Myoglobin Concentrations and Muscle-Enzyme Activities in Serum after Myocardial Infarction and Cardiac Arrhythmia

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Sera from patients with myocardial infarction and cardiac arrhythmias were analyzed for myoglobin concentration and the activities of total creatine kinase, creatine kinase isoenzyme-2, and lactate dehydrogenase isoenzyme-1 at the time of hospital admission and during the first few days of hospitalization. The nine patients with a final diagnosis of myocardial infarction had abnormally high values for total creatine kinase, creatine kinase-2, lactate dehydrogenase-1, and myoglobin. Myoglobin concentrations were highest on admission in six patients and on the day after admission in the other three patients. Creatine kinase-2 manifested maximum activity on the day after admission for all patients with myocardial infarction. Lactate dehydrogenase-1 did not reach maximal values until the second or third day after admission. The six patients with arrhythmias did not show any significant increases in creatine kinase-2 or lactate dehydrogenase-1. Myoglobin and total creatine kinase, however, were increased in the four patients who had received cardioversion. The specificity and diagnostic usefulness of these serum measurements are discussed.

Additional Keyphrases: creatine kinase • lactate dehydrogenase • isoenzymes • cardioversion • enzyme activity

Measurement of the activity of creatine kinase (CK; EC 2.7.3.2)1 and lactate dehydrogenase (LD; EC 1.1.1.27) in serum is widely used in the diagnosis of myocardial injury. The development of methods for separating and quantitating the isoenzymes CK-2 and LD-1 has increased the specificity and utility of enzyme measurements in the management of patients with suspected myocardial infarction (1–6). Recently, the concentration of a muscle protein, myoglobin, was found to be increased in serum after myocardial infarction (7).

With the availability of methods for the measurement of CK-2 and with the recent development of a sensitive radioimmunoassay for serum myoglobin in our laboratory (8), we studied the relative change in the values for myoglobin and some enzyme activities in serum in cases of myocardial infarction. We also examined the relative usefulness of these measurements in differentiating patients with myocardial infarction with or without complicating cardiac arrhythmias from patients with primary cardiac arrhythmias whose symptomatology may mimic myocardial infarction. Our findings are presented here.

Materials and Methods

Total CK activity was measured by the method of Rosalki at 32 °C (9). The upper limit of normal for this method is 70 U/liter. We separated CK-2 on “DEA Glyphase-G” glass beads (product No. 23537; Corning Glassworks, Medfield, Mass. 02052) by a modification of the batch absorption method of Henry et al. (10), using an increased serum sample size of 500 μl. The activity of CK-2 in the eluate was monitored by the method of Rosano et al. (11). A 200-μl aliquot of the eluate was used to further increase the sensitivity of the method. Normal values for CK-2 in our laboratory are 0 to 6 U/liter. The LD-1 activity was measured after electrophoretic separation on cellulose acetate by exposure to L-lactate substrate (60 mmol/liter) with subsequent reduction of nitroblue tetrazolium, followed by integrating densitometry (12). The activity of LD-1 was determined by relating the percentage of LD-1 activity found by electrophoresis to the total serum LD activity. Total LD was determined by a kinetic spectrophotometric method for measuring the rate of conversion of...
pyruvate to lactate (13). The normal upper limit for LD-1 activity in serum is 100 U/liter in our laboratory. All kinetic measurements of enzymatic activity were performed with an ENI GEMSAEC centrifugal analyzer (Electro-Nucleonics, Inc., Fairfield, N. J. 07006). Serum myoglobin concentration was measured by the radioimmunoassay method of Rosano and Kenny (8). Normal values are 10 to 68 μg/liter.

