Cerebrospinal Fluid Lactate Dehydrogenase Levels in Early Stroke and Transient Ischemic Attacks

Yair Lampl, MD, Yvonne Paniri, MSc, Yechiel Eshel, MD, MSc, and Ida Sarova-Pinhas, MD

We examined the concentrations of lactate dehydrogenase in the cerebrospinal fluid of 25 patients with strokes and 15 patients with transient ischemic attacks ≤8 hours after the onset of the vascular event and in a control group of 21 patients. We found significantly higher concentrations in the stroke patients (40.9 ± 14.5 units/l) than in the transient ischemic attack patients (11.8 ± 2.9 units/l, p < 0.001) and the controls (11.2 ± 6.7 units/l, p < 0.001). Among the stroke patients, we found a significantly higher lactate dehydrogenase concentration in those with cortical strokes (n = 12, 50 ± 123 units/l) than in those with lacunar white matter infarcts (n = 5, 26.4 ± 6.5 units/l; p < 0.001) and those with basal ganglia infarcts (n = 8, 36.37 ± 11.7 units/l; p < 0.05). Our study offers a supplementary examination for diagnosing cortical or subcortical infarction during the early stage of the event, with the possibility of distinguishing precisely stroke from transient ischemic attack during the first hours after onset of the event. (Stroke 1990;21:854–857)

Estimation of the recovery potential and neurologic outcome during the initial stages of ischemic cerebrovascular events is of therapeutic and prognostic importance. The limited value of computed tomography (CT) as a diagnostic procedure during the first hours after stroke onset justifies searching for an additional sensitive prognostic marker.

Previous studies have documented elevated concentrations of enzymes in the cerebrospinal fluid (CSF) of persons with stroke, and significantly elevated concentrations of lactate dehydrogenase (LDH), glutamic-oxaloacetic transaminase, and creatine kinase have been found in patients with cortical infarcts. An increase in the concentration of LDH without elevation of the concentrations of other enzymes in the CSF has been documented even in patients with lacunar infarcts and transient minor dysfunctions. However, these findings were demonstrated during a later stage of the event, at the peak of LDH levels (48–96 hours after infarction). The sensitivity of LDH as a marker in patients with mild and moderate strokes reflects the fact that this enzyme has a higher concentration in brain tissue than glutamic-oxaloacetic transaminase and is more thermostable than creatine kinase.

We investigated the concentrations of LDH in the CSF of patients during the initial stages of stroke and transient ischemic attack (TIA), and we correlated the concentrations with proximity of the infarcts to the subarachnoid space and with their volumes.

Subjects and Methods

We examined 25 patients with strokes (17 men and eight women, mean ± SD age 65.9 ± 12.1 years) and 15 patients with TIs (10 men and five women, mean ± SD age 59.8 ± 9.0 years). We excluded those with a history of previous stroke, convulsive disorder, or migraine from the study. Diagnosis of stroke or TIA was based on the findings of repeated neurologic examinations, electroencephalography (EEG), and brain CT. The patients were examined neurologically on five occasions by the same examiners; EEG was repeated 1, 2, and 10 days after the onset of symptoms; and brain CT was performed ≤24 hours and 8 days after admission. Volume of the infarct was calculated by dividing half of the product of the horizontal dimensions of the infarct by the number of CT cuts. We assayed LDH concentration in the CSF of all patients as a diagnostic procedure ≤8 hours after the onset of symptoms. We removed 3 ml CSF from each patient under similar conditions. The CSF
was stored at -70°C and examined ≤72 hours after the lumbar puncture. We determined the concentration of LDH using a centrifugation analyzer (Model N. 500, Medtechnica), with kits from Boehringer Mannheim GmbH (FRG). We also analyzed the cell count, the concentrations of protein and glucose in the CSF, and the concentration of LDH in the serum.

We compared the concentrations of LDH in the CSF of the stroke and TIA patients with that of 21 control patients (10 men and 11 women, mean±SD age 45.8±15.6 years). Statistical analysis consisted of one-way analysis of variance for the three groups, pair-wise comparison between subgroups using the Bonferroni test, and Pearson correlation with the variables infarct volume, time after lumbar puncture, cell count, protein and glucose concentrations, and LDH concentration in the serum. Results are reported as mean±SD.

