Evaluation of γ-Glutamyl Transpeptidase in Myocardial Infarction

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The activity of γ-glutamyl transpeptidase (γ-GTP) was determined serially in 64 patients with suspected myocardial infarction. Of 38 patients with proved myocardial infarction, only four showed early change of γ-GTP activity and six showed change between the fifth and seventh day. Of 26 patients shown not to have myocardial infarction, slightly over one-third had persistent false-positive elevation of γ-GTP. These studies failed to demonstrate a significant value to this enzyme determination.

Several previous studies1-3 have suggested that the determination of γ-glutamyl-transpeptidase (γ-GTP) activity might prove useful in the diagnosis of acute myocardial infarction. These studies have indicated that peak enzyme activity was found between the seventh and 11th days after infarction although elevation in some patients was present within 48 hours.

Since the clinical diagnosis of acute myocardial infarction is often difficult by conventional methods, it was thought useful to further explore the indications for this new enzyme and assess the usefulness of this diagnostic modality in a large series of patients with clear-cut myocardial infarction. Our earlier studies4-6 have indicated a high degree of accuracy with the use of enzyme diagnosis in myocardial infarction, and the addition of an enzyme which would be diagnostically helpful in older myocardiual infarctions would markedly enhance the employment of enzyme procedures at varying intervals following acute myocardial infarction.

The purpose of the present study was to correlate changes in γ-GTP activity at varying intervals following acute myocardial infarction and to ascertain the reliability of this new procedure in patients with myocardial infarction.

Methods

Serum γ-GTP activity was determined by a method originally described by Orlowski and Szewczuk.7,8 γ-Glutamyl-β-naphthylamine was used as a substrate and the β-naphthylamine liberated during enzyme incubation was determined by modification of the Bratton-Marshall procedure.9,10 The amount of β-naphthylamine was calculated from a standard curve (Figure). A unit of enzyme activity was defined as follows:

\[
\text{1 unit} = \frac{\mu\text{mol} \beta\text{-naphthylamine}}{\text{hour} \times 100 \text{ ml of serum}}
\]

The optical density was measured in a spectrophotometer against the blank at a wave length of 578 mμ.

Serum levels of γ-GTP activity were initially determined in 27 normal individuals and found to range between 2 and 25 units, with a mean of 14.5. No significant difference was demonstrated between activity of men or women, nor was any correlation found between age and enzyme activity.

Serum levels of γ-GTP activity were determined at varying intervals in 38 patients, following myocardial infarction and in 26 patients who were originally thought to have myocardial infarction and subsequently proved to have other diseases. Enzyme activity was determined daily on days 1, 2, 5, 6, 7, 9, and 12 after myocardial infarction. Other enzyme procedures performed in the same patients simultaneously included creatine phosphokinase (CPK), lactate dehydrogenase (LDH), and serum glutamic oxaloacetic transaminase (SGOT). All patients had serial electrocardiograms, sedimentation rates, white blood cell counts, and, in many cases, vectorcardiograms.

Results

A summary of the background and results obtained in patients with clear-cut myocardial infarction is shown in Table 1. These patients had definite histories of severe, prolonged pain in the chest, ECG changes of myocardial infarction, changes in SGOT, CPK, and LDH levels, and rise in sedimentation rates.

There were 13 anterior, 12 posterior, and 13 inferior wall in-

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Table 1.—Background Data and Enzyme Values on Patient Population

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age, yr</th>
<th>Location of Infarction</th>
<th>ECG Findings</th>
<th>CPK Level (Normal, 0-50)</th>
<th>SGOT Level (Normal, 0-40)</th>
<th>γ-Glutamyl Transpeptidase Activity *</th>
<th>1 to 2 Days</th>
<th>5 to 7 Days</th>
<th>7 to 14 Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>53</td>
<td>Posterior</td>
<td>Q-wave pattern</td>
<td>195</td>
<td>120</td>
<td>14</td>
<td>21</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>61</td>
<td>Anterior</td>
<td>Q-wave pattern</td>
<td>125</td>
<td>90</td>
<td>17</td>
<td>20</td>
<td>6.6</td>
<td></td>
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<tr>
<td>3</td>
<td>M</td>
<td>49</td>
<td>Inferior</td>
<td>Q-wave pattern</td>
<td>260</td>
<td>125</td>
<td>10.5</td>
<td>8.1</td>
<td>8.3</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>64</td>
<td>Anterior</td>
<td>Q-wave pattern</td>
<td>115</td>
<td>40</td>
<td>12</td>
<td>11.1</td>
<td>17.3</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>54</td>
<td>Inferior</td>
<td>STT changes</td>
<td>140</td>
<td>105</td>
<td>47</td>
<td>31.6</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>54</td>
<td>Anterior</td>
<td>LBBB</td>
<td>225</td>
<td>143</td>
<td>7</td>
<td>3.3</td>
<td>8</td>
<td></td>
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<tr>
<td>7</td>
<td>M</td>
<td>57</td>
<td>Posterior</td>
<td>Q-wave pattern</td>
<td>175</td>
<td>115</td>
<td>11</td>
<td>4</td>
<td>8.5</td>
<td></td>
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<tr>
<td>8</td>
<td>F</td>
<td>55</td>
<td>Inferior</td>
<td>STT changes</td>
<td>170</td>
<td>115</td>
<td>12</td>
<td>6.6</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>49</td>
<td>Posterior</td>
<td>LBBB with Q-wave pattern chest leads</td>
<td>48</td>
<td>28</td>
<td>9</td>
<td>1.6</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

*EGG signifies electrocardiographic; CPK, creatine phosphokinase; SGOT, serum glutamate oxaloacetic transaminase; and LBBB, left bundle branch block.

