CSF Lactate and CT Findings in Middle Cerebral Artery Infarction. A Comparative Study

O. Busse, M.D., and O. Hoffmann, Ph.D.

SUMMARY  The extent of edema related to infarction assessed by computed tomography was compared with the CSF-lactate concentration in patients with middle cerebral artery (MCA) infarction on the first, third and seventh day following the stroke. A linear correlation between the extent of infarction edema and CSF-lactate level was most distinct on the third day. CSF-lactate concentration on the third day can be considered as a measure of the extent of the accompanying edema which in our study reached its maximum at this time in comparison to the first and seventh day.

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AN INCREASE OF CSF LACTATE concentration which reflects an enhanced anaerobic glycolysis within ischemic brain tissue is a common finding.1-3 Our own measurements of lactate levels in the CSF during the acute phase of illness on the first, third and seventh day showed that the CSF lactate concentration correlates with the severity of the infarction regardless of the site of infarction.4 This relationship was particularly marked on the third day and was more distinct in superficial infarctions (fig. 1). The highest lactate levels with the most unfavorable prognosis were found in severe infarctions on the 3rd day of disease,4 when the maximum extent of the infarction edema is expected5,6 suggesting a relationship between the CSF lactate concentration and the development of infarction edema. Edema may cause a considerable increase in lactate in the cerebral tissue and the cerebrospinal fluid through increase of local tissue pressure resulting in a decrease of regional cerebral blood flow and enhanced anaerobic glycolysis.7,8

Cerebral edema is defined as an absolute increase of the brain tissue water content with a varying degree of space-occupying effect. In ischemic infarction the hypodense area visible in the CT scan in the first week after the onset is caused predominantly by the enhancement of intra- and extra-cellular fluid and to a minor extent through ischemic necrosis which cannot be differentiated precisely in CT.9,10 However, in the second week of the infarction the decreased attenuation of density is caused increasingly by ischemic necrosis. In our study it appears to be reasonable to designate the hypodense zone observed in the first week as ischemic and infarction edema respectively.

Thus, CT provides the opportunity to relate the development of the ischemic edema to biochemical changes in the CSF caused by metabolic dysfunction of the brain cells. The aim of the present study was to investigate the relationship between the CSF lactate level and infarction edema.

Patients and Methods

One hundred and thirteen patients were studied with an insult in the territory of the middle cerebral artery (MCA) who were admitted within 24 hours of the onset of the symptoms. Transient ischemic attacks were excluded. The mean age was 64 years (range 28–85). Based on the severity of the neurological deficit the patients were divided into three groups according to the rating scale of Patten et al.11 Twenty-nine were classified as mild, 29 as moderate and 55 as severe infarctions. The lactate concentration of the lumbar CSF was measured in all patients within 24 hours after the onset of infarction, on the third day in 109 and on the seventh day in 88 patients. The different number of examinations on the 1st, 3rd and 7th day was caused by the fact that some patients died and in a few patients no consent for another lumbar tap was obtained. Patients with an artificially blood-stained CSF were excluded from the study. On the same day, as soon as possible after the lumbar puncture CT was performed. This was practicable in 77 patients on the 1st day, in 85 on the 3rd day and in 76 on the 7th day of illness.

Measurements of CSF lactate concentration were first performed using the Biochemica-Test-Kombination of Boehringer, Mannheim. Later we used a more simplified electrochemical enzymatic method (Laktat­ analyzer 460 La Roche). The results of both methods do not differ according to Berger1 and our own examinations.12 In a control group of 77 patients the normal values of CSF lactate were 1.52 ± 0.48 mmol/l (mean ± two standard deviations). For statistical analysis lactate levels were divided into four classes (normal values = N, N-2.9, 3.0–3.9, ≥ 4.0 mmol/l). Non-enhanced CT scans, obtained with Siemens CT scanner (Siretom 2000, 256 × 256 — matrix) were evaluated. According to the extent of the ischemic edema changes in the CT scans were divided into four grades:

- grade 0: no edema
- grade I: involving one fourth or less of the hemisphere
- grade II: involving more than one fourth or less than one half of the hemisphere
- grade III: involving more than one half of the hemisphere

The volume of the hypodense zone was calculated on the basis of the planimetric measuring technique by means of a Siemens evaluscope13,14 in 28 cases examined on the first day and in 38 cases examined on the third day.

