Brain specific gravity and CT scan density measurements after human head injury

ROSS BULLOCK, F.R.C.S.(Sn), ROGER SMITH, F.R.C.S., JEAN FAVIER, M.D., MICHAEL DU TREVOU, M.B., CH.B., AND GORDON BLAKE, M.D.

Departments of Neurosurgery and Physiology, University of Natal, Durban, South Africa

White matter specific gravity was measured using the microgravimetric method in 20 comatose patients with diffuse head injury who were undergoing intracranial pressure (ICP) monitoring, and in 19 patients with focal injuries who were undergoing evacuation of contusions or intracerebral hematomas. Computerized tomography (CT) density readings were obtained for each site of white matter sampling by locating the sampling site on the preoperative CT scan. A significant correlation was found between the specific gravity values and the CT density numbers \( r = 0.775; p < 0.001 \). Patients with focal injuries demonstrated reduced perifocal specific gravity, suggesting brain edema. The mean specific gravity in patients with diffuse injury was within the normal range. In 10 of 12 patients in whom the specific gravity was above the normal range, the CT density was also above the normal range. These data suggest that cerebral vascular engorgement is the cause of the high specific gravity. Six (60%) of this small subgroup of 10 patients also demonstrated a high ICP.

KEY WORDS - head injury - brain specific gravity - cerebral edema - computerized tomography density

The factors that determine the formation of brain edema following human head injury remain poorly understood since human head injury consists of an interplay between a number of different pathological mechanisms, such as diffuse axonal injury, brain ischemia, direct brain contusion, and brain engorgement. Although animal studies have provided a great deal of information regarding the pathophysiology of brain edema in diffuse head injury, ischemia, and tumors, the relevance of these data when applied to human head injury is questionable. No single animal model is likely to closely approximate human head injury because of the complexity of the pathophysiology in man.

Neuropathological studies have yielded relatively little information regarding edema after human head injury. Interpretation is difficult because of the effects of postmortem change and the shrinkage artifacts of fixation and staining techniques. Likewise, electron microscopy, which has yielded so much valuable data in animal studies, has not been used extensively following human head injury because brain tissue must be taken directly from the living patient and placed into fixative in order to avoid shrinkage artifacts.

Computerized tomography (CT) scanning has provided the most valuable information to date regarding the evolution of brain edema after head injury. Modern CT scanners are able to clearly define areas of low density in relation to focal brain injury such as contusions and hematomas, and more recently authors have sought to relate increases in CT density values to brain engorgement by correlating those values with cerebral blood volume and cerebral blood flow measurement. Relatively few studies, however, have directly correlated CT scan findings with objective measurements of brain edema, either by light or electron microscopy.

In this report we have analyzed the relationship between regional brain specific gravity, as measured by the microgravimetric technique, and CT scan density measurements made in the same region. The effect of increased intracranial pressure (ICP) and other clinical variables on the specific gravity of brain was also assessed.

Clinical Material and Methods

Summary of Cases

Thirty-nine patients who had sustained severe head injury were studied. In 19 patients, samples of white
Brain specific gravity and CT scan density

**TABLE 1**

<table>
<thead>
<tr>
<th>Head Injury</th>
<th>No. of Cases</th>
<th>Specific Gravity</th>
<th>CT Density</th>
<th>ICP (1st 24 hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>focal</td>
<td>19</td>
<td>1.0343 ± 0.0007</td>
<td>30.3</td>
<td>26.2 ± 3.1†</td>
</tr>
<tr>
<td>diffuse</td>
<td>20</td>
<td>1.0386 ± 0.0010</td>
<td>36.2</td>
<td>20.4 ± 3.7</td>
</tr>
<tr>
<td>significance</td>
<td></td>
<td></td>
<td>p &lt; 0.001</td>
<td>p &lt; 0.01</td>
</tr>
</tbody>
</table>

* Values are means ± standard error. CT = computerized tomography (Hounsfield units); ICP = intracranial pressure (mm Hg).
† Values derived from monitoring 13 patients.
‡ Calculated according to Student’s t-test. NS = not significant.

