were comparable with those by the reference assays. However, the results emphasize the well-established fact that antibodies of different origin do not necessarily provide identical results across the broad range of analyte concentration encountered clinically (14). The clinical correlation between the results by the kit and those by A1 in the limited clinical groups studied was closer than that between A2 results and the kit results. Some of this latter discrepancy might be attributable to a dilution of serum samples with the human serum supplied with the kit but, more probably, the magnitude of differences is simply intrinsic to two assays that involve different sample volumes and different antibodies to thyrotropin.

Finally, our studies did not confirm the previously noted possibility of chorionicadotropin cross-reactivity with thyrotropin (2). We conclude there is no need to adjust normal ranges or alter reportability of the assay for pregnant patients, at least for the lot of antibody to thyrotropin used in this study.

References


Early Detection of Myocardial Infarction by an Immunoradiometric Procedure for Creatine Kinase MB
Richard F. Dods

I investigated the diagnostic efficacy of the Embria-CK immunoradiometric assay (IRMA) in detecting myocardial infarction, using a single blood sample drawn at hospital admission 0 to 10 h after the onset of chest pain and serial testing over a 24- to 48-h interval after hospital admission. The sensitivity, specificity, and efficiency for hospital admission samples were 87.5, 83.3, and 85.0%, respectively, and for serial testing, 100, 79.2, and 87.5%, respectively. The diagnostic efficacy was comparable to that of electrocardiography and significantly better than the Du Pont CK-MB method.

Additional Keyphrases: heart disease • diagnostic efficacy • isoenzymes • cutoff value

Increased creatine kinase isoenzyme MB (CK-MB, EC 2.7.3.2) in serum has become widely accepted as suggestive of myocardial infarction (MI), even in the absence of electrocardiographic changes and even before there are increases in other indices to cardiac status such as lactate dehydrogenase isoenzyme 1. Rapid, accurate, and analytically sensitive methods for assay of CK-MB are therefore highly desirable.

The ideal CK-MB assay would have an analytical sensitivity and precision such that changes in CK-MB could be detected promptly after the onset of chest pain. Electrophoresis on cellulose acetate or agarose and ion-exchange column chromatography, until recently the accepted methods for the separation, identification, and quantification of the CK isoenzymes, generally require serial testing during a 24- to 48-h interval. The clinician thus must wait one to two days before he can include the CK-MB data in his diagnosis. Elser and McKenna (1) evaluated the diagnostic efficacy for CK-MB at various times after the onset of chest pain as determined by three CK-MB techniques: column chromatography on DEAE-Sephadex A-50, electrophoresis on agarose, and immunoinhibition. The diagnostic sensitivities for these methods in the detection of MI 0 to 8 h after the onset of symptoms ranged from 11 to 45%. They obviously are not suitable for the early detection of MI.

Shell et al. (2) reported considerably improved diagnostic efficacy when they used an analytically sensitive Sephadex ion-exchange column-chromatographic method reportedly

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Results and Discussion

The between-run CVs for the IRMA procedure were 9.7 and 6.0% with means of 6.56 and 28.3 EU/L, respectively, as determined on two control samples. The within-run CVs were 8.8 and 5.8% with means of 7.50 and 30.1 EU/L, respectively, as determined on the same two controls. The between-run CVs for the Du Pont CK-MB column-chromatographic method were 10.7 and 6.7%, with means of 11.0 and 42.8 U/L, respectively, as determined on the two control materials. The within-run CVs were 9.1 and 5.3% with means of 12.5 and 40.5 U/L, respectively, as determined on the same two controls. Results from the electrophoresis method were used qualitatively.

In a preliminary study of 30 non-MI patients, the IRMA method produced a mean value for CK-MB of 2.19 EU/L (SD 0.32 EU/L). For the same samples the Du Pont column-chromatographic method gave a mean of 1.20 U/L (SD 0.80 U/L). From these results, I established upper limits of normal of 3.0 EU/L and 3.0 U/L for the IRMA and column-chromatographic methods, respectively. To assess the IRMA data I used three values for the upper limit of normal: 3.0 EU/L, the value determined in the preliminary study; 4.5 EU/L, an arbitrarily chosen value; and 5.0 EU/L, the value suggested by International Immunoassay Labs. I evaluated diagnostic efficacy for the column-chromatographic method at two upper-limit-of-normal values for CK-MB when total CK activity was <450 U/L: 3.0 U/L, the value determined in the preliminary study, and 8.0 U/L, the value suggested by Du Pont. For samples exceeding 450 U/L the non-MI range was defined as a CK-MB activity that was less than 1.8% of the total CK activity.

In the electrophoresis method, the resolved CK isoenzymes were viewed in ultraviolet light, and the presence or absence of CK-MB was noted. In confirmation, I scanned the plates with a Helena Quick Scan densitometer.