Results

The number of pathological CT findings increased with the severity of the infarction as measured by the scores of the rating scale. Mild infarctions most fre-
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Figure 1. CSF lactate in relation to the severeness of the infarction measured by a rating scale on the third day of disease. Only superficial infarctions (n = 90).

Figure 2. CSF lactate in relation to the extent of the infarction edema (grade 0–III) on the first, third and seventh day.

Discussion

A comparative study in the acute stage of MCA infarction revealed the interdependence between the extent of the hypodense zone and the CSF lactate level. The assumption that the hypodense area in the CT scan corresponds to the ischemic edema alone is not quite correct. On the first day of the disease the correlation between CSF lactate and the extent of the lesion in CT was significantly weaker than on the third day. In that by the seventh day, 40% of the patients with severe infarctions had died, the correlation at this time was somewhat less distinct. These results were confirmed by the volume determinations. On the first day a relationship between the volume of ischemic edema and CSF lactate concentration was only slight, while on the third day these two variables correlated to a high degree (p < 0.01). Our previous and present results agree with the findings of Terent et al., who reported a small group of patients, in whom on the second and third day

spurious correlation the first day had to be subdivided into the time periods of 0–8 and 9–24 hours after the onset of infarction because of the different rate of development of edema and CSF lactate rise. Chi-square test was used to examine the independence of the two variables. Since the expected cell frequencies have to be at least near 1 combining of rows and columns was necessary. For the first day the result was insignificant for the time 0–8 hours, but significant at the 0.05 level for 9–24 hours.

For the third and the seventh day the results obtained were significant at the 0.01 level. Hence there is clear statistical evidence that the CSF lactate concentration and extent of the infarction edema, as evaluated in the CT scan, are not independent. Additional calculation of the corrected coefficients of contingency showed a more distinct correlation between these two variables on the 3rd day than on the 1st or 7th day (table 2). More detailed information about the nature of this relationship could be obtained in those cases where the volume of the edema was calculated from the CT cuts. Figure 3 demonstrates a correlation between the CSF lactate level and the volume of the infarction edema on the 3rd day (linear regression, r = 0.65, p < 0.01). The same analysis for the data of the 1st day provides a significantly lower correlation coefficient of r = 0.34 (p < 0.05), although a linear relation was indicated already at this time.

Two way classification of the data according to CSF lactate levels and CT grades yields contingency tables for the first, third and seventh day. In order to avoid
the maximum extent of the edema corresponded with the maximum average of CSF lactate concentration. In accordance with the different rates of development of the infarction edema and the CSF lactate concentration the relationship between both the variables on the first day was less distinct. The increase of the CSF lactate concentration precedes the formation of the edema in terms of its detection by CT scan. Several patients who were admitted within a few hours of the stroke, had considerable increase of CSF lactate prior to the development of a noticeably hypodense zone in the CT scan. We think, therefore, that during the initial phase the circumscribed increase of cerebral lactate transmitted to CSF is not a consequence of the edema, but rather the result of local ischemia of the brain. According to the results of Hossmann et al and Bandaranayake et al the increase of osmolality in the ischemic tissue as a consequence of increasing lactate causes an enhanced inflow of water from the vascular network, favouring development of edema. The high correlation between the CSF lactate level and the recognizable infarction edema on the third and seventh day supports the presumption that CSF lactate concentration is a measure of the ischemic lesion of the brain, expressed by the slowly developing infarction edema. The results, however, do not substantiate the supposition that the formation of the edema in the first few days always has an additional effect on the lactate level. Characteristic for mild and moderate infarcts was the development of edema, demonstrable in the CT, limited to grade I or II with no increase of lactate concentrations (table 1). Severe infarctions, however, showed a tendency to increased concentration of CSF lactate up to the third day. In these patients the time of maximal extension of the edema corresponded to the maximum CSF lactate concentration. Therefore, CSF lactate concentration on the third day can be considered to be the measure of the extent of the infarction edema. Unfortunately cerebral blood flow was not measured. We suppose like Bartko et al and Hadjidimos et al that the development of extensive edema is followed by progressive focal reduction of CBF due to microcirculatory compression. The decrease of CBF coincides with an enhanced anaerobic glycolysis and accumulation of lactate, first in the area of edema, shortly thereafter also in the CSF. Hossmann has shown in animal experimental studies that in peritumoural edematous tissue CBF and autoregulation remain stable. He postulates that the edematous tissue can become hypoxic if an increase of intercapillary distance impedes the oxygen exchange between the blood vessels and viable parenchyma. On the other hand it is possible that the increase of CSF lactate due to anaerobic glycolysis reflects an extension of infarcted tissue which cannot be differentiated from edema fluid by CT scanning. Without doubt, factors other than decreased CBF following infarction edema must be taken into account to explain the rise of lactate in severe infarction. Hyperventilation alkalosis which is not rarely seen in severe infarctions gives rise to a decrease of CBF and an increase of lactate due to the vasoconstriction. A general lowering of CBF due to an increase of intracranial pressure following extensive edema also may have to be considered. The so-called diachisis, namely the CBF and metabolism reduction in the contralateral hemisphere with increase of anaerobic glycolysis must be considered. The role of the blood-brain barrier (BBB) is not clear. Under normal conditions the

