ECG AND ENZYMATIC INDICATORS OF THERAPEUTIC SUCCESS AFTER INTRA-VENOUS STREPTOKINASE FOR ACUTE MYOCARDIAL INFARCTION - A PILOT STUDY

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ABSTRACT

The effect of intravenous streptokinase (SK) on time course of creatine kinase-MB (OK-MB) release and rapid reduction in ST-segment elevation as two non-invasive markers of reperfusion was prospectively studied in 83 patients with first anterior wall AMI (SK group, n = 61; control group, n = 22). OK-MB evidence of reperfusion in the SK group was significantly higher than that in the control group (80% versus 32%; P < 0.0001). The rapid resolution of sum of ST segment elevations as an evidence of reperfusion was found in 82% patients in SK group versus 23% in the control group (P < 0.0001). Both GK-MB and rapid resolution of ST segment elevations as evidences of reperfusion were found in 69% patients in SK and 14% in the control group (P < 0.0001). The proportions of patients with non-invasive evidence of reperfusion with half-dose SK (750,000 units) regimen were comparable to that reported in the literature with full dose SK (1.5 million) regimen. Thus, serial CK-MB and EGG analysis in patients with AMI undergoing streptokinase therapy provides a non-invasive means for assessing therapeutic success. A dose of 750,000 units of SK was found clinically satisfactory using previously validated non-invasive markers of coronary reperfusion and produced results previously reported with 1.5 million units of SK (JPMA 42: 288, 1992).

INTRODUCTION

Thrombolytic therapy in acute myocardial infarction (AMI) has been shown to be effective in limiting infarct size, preserving left ventricular functions and reducing short and long term mortality. Coronary angiography immediately after thrombolytic therapy is the most accurate way to document coronary artery patency. However, only a few medical centres can provide timely angiographic evidence of reperfusion for each patient with AMI. Early relief of chest pain, rapid reduction in ST segment elevation, early peaking of serum creatine kinase and reperfusion arrhythmias are some of the markers used to predict reperfusion noninvasively. The present study was done to assess the usefulness of rapid resolution (reduction) of ST segment elevation and early peaking of CK-MB as noninvasive markers of myocardial reperfusion in patients treated with intravenous streptokinase or conventional therapy and assess the relative efficacy of half-dose (750,000 units) of intravenous streptokinase in causing coronary reperfusion (determined by above-mentioned non-invasive markers) as compared to the efficacy of full-dose (1.5 million units) of streptokinase (reported in the literature).

PATIENTS AND METHODS

Eighty-three patients with acute anterior wall myocardial infarction seen between May, 1990 and October, 1991 at National Institute of Cardiovascular Diseases, Karachi were included in the study. Sixty-one patients were given streptokinase (SK group) and twenty two patients (control group) were treated with conventional therapy. Inclusion criteria were ischemic chest pain of at least 30 minutes or more but less than 4 hours duration, ST segment elevation of at least 2 mm in two consecutive
precordial leads, persistence of chest pain and ECG changes after sublingual nitroglycerin and age less than 60 years. Exclusion criteria were inferior and isolated high lateral wall M.I., age over 60 years, left bundle branch block, dilated cardiomyopathy and contraindication to streptokinase. A dose of 750,000 units streptokinase (streptase) diluted in 50 ml 5% D/W was given intravenously in 30 minutes. Concomitantly, a bolus of 5000 IU of heparin was infused followed by 24,000 IU per 24 hours. The dose was adjusted to keep the activated partial thromboplastin time 1.5 to 2 times the baseline. Heparin infusion was continued for at least five days except when patients bled. Disprin (150 mg) was given daily. Conventional anti-anginal and anti-congestive treatment was used as needed. Blood samples were obtained before the start of streptokinase infusion and sent to laboratory for baseline CK-MB and activated partial thromboplastin time (APTr). Thereafter blood samples were taken at 4 hour intervals for the first 24 hours for determination of CK-MB activity. For each patient, the time from streptokinase administration to peak CK-MB was noted. Electrocardiograms recorded before thrombolysis and 4 hours after start of streptokinase were analysed for resolution of ST segment elevations. The sum of ST segment elevations on the electrocardiograms recorded at admission and 4 hours after the start of treatment was calculated. The reduction in sum of ST segment elevations after thrombolytic treatment was expressed as a percentage reduction from the initial value of sum of ST elevations. Maximal CK-MB activity within 12 hours after the start of streptokinase therapy was considered a positive marker of infarct-related artery reperfusion. A positive ST marker was defined as a reduction in sum of ST segment elevation of?: 50% within 4 hours after the start of thrombolysis. The statistical analysis was performed using the Z-test for comparing the difference of two proportions. P< 0.05 was taken as statistically significant. In addition Student’s t test for independent samples was used for comparing the means of two groups.

