Creatine Kinase MB and Lactate Dehydrogenase 5 Isoenzymes in Rhabdomyolysis

To the Editor:

Although the percentage of the three major CK (creatinine kinase; EC 2.7.3.2) isoenzymes varies in different organs and animal species and depends in part on the techniques used for their separation, it is unanimously accepted that isoenzyme MB is found predominantly in the myocardium. The fact that this enzyme is seldom if ever detected by conventional methods in serum of normal people makes its detection in serum strongly suggestive of myocardial damage.

Reports on the CK isoenzyme composition of skeletal muscle are controversial; various percentages of MB isoenzyme are reported in skeletal muscle, ranging from 0 to 20% (1-4). CK-MB was detected in the serum of six patients with polymyositis, dermatomyositis, and viral myositis, but lactate dehydrogenase (EC 1.1.1.27) isoenzyme 5 activity was not increased in the serum of these patients (4). Although the highest total CK activity detected in these series was 82 kU/liter, a patient with massive skeletal muscle injury and a total CK activity of 104 kU/liter did not show CK-MB in the serum (5). CK-MB was not detected in serum in patients with status epilepticus (6) or after cardioversion (6, 7), but was consistently found in cases of Duchene muscular dystrophy and dermatomyositis of children and in cases of severe gangrene of the extremities (6). In Duchenne muscular dystrophy the MB isoenzyme is believed to originate from striated muscle, but a myocardial origin has not been ruled out (8, 9). It was also suggested that metabolic disturbances may induce hybrid isoenzyme formation, resulting in the appearance of MB isoenzyme in the serum.

Why is CK-MB found in serum in some muscular diseases but not in others? We report here a case of viral rhabdomyolysis with increased serum total CK activity, myoglobinuric, and with CK-MB and high lactate dehydrogenase activity present in the serum.

A young woman was admitted to the hospital because of increasing myalgia, dark urine, and increase in frequency and urgency of micturition.

At admission the urine showed myoglobin by immunodiffusion of a 1000-fold diluted sample. Serum lactate dehydrogenase activity exceeded 2700 U/liter, aspartate aminotransferase (EC 2.6.1.1) activity was 3050 U/liter, and CK activity exceeded 3000 U/liter. Separation of the lactate dehydrogenase isoenzymes in the serum showed an increase of lactate dehydrogenase isoenzymes 4 and 5 (24.2 and 42.6% of the total lactate dehydrogenase activity, respectively), and CK isoenzyme assay showed about 6% of the total activity to be CK-MB, even when the serum was diluted to about 100 U/liter. CK isoenzymes were separated by electrophoresis on agarose gel and quanitifed by fluorometric scanning. A linear relationship was observed between enzyme concentration and fluorescence for samples with CK activity of up to 800 U/liter (10).

In cases of electrical countershock (electric shock applied to the heart to terminate a disturbance of its rhythm) there is a release of CK from skeletal muscle, presumably from the chest wall (11). However, CK-MB is usually not found in the serum of countershock-treated patients, patients who are undergoing various surgical procedures (7), or patients with convulsions or hypothyroidism, even though the total CK activity is high (12). When myocardy is induced by 5-hydroxytryptamine in aorta-ligated animals, such experimental skeletal muscle damage increases serum CK-MB isoenzyme (3). It was considered that only the "red" muscle fibers of type II (e.g., soleus) contain significant amounts (up to 10%) of MB isoenzyme, while type I (e.g., gastrocnemius) contain negligible amounts (<1%) (6, 13). Interestingly, there are developmental changes in CK isoenzyme patterns; i.e., CK-MB is found in increased amounts in muscles of the fetus after three months as compared to an earlier fetal stage, and remains increased until the sixth month of gestation (14). It was suggested that the mechanism of skeletal muscle breakdown in Duchenne dystrophy differs from that in other kinds of neuromuscular diseases (8) and that various muscular diseases preferentially affect some types of fibers. Our case showed an increased serum lactate dehydrogenase 5, conceivably of muscular origin.

Further studies are needed to ascertain if the CK isoenzymes would be useful in determining the stage and the extent of neuromuscular diseases (8).

References

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Measurement of Total Protein in Cerebrospinal Fluid with the Perkin-Elmer Amylase-Lipase Analyzer

To the Editor:

The most widely used method for cerebrospinal fluid total-protein determination is turbidimetric (1). We use a modification of the Dennis-Ayer method (2), with sulfofascic acid as the precipitant. The most accurate method of measurement is with a nephelometer, rather than by spectrophotometry (3). Many hospitals do not have a nephelometer but do have a Model 91 Amylase-Lipase Analyzer (Perkin-Elmer Corp., Coleman Instruments Division, Oak Brook, Ill. 60521) (4). Use of this analyzer as a nephelometer has de-