repeated hemorrhages from capillaries or "mesothelial-lined blood spaces." Gardner took exception to this on the basis that the gross contents of clinically progressive hematomas are usually found to be perfectly homogeneous. Again, wider pathological experience has shown that many chronic hematomas tend to have a laminated structure, probably indicating sequential hemorrhages. As Gardner himself pointed out in the discussion of his paper, normal-looking red blood cells were found in fluid carefully aspirated by needle in a hematoma that was at least 2½ months old. This was a routine finding in this study. The results of animal experiments have not been thought to support the osmotic theory.

It seems unlikely that there is any simple or indeed single mechanism for the development of subdural hematomas with late onset of symptoms. The initial bleeding sites are probably bridging veins. Rebleeding may occur from these venous stumps or from the fragile blood vessels of the external subdural membrane. There may be an effusion of albumin-rich fluid through these abnormal blood vessels into the subdural hematoma. It seems unlikely that the breakdown of red blood cells can account for the content of albumin that occurs in the subdural hematoma.

In their analysis of fluid from a subdural hematoma, Hill, et al., found no prealbumin. They felt that, except for the presence of an increased amount of alpha I globulin, the hematoma fluid resembled serum in composition. They did not find prealbumin in two cases of subdural hygroma. They felt that the protein in the fluid of subdural hematomas was probably derived locally from the serum and owed its composition to the interplay of physical-chemical factors including the size of the serum protein mole-
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cules and their gradient of concentration across a separating membrane.

It may be that the late onset of symptoms is due to a dynamic decompensation of cerebral tissue adjacent to the hematoma, possibly without any change in the size of the hematoma. The fact that most patients recover uneventfully with only burr hole drainage of the hematoma without removal of the external membrane argues that the late progressive rebleeding is probably not uniformly important. If the hyperosmolar theory with the progressive increase in size of subdural hematomas were correct, it would be necessary to postulate a reverse phenomenon in many cases that undergo spontaneous shrinkage during organization.

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