Results

All 25 patients with an acute stroke had motor deficits; 15 suffered from hemihypesthesia, seven had mixed aphasia, seven had motor aphasia, one had sensory aphasia, and six had hemianopia. Among the 15 patients who had a TIA, 12 had motor deficits, four had sensory deficits, one had mixed aphasia, six had motor aphasia, and two suffered from transient global amnesia. All neurologic deficits disappeared ≤24 hours after the onset of the event. We found no evidence of a brain lesion on repeated CT scans and no paroxysmal discharge in any EEG examination in any TIA patient.

We further divided the stroke patients into three subgroups according to the location of the infarct on CT. Twelve patients (nine men and three women) had cortical infarcts, with focal slow disturbances on EEG that confirmed the CT findings; five patients (three men and two women) had lacunar infarcts of the white matter; and eight patients (four men and four women) had infarcts of the basal ganglia with no EEG abnormalities.

We found significantly higher CSF LDH levels in the stroke patients than in the TIA patients (40.9±14.5 vs. 11.8±2.9 units/l, p<0.001) and the controls (40.9±14.5 vs. 11.2±6.7 units/l, p<0.001) and no significant differences between the TIA patients and the controls (p=0.974) (Figure 1). Among the stroke patients, a significantly higher CSF LDH concentration was found in the subgroup with cortical strokes than in the subgroup with lacunar infarcts (50±12.3 vs. 26.4±6.5 units/l, p<0.001) and the subgroup with basal ganglia infarcts (50±12.3 vs. 36.37±11.7 units/l, p<0.05). There were no significant differences in CSF LDH level between the subgroup with lacunar infarcts and the subgroup with basal ganglia infarcts (p=0.2128) (Figure 2) and no correlation between the timing of lumbar puncture and the CSF LDH level (r=0.247, p=0.117).

There was also no correlation between the infarct volume and the CSF LDH levels in any subgroup (p=0.2) or between the LDH concentrations in the CSF and the serum. There was no correlation between the CSF LDH concentration and the cell count or the protein and glucose levels in the CSF (Table 1).

Discussion

There have been few studies of the levels of enzymes in the CSF after cerebrovascular events. Most studies have demonstrated an increase in the concentration of creatine kinase,6-9 LDH,1-3-89 and glutamic-oxaloacetic transaminase45-8-9 from 8 hours to several days after the onset of stroke. Creatine kinase concentration, which peaks earlier than that of the other enzymes, was found to be diagnostic only in patients with severe global brain damage, especially after transient cardiac arrest,11-14 open heart surgery with cardiopulmonary bypass,15 and severe
The difference between these findings can be explained by the very early stage of examination in our study. We believe that during the initial stage, the increase in LDH concentration is related more to proximity of the lesion to the subarachnoid space than to volume of the infarct.22 Considering our results, we suggest that the examination of LDH concentration in the CSF during the first hours after stroke onset may be of diagnostic and prognostic usefulness. This examination offers a simple procedure with which to recognize patients with poor prognoses. Diagnosis of a patient's recovery potential within the first hours after the event is important for management of such cases. In addition, the appearance of LDH in the CSF may provide supplementary information for the diagnosis of cortical versus subcortical infarction, even before evidence of a brain lesion can be found on CT. We also suggest that LDH in the CSF may be useful for recognizing those patients at high risk of developing severe stroke. Such findings could be important for preventive treatment.

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References


Table 1. Concentrations in Cerebrospinal Fluid

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Age (yr)</th>
<th>Cells (per mm³)</th>
<th>Protein (mg%)</th>
<th>Sugar (% blood sugar)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>25</td>
<td>65.9±12.1</td>
<td>4.2±5.8</td>
<td>34.5±5.8</td>
<td>69.5±8.2</td>
</tr>
<tr>
<td>TIA</td>
<td>15</td>
<td>59.8±9.0</td>
<td>1.6±1.2</td>
<td>17.3±5.8</td>
<td>71.9±7.4</td>
</tr>
<tr>
<td>Control</td>
<td>21</td>
<td>45.8±15.6</td>
<td>1.4±0.7</td>
<td>21.6±8.3</td>
<td>68.3±9.3</td>
</tr>
</tbody>
</table>

TIA, transient ischemic attack. Data are mean±SD.

KEY WORDS • cerebral ischemia, transient • cerebrovascular disorders • lactate dehydrogenase
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