Cerebrospinal fluid lactate and lactate/pyruvate ratios in hydrocephalus

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Cerebral metabolism in 21 hydrocephalic patients was studied. Preoperative and postoperative specimens of cerebrospinal fluid (CSF) were obtained and the cerebral perfusion pressure (CPP) was calculated in each instance. The specimens of CSF were analyzed for lactate and pyruvate and the lactate/pyruvate (L/P) ratio was calculated for each sample. The L/P ratio, which reflects the redox state of the cell, was used to determine the extent of anaerobic metabolism. An inverse relationship was noted between CPP and lactate as well as the L/P ratio. In general, the level of anaerobic metabolism was decreased after insertion of a shunt.

KEY WORDS: hydrocephalus, shunt, anaerobic metabolism, lactate/pyruvate ratio, cerebral perfusion pressure

The status of cerebral metabolism in hydrocephalus has not been thoroughly investigated. Previous experiments have demonstrated that a moderate increase in intracranial pressure (ICP) may significantly reduce cerebral blood flow due to a decrease in the cerebral perfusion pressure (CPP). In the presence of a decreased CPP there is a shift from aerobic to anaerobic metabolism. The anaerobic metabolism results in a rise in the lactate and lactate/pyruvate (L/P) ratio in brain tissue and the cerebrospinal fluid (CSF). Granholm and Siesjö noted that the lactate and the L/P ratio were elevated in the CSF of hydrocephalic patients, but the effects of CPP and the results of shunting on cerebral metabolism were not considered in their report.

In this study the extent of anaerobic metabolism in hydrocephalic patients was determined by measuring the lactate and the L/P ratio in CSF before and after shunting procedures. The postshunt metabolic values were used as controls and compared with preshunt values. A correlation of metabolic parameters, that is, lactate and the L/P ratio, was made with the CPP of individual patients.

Clinical Materials and Methods

A total of 21 patients with communicating and noncommunicating hydrocephalus were studied. Patients with disease processes such as posterior fossa tumors or active meningitis were excluded. Ventricular fluid was obtained either at the time of ventriculogram or intraoperatively prior to the placement of a ventriculoatrial shunt. Approximately 1 week after the operative procedure, additional...
specimens were obtained by tapping the shunt reservoir. Care was taken to obtain enough fluid to ensure a fresh ventricular sample by discarding the first 0.5 to 1.0 cc.

The CSF was immediately placed in 6% perchloric acid, mixed thoroughly, and stored in ice. If a precipitate formed the specimen was centrifuged. The supernatant was decanted and frozen for later analysis. Duplicate aliquots of these specimens were then analyzed by enzymatic technique for lactate and pyruvate. The L/P ratio was calculated from these values. Some specimens of CSF were obtained under anaerobic conditions for determination of pH and pCO₂. Mean ventricular pressure and mean systemic arterial pressure were recorded when the CSF sample was obtained, and the CPP was calculated.

### Results

Data were collected from 21 patients before shunting and from 11 of these patients after shunting. The values for these individual patients are recorded in Table 1. Postoperative values were not obtained on 10 patients either because of difficulty with fluid aspiration from the shunt or because the CSF was bloody or xanthochromic. The problem encountered when aspirating postoperative samples was most likely due to collapse of the ventricle around the ventricular catheter. Postoperative blood-tinged or xanthochromic samples were discarded since they would falsely elevate lactate values. The pH and pCO₂ values obtained on the specimens collected under anaerobic conditions were within normal ranges, 7.32 to 7.45 pH and 28 to 40 mm Hg respectively. No complications occurred because of the CSF aspirations.

The results suggest an inverse relationship between the CPP and the L/P ratio, as well as between CPP and the lactate. When the lactate and the L/P ratios were correlated with the CPP values as shown in Table 2, three categories of CPP were used: low (45–59 mm Hg); marginal (60–69 mm Hg); and normal (70 mm Hg and higher). The lactate values and the L/P ratios were averaged for each of these ranges. Low CPP was associated with a high lactate and L/P ratio, and conversely, a
CSF lactate/pyruvate ratios in hydrocephalus

**TABLE 2**

<table>
<thead>
<tr>
<th>Cerebral Perfusion Pressure</th>
<th>No. of Cases</th>
<th>Average Lactate (mM/l)</th>
<th>Average L/P</th>
</tr>
</thead>
<tbody>
<tr>
<td>low (45 - 59 mm Hg)</td>
<td>10</td>
<td>2.5</td>
<td>19.2</td>
</tr>
<tr>
<td>marginal (60 - 69 mm Hg)</td>
<td>6</td>
<td>2.2</td>
<td>15.6</td>
</tr>
<tr>
<td>normal (70 - 100 mm Hg)</td>
<td>5</td>
<td>2.1</td>
<td>11.8</td>
</tr>
</tbody>
</table>

**TABLE 3**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Preoperative Data</th>
<th>Postoperative Data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CPP (mm Hg)</td>
<td>Lactate (mM/l)</td>
</tr>
<tr>
<td>2</td>
<td>56.2</td>
<td>2.3</td>
</tr>
<tr>
<td>4</td>
<td>56.2</td>
<td>2.3</td>
</tr>
<tr>
<td>5</td>
<td>56.8</td>
<td>1.7</td>
</tr>
<tr>
<td>6</td>
<td>57.5</td>
<td>3.7</td>
</tr>
<tr>
<td>13</td>
<td>54.0</td>
<td>2.3</td>
</tr>
</tbody>
</table>

low lactate and L/P ratio was noted with a normal CPP (Table 2).