†Normal, 2 to 25; mean, 14.5.

Table 2.—γ-Glutamyl Transpeptidase in Myocardial Infarction

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of Patients With Elevation in Activity</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>24-48 hr</td>
</tr>
<tr>
<td>Myocardial infarction (38 patients)</td>
<td>4</td>
</tr>
<tr>
<td>Not myocardial infarction (26 patients)</td>
<td>9</td>
</tr>
</tbody>
</table>

Standard curve used to calculate amount of β-naphthylamine liberated during enzyme incubation.

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Infarctions. All of these patients showed a marked rise in CPK and SGOT levels and most patients showed a rise in LDH level. These enzyme changes appear within 12 to 24 hours, persisted for an average of four days in the case of CPK, five days in the case of SGOT, and five to seven days in the case of LDH. Table 1 illustrates that only four patients showed significant elevation within 24 to 48 hours, with several other patients demonstrating top normal values and the majority of the results being well within the normal range. A review of data obtained from the fifth to the seventh days revealed six patients with elevated levels, two of whom had shown elevation early; these patients both had severe myocardial infarctions. Again, the remaining patients demonstrated values...
that were well within normal limits.

Between the seventh and 14th days, only one patient showed an elevated enzyme value; this was a patient with an extensive infarction, and he had elevated values persisting from the first 24 hours until the 12th day.

Table 2 illustrates the results obtained in both patients with definite myocardial infarction and in patients subsequently found not to have myocardial infarction.

Slightly over one third of the patients who did not have acute myocardial infarction showed elevation up to seven days and one patient exhibited elevation for 13 days. There was limited correlation between the location or severity of the infarction and the rise in γ-GTP activity, nor was the rise specific for age groups, complications of myocardial infarction, or other laboratory measurement of severity.

Comment

This study failed to demonstrate the previously described correlation between change in γ-GTP activity and acute myocardial infarction. A similar technique was employed for the assay of the enzyme and our normal values corresponded with those cited in the literature.1-8 In several of the patients with definite myocardial infarction, the enzyme procedure was repeated several times and results were consistently normal.

It has been postulated that the increased enzyme activity may be lacking in the first 48 hours as the result of washout of soluble enzyme from heart muscle without release of the particle-bound fraction. Most of the γ-GTP is particle-bound and can be released by conditions which affect particle membranes of the lysosomes.

The activity of γ-GTP has been shown to be elevated during viral hepatitis, chronic hepatitis, obstructive jaundice, liver cirrhosis, and intrahepatic metastatic carcinoma.9 Distribution of the enzyme in human tissues indicates that the highest enzyme activity is present in the kidneys, with the pancreas, liver, and spleen the next most common locations of high enzyme activity.

The discrepancy between our results and several prior studies may be related to several factors including heterogeneity of serum γ-GTP, lack of correlation between enzyme rise and severity of disease process, the many forms of liver disease affecting the behavior of this enzyme, technical problems in the handling of enzyme substrate, and differences in enzyme activity reported by differing investigators.

Kokot and Kuska9,10 demonstrated γ-GPT heterogeneity on starch electrophoresis with three separate peaks of protein activity. They indicated that leakage of enzyme from different organs may be responsible for the observed heterogeneity; large increase in serum activity of γ-GTP is only noted in the presence of liver disease. Szczeklik et al11 demonstrated a marked discrepancy between degree of tissue injury and enzyme activity. This probably accounts for some of the differing values noted in several studies.

Our many false-positive results are also probably related to the known presence or subclinical presence of liver disease and also liver congestion secondary to heart failure in many of the patients studied. A higher rate of synthesis of enzyme in the liver as an adaptive mechanism to abnormalities elsewhere has also been hypothesized to explain the lack of correlation between tissue injury and degree and duration of enzyme response. Agostoni et al12 also failed to demonstrate the early rise of enzyme activity after infarction and their data correlated well with ours in this regard. Poor solubility of substrate used in the laboratory procedure required the use of additional serum dilutions and this might affect the final data obtained.

These multiple factors would appear to account for the discrepancy between our study and several previously reported, and appear to make the use of this enzyme procedure less desirable than other enzyme procedures offering greater specificity and sensitivity. The patients originally thought to have acute myocardial infarction but later shown not to have this disease who exhibited rise in γ-GTP activity were reassessed for possible liver or kidney disease in an effort to determine the cause of the false-positive elevation. In three of the nine patients, liver disease was demonstrable, though not in an acute form; four other patients had hepatic congestion secondary to heart failure; in one of the remaining two patients, heavy alcohol ingestion preceded the elevation of γ-GTP activity; the other patient had a pulmonary embolus.

It would appear from this study that γ-GTP activity is not a sufficiently reliable indicator of acute myocardial infarction and is rarely elevated for any period of time so as to provide useful information on a patient with an older myocardial infarction. This enzyme procedure clearly has significant limitations in that elevation may be shown in a number of diverse conditions. Sensitivity is also low, with less than one third of patients with myocardial infarction showing an elevated enzyme activity.

References