### Table 1: Mean Values ± sd of CSF Lactate in Relation to the Extent of the Infarction Edema

<table>
<thead>
<tr>
<th>CT-grade</th>
<th>1st day</th>
<th>3rd day</th>
<th>7th day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CSF-lactate (mmol/l)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1.9 ± 0.6 n=37</td>
<td>1.7 ± 0.3 n=21</td>
<td>1.6 ± 0.4 n=19</td>
</tr>
<tr>
<td>I</td>
<td>2.0 ± 0.6 n=21</td>
<td>2.1 ± 0.7 n=30</td>
<td>1.9 ± 0.5 n=30</td>
</tr>
<tr>
<td>II</td>
<td>2.3 ± 0.5 n=9</td>
<td>2.5 ± 0.9 n=14</td>
<td>2.3 ± 0.7 n=16</td>
</tr>
<tr>
<td>III</td>
<td>3.7 ± 1.5 n=7</td>
<td>4.5 ± 1.4 n=19</td>
<td>3.7 ± 1.3 n=6</td>
</tr>
</tbody>
</table>

### Table 2: Relation Between Extent of Edema and CSF Lactate Level. Results of Chi-square Test

<table>
<thead>
<tr>
<th>Dimension of table</th>
<th>Result of Chi-square test</th>
<th>Coeff. of contingency (corr.)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–8 hrs</td>
<td>20 3 × 2</td>
<td>0.61</td>
<td>0.24</td>
</tr>
<tr>
<td>9–24 hrs</td>
<td>54 3 × 3</td>
<td>10.68</td>
<td>0.50</td>
</tr>
<tr>
<td>3rd day</td>
<td>84 4 × 4</td>
<td>65.29</td>
<td>0.76</td>
</tr>
<tr>
<td>7th day</td>
<td>71 3 × 4</td>
<td>20.44</td>
<td>0.57</td>
</tr>
</tbody>
</table>

*Figure 3.* CSF lactate in relation to the volume of the hypodense area on the third day of disease (n = 38, r = 0.65, p < 0.01).
BBB guarantees that the lactate level can vary independently in blood and CSF. One can imagine that a lactatemia, as observed in some of our patients, might influence the CSF lactate level, when the BBB is damaged in the region of infarction.

For clinical purposes the extent of the infarction edema is of importance because the prognosis can be partly determined from combined CT and CSF lactate data. Severe infarctions with a CT finding of grade III or a CSF lactate concentration of more than 4-mol/l were always fatal (fig. 2). Both findings were most frequent on the third day of disease, the time of maximal extension of the edema, thereby providing an important prognostic indicator.

Measured on the third day of the stroke the critical limit for the volume of the edema was 100 ml; however, the number of volume determinations was too small for significant conclusions. Recently Takagi et al. have pointed out the interdependence of the prognosis and the extent of infarction calculated by the measurement of volumes. Their studies, however, were performed three weeks and later after the stroke in order to exclude the simultaneous presence of edema and an ischemic necrosis.

References

5. Shaw C, Alvord EC, Berry RG: Swelling of the brain following ischemic infarction with arterial occlusion. Arch Neurol 1: 161-177, 1959
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