Serum samples were obtained from nine patients with myocardial infarction and six patients with cardiac arrhythmias. The samples were collected at the time of hospital admission, within 6 h of onset of symptoms for all patients. Subsequent samples were collected each morning after admission. The categorization of disorders was based on the final diagnosis. The diagnostic criteria for myocardial infarction included the following: intense precordial chest pain, characteristic electrocardiographic changes (including the development of pathologic Q waves and QRS deformity, inversion of T waves, and ST segment shifts), as well as elevations in LD-1 and total CK activities. All of the electrocardiograms were interpreted by hospital staff cardiologists who had no knowledge of the laboratory results. The diagnosis of arrhythmias was based on symptomatology, characteristic electrocardiographic findings, and the absence of significant increases in LD-1 activity. The types of cardiac arrhythmias were as follows: patient 10, ventricular tachycardia; patient 11, premature ventricular contractions, paroxysmal atrial tachycardia, and heart block; patient 12, ventricular fibrillation and episodic atrial fibrillation; patient 13, supraventricular tachycardia and atrial fibrillation; patient 14, paroxysmal atrial fibrillation; and patient 15, atrial flutter. Patients 10, 11, 12, and 13 received direct-current countershock (cardioversion). Patients 14 and 15 did not receive cardioversion.

Results

Figure 1 shows the change in myoglobin, total CK, CK-2, and LD-1 in patients with myocardial infarction. The maximal concentrations of myoglobin (Figure 1a) in these patients ranged from 86 to 362 μg/liter. Maximal values were observed on admission in six patients and on the day after admission in three patients. Total CK (Figure 1b) had a peak activity ranging from 150 to 1200 U/liter. Maximal activity was detected on the first or second day after admission. Maximum detected CK-2 activity (Figure 1d) ranged from 16 to 135 U/liter; these maximum values were seen on the day after admission for all patients. The highest measured activities of LD-1 (Figure 1c), ranging from 201 to 897 U/liter, were observed on the second or third day after hospital admission.

Figure 2 illustrates the concentrations of myoglobin and the enzyme activity in the serum of patients with cardiac arrhythmias. CK-2 and LD-1 did not become significantly increased in the patients in this category. However, myoglobin and total CK did show significant increases above normal in the four patients who received cardioversion (patients 10–13). In these patients, the magnitudes and patterns of increases in myoglobin and total CK were similar to those in patients with acute myocardial infarction. The two patients (14 and 15) who showed no increase in any of the measured variables had not received cardioversion.

Discussion

The diagnostic value of serial determinations of CK, CK-2, LD, and LD-1 activity in the management of patients with myocardial infarction, ischemic cardiac disease, angina pectoris, and cardiac arrhythmias is well established (1–6). In this study, all patients were evaluated with the aid of these laboratory measurements, as well as with the use of a more recently developed laboratory tool, the serum myoglobin assay.

The results show that myoglobin was increased before total CK in six of nine patients with acute myocardial infarction, an observation consistent with that of Stone et al. (7), who also found that the peak value of serum myoglobin in patients with myocardial infarction preceded that of total CK. The present study further extends this observation to the relationship between myoglobin and CK-2, and indicates that myoglobin is the earliest detectable serum indicator of a myocardial infarction. However, the group of patients with cardiac arrhythmias demonstrates the poor cardiac specificity of the serum myoglobin measurements. In this instance, both
myoglobin and total CK were increased in the absence of any significant increase in CK-2 or LD-1. These data correlated with cardioversion of patients and may reflect pectoralis muscle injury, subendocardial ischemia, or trauma secondary to intramuscular injections, or some combination of these. Further studies of larger numbers of arrhythmia patients will be necessary to clarify the exact etiologies of the myoglobin increases in the cardioverted patients. Nevertheless, it is interesting to note that these findings are in conflict with the preliminary data of Stone et al. (7), which revealed no marked alterations of serum myoglobin concentration in patients receiving cardioversion.

In conclusion, this study demonstrates that after myocardial injury, serum myoglobin increases and does so before CK-2 appears in the serum. Notwithstanding, the inability to distinguish between serum myoglobin originating from cardiac and skeletal muscle and the sophisticated methodology required for the analysis indicate that routine measurement of serum myoglobin in instances of suspected myocardial infarction is not clinically warranted at this time. This study confirms the observation of others (1–3) that CK-2 measurement is of significant usefulness in the laboratory differential diagnosis of myocardial infarction. The potential value of serum myoglobin and CK-2 determinations in the management of patients with other endocardial, myocardial, and/or pericardial disorders remains to be established.

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References