Microgravimetric Measurement of Brain Water

Density gradient columns were generated by the semiautomatic method described by Shigeno, *et al.*

The column was housed in a temperature-controlled room close to the operating theater, and white matter specimens were immersed in a solution of bromobenzene and kerosene immediately after being removed from the patient. The bromobenzene and kerosene solution was of similar specific gravity to the mean value for the density column. These procedures were used in order to counteract evaporative water loss in the specimen during transit, as advocated by Symon, *et al.*

Specific gravity readings were made 1 minute after immersion of the specimen in the density column. Standardization of the column was performed using six standards of known specific gravity, as described by Shigeno, *et al.* The column was standardized prior to every observation, and a new column was generated wherever the linearity of the column deviated significantly (r = 0.998 or less).

**Computerized Tomography Scan Density Data**

At the time of surgery the site of the white matter biopsy was annotated onto two-dimensional line diagrams by the surgeon. These data were then used to locate the biopsy site on the CT scans. A standard 12-cu mm region of interest was then marked on this site at the appropriate CT scan cut using the cursor facility of the GE 8800 scanner, and the mean value of three readings of CT density number was recorded. The CT scanner was calibrated weekly using phantoms of known CT scan density.

**Results**

In the five patients designated as “normal,” white matter specific gravity was found to be 1.038 ± 0.0006 (± standard deviation), which agreed with the normal value of 1.038 ± 0.00058 reported by Tagaki, *et al.*

**White Matter Specific Gravity and ICP**

The mean white matter specific gravity for patients with focal brain injury was 1.0343 ± 0.0007. This was significantly below the normal range (p < 0.001) (Table 1 and Fig. 1). The mean ICP for this group was 26 ± 3 mm Hg. In the patients with diffuse injuries, however, the mean white matter specific gravity, at 1.0386 ± 0.0010, was within the normal range, and the mean ICP was found to be 20 ± 4 mm Hg. No relationship was found between ICP and specific gravity, either for the entire group (correlation coefficient = 0.448) or when the data for patients with focal and diffuse injuries were analyzed separately (Fig. 1 left).

Twelve patients were found to have a white matter specific gravity value above the normal range. Ten of these underwent ICP monitoring, and in six the mean ICP was greater than 20 mm Hg. In only nine of the remaining 23 patients with normal or low white matter specific gravity who underwent ICP monitoring was the ICP raised (Table 2).
White Matter Specific Gravity and CT Scan Density

For the total group of 39 patients, the relationship between focal CT scan density and white matter specific gravity was striking (Fig. 1 right). A correlation coefficient of 0.775 was found ($p < 0.001$). The majority of patients with a low white matter specific gravity fell within the normal range for CT scan density. When the CT density values for the 12 patients with an abnormally high white matter specific gravity were considered, 10 of the 12 patients had CT white matter density values above the upper limit of normal. Eight of these 12 patients had sustained diffuse injuries, while only four had focal injuries. The mean CT density number for white matter in this group of 12 patients with high specific gravity was 37.0 as compared to a mean of 30.5 for the remaining 27 patients (Table 2).

Influence of Ischemic Episodes

In eight patients, ischemic episodes had been documented prior to admission to the neurosurgical service. Low white matter specific gravity values were obtained in six of these eight patients.

Discussion

Although CT scanning currently provides the most useful clinical indication of brain edema, conclusions based on CT scans must be founded upon pathological and microanatomical correlates for this interpretation to be valid. Nuclear magnetic resonance scanning is likely to revolutionize concepts of brain edema resulting from head injury, but, even with this mode of imaging, validation by some form of tissue analysis is necessary prior to interpretation.

