Serum Lactate Dehydrogenase Isoenzymes in the Diagnosis of Myocardial Infarction

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ABSTRACT

The ratio of lactate dehydrogenase (LD-1: LD-2) in serum was studied in 101 patients admitted to a coronary care unit. The clinical reliability of the test could not be predicted from the normality or abnormality of the total serum lactate dehydrogenase (LD) activity. However, for samples with total LD activity below the middle of the normal range, no information was provided by the test. In contrast, the test provided reliable information when the total LD activity in the specimen was above the middle of the reference range (220 IU per L).

Introduction

Measurements of the serum isoenzymes of creatine kinase (CK) and lactate dehydrogenase (LD) are recognized to be of value in the diagnosis of myocardial infarction. These isoenzyme determinations often are used to improve upon the diagnostic specificity of measurements of total serum enzyme activities. In this context, the isoenzymes have been measured only when the total enzyme activity was increased. However, increases in isoenzyme 2 of CK (CK-MB) can be used for the early diagnosis of myocardial infarction before the total CK activity becomes elevated. This observation raises the question of whether or not LD isoenzyme determinations might also be useful in the diagnosis of myocardial infarction when the total LD activity is normal.

Occasional abnormalities of LD isoenzyme patterns in samples with normal total LD have been noted. However, no published study has been found evaluating the sensitivity and specificity of LD isoenzyme changes in specimens with normal total LD activity. Moreover, in an informal survey of six hospital laboratories, a lack of agreement exists on when to perform isoenzyme testing for LD. In some laboratories testing is performed on all samples, whereas in other hospitals, testing is restricted to samples with increased total LD activity.
The present study was undertaken to establish the value in performing serum LD isoenzyme measurements when the total LD activity is within the normal reference range. Our results suggest that LD isoenzyme testing is useful whenever the total LD activity of the sample exceeds the middle of the normal range and is of no value for samples with LD activities in the lower part of the reference range. This unanticipated result may explain why laboratories have not agreed on whether or not to analyze samples with normal total LD activity.

**Methods**

One hundred and one patients admitted to the coronary care unit at the University of Virginia Medical Center were studied prospectively. A diagnosis of myocardial infarction was established in 29 of the patients based upon standard clinical criteria, including the clinical history, evolutionary electrocardiographic changes, serial enzyme patterns, and the CK-MB activity. The diagnoses were established independently of the LD isoenzymes. Lactate dehydrogenase and its isoenzymes were measured in 334 serum samples from the 101 patients. Total LD activity in serum was measured at 30°C using a kinetic assay, pyruvate-to-lactate, adapted to a centrifugal analyzer.* Lactate dehydrogenase isoenzyme patterns were assessed electrophoretically using commercially available cells and reagents.† An electrophoretic method widely used for clinical determinations was employed. Results were recorded as positive (LD-1 > LD-2) or negative (LD-1 < LD-2) following visual inspection of the stained gel with confirmation by integrating-densitometry. Equivocal results (LD-1 = LD-2) were recorded with similar frequency in samples from patients with (17 percent) and without (20 percent) myocardial infarction. These results were not tabulated for further analysis in the present study. The LD-1:LD-2 ratio was evaluated in terms of its sensitivity (positivity in samples from patients with myocardial infarction) and specificity (negativity of the test in samples from patients without infarction).

**Results and Discussion**

The results of the study are summarized in table I. The sensitivity and specificity of the LD electrophoresis were acceptable only on samples which had a total LD activity above 220 IU per L (reference range 100 to 350 IU per L). One-third of all the samples tested (116/334) had an LD activity in the lower half of the reference range (i.e., <200 IU per L); no true positive electrophoretic result was found in this group and the only false positive re-

<table>
<thead>
<tr>
<th>Table I: Sensitivity and Specificity of Lactate Dehydrogenase (LD) Isoenzymes for the Diagnosis of Myocardial Infarction (MI)</th>
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<tbody>
<tr>
<td>Specimens*</td>
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<tr>
<td>Total LD†</td>
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<tr>
<td>(IU/L)</td>
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<td>221-350</td>
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<td>&gt;350</td>
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*Note that 4.9 samples were analyzed for each patient with myocardial infarction versus only about three samples for the others. The conclusions are not affected if the excess samples for infarct patients are excluded. The sensitivities (and numbers of samples) then become 0 percent (10), 42 percent (31), and 59 percent (37), respectively, for samples with total LD of <220, 220 to 350, and >350 IU per L. The small changes compared to the table reflect the fact that later samples tended to have both higher LD activities and positive LD-1:LD-2 results.

†Reference range for serum LD was 100 to 350 IU/L.

‡Sensitivity: proportion of samples from infarct patients that had a flipped LD-1:LD-2 ratio (LD-1>LD-2).

§Specificity: proportion of samples from non-infarct patients that had a normal LD-1:LD-2 ratio (LD-1<LD-2).

Numbers in parentheses indicate the number of serum samples analyzed.

* Lyophilized reagent was purchased from BMC, Indianapolis, IN.
† Coming Medical, Medfield, MA.
result in the study occurred among these samples. Thus, in samples with LD < 220 IU per L, no useful information was obtained from LD electrophoresis. For samples in the upper portion of the reference range for total LD (i.e., 221 to 350 IU/L), LD electrophoresis provided useful information. Twenty-one positive results occurred in patients diagnosed as having had a myocardial infarction and, moreover, three patients with myocardial infarctions had positive LD electrophoresis results but had no LD values which exceeded 350 IU per L during their hospitalization.

In four other patients with myocardial infarction, a positive LD-1:LD-2 ratio was documented before the total LD exceeded 350 IU per L. Thus, in 24 percent of infarct patients (7/29), the use of LD electrophoresis on samples with normal total LD provided a laboratory confirmation of the diagnosis which would otherwise have been absent or delayed.

The findings from this study suggested that LD electrophoresis was useful only when the total LD exceeded approximately 220 IU/L. During a subsequent three week period, three more false positive electrophoretic results were observed and no true positive results on samples with total LD less than 220 IU per L. It has been concluded that for samples with total LD less than 220 IU per L, no further useful information can be obtained from LD electrophoresis. It is recommended that limited laboratory resources can be better utilized than in the performance of LD electrophoresis on samples with total LD activity below the middle of the normal range. Since one-third of our samples fell into this category, the cost savings can be appreciable. On the other hand, it appears that LD isoenzyme determinations can provide reliable information on selected samples with normal total LD activity, i.e., on samples with LD above 220 IU per L. The cost of obtaining this information must be weighed against its value in a given patient. Finally, the results of this study suggest that newer assays which are specific for LD-1 may provide a more sensitive early test for myocardial infarction than would be expected based upon current experience with measurements of total LD activity. Studies in our laboratory indicate that LD-1 is indeed increased very early following myocardial infarction. This result would not have been expected from experiences with LD isoenzymes in which increased total LD was a prerequisite for measuring LD isoenzymes.

References