The diagnostic sensitivity, specificity, and efficiency for each of the three CK-MB assay procedures, based on single blood samples drawn at the time of hospital admission, were calculated by the standard equations of Galen and Gambino (9). As Table 1 shows, the IRMA results were the most useful diagnostically for admission-sample analysis. Use of the 3.0

Table 1. Diagnostic Efficacy of Three Methods for CK-MB Assay in the Detection of Myocardial Infarction

<table>
<thead>
<tr>
<th>Method</th>
<th>Cutoff Value</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Efficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embria-CK, EU/L</td>
<td>3.0</td>
<td>87.5</td>
<td>83.3</td>
<td>85.0</td>
</tr>
<tr>
<td></td>
<td>4.5</td>
<td>56.3</td>
<td>100.0</td>
<td>82.5</td>
</tr>
<tr>
<td></td>
<td>5.0</td>
<td>56.3</td>
<td>100.0</td>
<td>80.0</td>
</tr>
<tr>
<td>Du Pont CK-MB, UIL</td>
<td>3.0</td>
<td>56.3</td>
<td>75.0</td>
<td>67.5</td>
</tr>
<tr>
<td></td>
<td>8.0</td>
<td>50.0</td>
<td>83.3</td>
<td>70.0</td>
</tr>
<tr>
<td>Electrophoresis</td>
<td></td>
<td>75.0</td>
<td>87.5</td>
<td>82.5</td>
</tr>
<tr>
<td>Embria-CK, EU/L</td>
<td>3.0</td>
<td>100.0</td>
<td>79.2</td>
<td>87.5</td>
</tr>
<tr>
<td></td>
<td>4.5</td>
<td>87.5</td>
<td>95.8</td>
<td>92.5</td>
</tr>
<tr>
<td></td>
<td>5.0</td>
<td>75.0</td>
<td>100.0</td>
<td>90.0</td>
</tr>
<tr>
<td>Du Pont CK-MB, UIL</td>
<td>3.0</td>
<td>94.1</td>
<td>75.0</td>
<td>85.0</td>
</tr>
<tr>
<td></td>
<td>8.0</td>
<td>75.0</td>
<td>87.5</td>
<td>82.5</td>
</tr>
<tr>
<td>Electrophoresis</td>
<td></td>
<td>100.0</td>
<td>83.3</td>
<td>90.0</td>
</tr>
</tbody>
</table>

*n = 43 patients
EU/L value for the upper limit of normal resulted in the highest sensitivity (87.5%) and the highest efficiency (85.0%), while the other two cutoff values gave the highest specificity (100%). For serial testing on the same patients, the electrophoresis method has a sensitivity of 100%, a specificity of 83.3%, and an efficiency of 90.0%. The IRMA procedure had a sensitivity that ranged from 75.0 to 100%, depending on the value used as the upper limit of normal. In general, all of the methods I studied produced diagnostic sensitivities, specificities, and efficiencies for admission sample testing that were lower than for serial testing.

A test for MI should have a high efficiency, a false negative being as undesirable as a false positive (9). The Embria-CK IRMA method produced comparable efficiencies for both hospital-admission-samples and serial testing, 85.0 and 87.5%, respectively. Cellulose acetate electrophoresis is about as efficient as the IRMA method (82.5%), but less sensitive. The Du Pont CK-MB method, a relatively rapid procedure that may be used in an urgent situation, has the lowest diagnostic efficacy of the three methods studied for admission sample testing.

I conclude that, although not ideal, IRMA provides good diagnostic efficacy for the detection of MI 0 to 10 h after the onset of chest pain. Nonetheless, serial testing at 12-h intervals, beginning when the patient is admitted, remains necessary to confirm the diagnosis.

References


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Cell Membrane Abnormality Detected in Erythrocytes from Patients with Multiple Sclerosis by Partition in Two-Polymer Aqueous-Phase Systems

James M. Van Alstine1 and Donald E. Brooks1,2

Erythrocytes from multiple sclerosis patients differ significantly (p < 0.005) from those from controls with regard to hydrophobic affinity partition in two-polymer aqueous-phase systems containing dextran, poly(ethylene glycol) and poly (ethylene glycol)-fatty acid esters. The most likely source of the abnormality is the cell membrane.

Additional Keyphrases: polyethylene glycol • dextran • fatty acid esters

Among the abnormalities reported for erythrocytes from patients with multiple sclerosis (MS) are increased cell diameter, enhanced osmotic fragility, altered linoleic and arachidonic acid composition in the membranes (I and references therein) and the effect of exposure to polyunsaturated fatty acids (50 μg/mL) on the electrophoretic mobilities of both fresh and glutaraldehyde-fixed erythrocytes (1–3). Alterations in cell function or membrane lipid composition have also been reported for platelets (4, 5) and lymphocytes (6–8) from MS patients. These blood cell abnormalities may be related to changes in plasma lipids or other plasma components (I, 5, 8–10).

Cell partition in two-polymer aqueous-phase systems is an analytical and preparative technique that is sensitive to cell-membrane properties. When the neutral polymers dextran and poly(ethylene glycol) (PEG) are mixed in aqueous solution above certain concentrations, two phases form, with PEG predominating in the upper phase and dextran in the lower.

These systems can be rendered isotonic and buffered to physiological pH by the addition of various salts. Cells can be selectively partitioned into the upper phase in appropriately buffered systems on the basis of several cell-surface properties, including affinity for PEG molecules esterified to various saturated and unsaturated long-chain fatty acids (11–14). In the latter case the fatty acyl tails appear to intercalate into the lipid bilayer and (or) bind to other hydrophobic sites on the cell surface, coating the cell with PEG molecules. The PEG-coated cells exhibit dramatically increased affinity for the upper, PEG-rich phase.

In recent experiments we have attempted to differentiate between normal and MS erythrocytes with respect to their hydrophobic surface properties on the basis of their partition in two-phase systems containing micromolar concentrations of PEG esters of stearic (18:0) acid and linoleic (18:2) acid.

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