The introduction of the microgravimetric technique for measurement of brain edema, which allows specific gravity estimations of small volumes of brain tissue, has stimulated research into brain edema. Although the technique suffers from certain methodological limitations, it has been well validated against the dry/wet weight method and has been found to be satisfactory.

Although the relationship between brain specific gravity and CT scan density has been evaluated by Takagi, et al., in patients with tumors and vascular lesions, this association has not hitherto been determined in head-injured patients. The study by Takagi, et al., showed that areas of low CT density frequently correlated with low white matter specific gravity. Our data now confirm this in head-injured patients. We have shown a correlation between CT density values and white matter specific gravity over a wide range, and have confirmed the findings of Galbraith, et al., that white matter specific gravity is decreased in patients with focal brain injuries. However, in contrast to the findings of Galbraith, et al., we have shown no reduction in the white matter specific gravity in patients with diffuse injury.
Brain specific gravity and CT scan density

In 12 of our patients, specific gravity values were increased above the normal range. This would suggest an increase in tissue solids or a reduction of tissue water. Although the elevated values may possibly be explained by a methodological error, such as loss of tissue water in transit, we think that this is unlikely because specimens were transported immersed in a mixture of bromobenzene and kerosene of a specific gravity similar to that of the density column. Another explanation might be the inclusion of gray matter fragments, although this is unlikely in view of the techniques used.

Shigeno, et al., have shown that cerebral blood volume exerts an important influence upon brain specific gravity and that an increased cerebral blood volume increases tissue solids, giving a higher specific gravity value. These authors reported that changes in cerebral blood volume may account for specific gravity variations of up to 0.001 in white matter of cats. We support the view of Shigeno, et al., that cerebral blood volume change constitutes an important variable which must be considered when basing conclusions upon the microgravimetric determination of specific gravity. It is proposed, therefore, that brain water content should not be calculated from specific gravity values for this reason.

Of our 12 patients with increased white matter specific gravity, eight had sustained diffuse brain injury. The propensity for diffuse brain injury to produce cerebral engorgement has been well described. The mean age of our patients with increased white matter specific gravity was 27 years, as compared to 33 years in patients whose white matter specific gravity was within or below the normal range. Bruce, et al., have attributed increased CT scan density values to an increased cerebral blood volume after head injury. The relationship between white matter specific gravity and CT density values demonstrated in our patients (Fig. 1 right) supports the contention that the 12 patients with high white matter specific gravity in our series displayed brain engorgement or hyperemia. Obrist, et al., have recently reported acute hyperemia in 55% of 75 patients undergoing xenon-133 cerebral blood flow measurement after head injury. Hyperemia thus appears to be a frequent finding in the acute phase after diffuse head injury.

We were unable to demonstrate any correlation between ICP and white matter specific gravity for the group as a whole (Fig. 1 right), or when the two groups with focal and diffuse injuries were considered separately (Table 1). However, since six of the 10 patients with a high white matter specific gravity who underwent ICP monitoring had mean pressures above 20 mm Hg and only nine of the remaining 23 patients who underwent ICP monitoring had pressures greater than 20 mm Hg on the 1st postoperative day (Table 2), our data support the contention of Obrist, et al., that high ICP is frequently associated with brain engorgement.

The lowest readings for white matter specific gravity were found in patients who had undergone prior ischemic insults. The tendency for cerebral ischemia to produce increased brain edema has been well demonstrated in animal studies.

The microgravimetric method of measurement of brain specific gravity may improve our understanding of the dynamics of edema following human head injury. Density readings from more modern CT scanners may provide a readily available indication of the pathophysiological process occurring after head injury, but evaluation of these data must be corroborated by such modalities as cerebral blood flow measurement, cerebral blood volume estimation, and measurement of brain water or specific gravity.

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References


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Address reprint requests to: Ross Bullock, F.R.C.S.(Sn), Department of Neurosurgery, University of Natal, Durban, South Africa.