In general, a decrease in the CSF lactate and the L/P ratio occurred following insertion of a shunt. For Table 3, the data are taken from the five patients with low CPP (less than 60 mm Hg) who had both preoperative and postoperative specimens sampled. All of these patients showed a reduction in both lactate and the L/P ratio following a shunting procedure.

**Discussion**

The exact etiology of “brain damage” in hydrocephalus is not known. Most likely it is a combination of mechanical distortion that results from ventricular dilatation and metabolic changes induced by increased pressure. Marked ventricular dilatation in congenital hydrocephalus is, in many instances, associated with permanent brain dysfunction. However, there has not been a good correlation between the thickness of the cortical mantle and the neurological state of the patient. Elevated ICP may also result in brain damage independent of mechanical distortion.

When the ICP rises significantly, the CPP is decreased and ischemia occurs. If the ischemia is marked, there is a decrease in high-energy phosphorylated compounds such as phosphocreatine and ATP. A marked decrease in these compounds is ultimately associated with permanent brain damage. The early effect of a reduced CPP is a mild ischemia resulting in a shift toward anaerobic metabolism. This shift may be detected by the elevation of the CSF lactate and the L/P ratio. The L/P ratio conveniently reflects the oxidation-reduction state (NADH/NAD+) of the tissue, provided the pH is within relatively normal limits. The NADH/NAD+ ratio within the cytoplasm of the cell is in near equilibrium with the L/P ratio of brain tissue. Lactate and pyruvate differ quantitatively across the cell membrane but their ratio remains similar. The intracellular lactate and pyruvate are therefore reflected in the CSF values.

Zwetnow and Siesjö, in a series of animal experiments, showed the close relationship of cerebral metabolism with CPP. More specifically, they demonstrated that it was necessary to reduce the CPP to approximately 30 mm Hg before a decrease in tissue high-energy compounds such as phosphocreatine and ATP occurred. However, with a small reduction in CPP there was a rise in the lactate and L/P ratio in brain. Their results indicate that elevated lactate values and L/P ratios in brain tissue are earlier and more sensitive indicators of tissue hypoxia than are changes in tissue high-energy phosphorylated compounds.

We have attempted to correlate the CPP with the metabolic state of brain tissue in a clinical situation. The CPP was determined and the CSF analyzed for lactate and pyruvate in hydrocephalic patients with elevations in their ICP. Correlation between metabolic parameters representing anaerobic metabolism (lactate and L/P ratio) and the CPP was made before and after the placement of a ventricular shunt (Table 1). A graphic illustration of the preoperative data is shown in Fig. 1, which plots the L/P ratio against the CPP. The line that best fits these values was determined by standard linear regression techniques. Previously reported animal experiments demonstrated a similar
The relationship between a CPP of 40 and 110 mm Hg.\textsuperscript{13} The patients were placed into three categories based on the ranges of CPP as demonstrated in Table 2. When the CPP was low, the lactate and L/P ratios were elevated. When the CPP was marginal, these metabolic parameters were somewhat lower. This pressure range (60 to 69 mm Hg) probably included cases in which the CPP was adequate to maintain oxidative metabolism, and some in which the CPP was inadequate and resulted in a shift toward anaerobic metabolism. In the final category, the CPP was normal and the lactate and L/P ratios were their lowest. Statistical analysis that used the Pearson correlation coefficient demonstrated a significant inverse relationship between CPP and the L/P ratio ($r = -0.66, p < 0.005$). With the same test there was a trend toward a similar relationship between CPP and the lactate values, but this was not statistically significant ($r = -0.17, p > 0.10$). The data demonstrate the dependence of cellular oxidative metabolism upon the maintenance of an adequate CPP in patients with increased ICP.

The level of anaerobic metabolism was decreased after the placement of a ventricular shunt as shown by a decrease in L/P ratio in 64% of the patients (Table 1). This resumption of aerobic metabolism coincided well with the reduction of ICP and the restoration of a higher CPP. The data from five patients with low preoperative CPP values are given in Table 3. In these five patients we were able to obtain postoperative specimens of CSF for comparison with preoperative values. In each of these patients there was a reduction in the lactate and the L/P ratio following the placement of a shunt with restoration of a higher CPP. When the paired t test was used this reduction was significant at the 0.001 level for both lactate and the L/P ratio. These results indicate that shunting hydrocephalic patients with significantly decreased CPP restores and maintains cellular oxidative metabolism.

The status of cellular metabolism in brain tissue, as reflected by the lactate and the L/P ratio in CSF, might be used to aid in the diagnosis of clinical problems. Measurements of these metabolic parameters may be useful in the evaluation of various CSF shunting devices and may possibly aid in the detection of intermittently malfunctioning valves. In addition, the CSF lactate and L/P ratio could be of assistance in the evaluation of patients who have arrested hydrocephalus. Caution should be used in correlating metabolic changes with neurological deficits until more information is available. The presence of anaerobic metabolism, however, is indicative of cellular hypoxia and, if it is longstanding or severe, may ultimately result in cellular damage.

Acknowledgment

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References

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