RESULTS
The study included 83 patients, 22 in the control group and 61 in the streptokinase (SK) group. Clinical characteristics were similar between the two groups. There was a significant difference in time from streptokinase administration to peak CK-MB, between the control and streptokinase groups. This difference resulted in a higher proportions of patients in the streptokinase group having enzymatic evidence of reperfusion (80% versus 32%, P <0.0001) (Table I).

<table>
<thead>
<tr>
<th>TABLE I. Proportions of patients with ECG and enzymatic indicators of therapeutic success.</th>
<th>Control (n=22)</th>
<th>Streptokinase (n=61)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with CK-MB reperfusion</td>
<td>7 (32%)</td>
<td>49 (80%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Patients with rapid resolution of ST segment elevations</td>
<td>5 (23%)</td>
<td>50 (82%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Patients with both markers of myocardial reperfusion</td>
<td>3 (14%)</td>
<td>42 (69%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
As shown in Table II there was no significant difference in the mean sum of ST-segment elevations (in mm) at presentation between the SK and control groups 120.4 (4-56) versus 20 (6-48). However, there was marked difference in the mean sum of ST segment elevations (in mm) at 4 hours from initiation of streptokinase between SK and control groups [5.9 (0-22)] versus [13.4 (6-34)]. Similarly the mean percent resolution of the sum of ST segment elevations at 4 hours was also markedly different in SK and control groups [7 1.5% (100%-No resolution)] versus [33% (11%-No resolution)]. These differences resulted in a much higher proportion of patients in the streptokinase group having?: 50% reduction in the sum of ST segment elevations at 4 hours from the initiation of streptokinase as compared to initial sum as an indicator of reperfusion (i.e., therapeutic success) (82% versus 23%, P <0.0001). The combined analysis of two markers of reperfusion also revealed highly significant between SK group and P<0.0001) (Table I).

**DISCUSSION**

Results of the present study suggest the ability of non-invasive methods to identify patients who benefit from thrombolysis for AMI and to predict reperfusion status to a clinically useful degree. The study describes the assessment of myocardial reperfusion by two non-invasive methods (early peak of CK-MB and rapid resolution of sum of ST segment elevations). Considering CK-MB peak, a cut off value of 12 h after the start of thrombolysis was derived from a trial conducted by Meinertz et al\(^1\). In a recent study, Hohnloser et al\(^9\) used the same cut off value as a non-invasive marker of coronary artery patency and revealed a sensitivity of 84% and a specificity of 95%. Gottlich et al\(^13\) used following
criteria for CK-MB determined reperfusion: time from onset of chest pain to peak CK < 17 hours and
time from SK to peak CK< 15 hours. In their study, CK-evidence of reperfusion was found in 75%
patients given 500,000 units SK, 89% given 750,000 units SK and 67% given 1.5 million units SK. The
present study documents the usefulness of the standard ECG ST segment as a non-invasive predictor of
coronary artery reperfusion after intravenous SK for AML In the present study, _ 50% reduction in sum
of ST segment elevations at 4 hours after SK was used as an indicator of reperfusion; 82% patients
fulfilled this criteria versus 23% control group, (P<0.0001). These findings are consistent with many
recent studies. Hogg et al reported a high sensitivity (93%) for a fall of _ 50% in the lead showing
maximum ST elevation, with a specificity of 67%. Workers evaluated whether angiographically deter-
mined reperfusion could be predicted from changes in ST segment elevation. According to Saran et
at reduction in ST elevation of >25% within 3 hours of thrombolysis indicates either a patent infarct
artery or preservation of left ventricular function. When the ST segment elevation does not fall by
>25% persistent coronary occlusion is likely (predictive accuracy 86%). Clemmensen et al compared
the sum of ST segment elevation before and after (<8 hours, pre-angiographic from onset of symptoms)
thrombolytic therapy and concluded that a decrease of only 20% in the sum of ST elevation in the
standard ECG after thrombolytic therapy is a useful non-invasive predictor of reperfusion status in
patients with evolving AMI. In a recent study, Hohnloser et at defined _ 50% reduction in ST segment
elevation as a positive non-invasive marker of coronary reperfusion and found a value of 60%
sensitivity, 95% specificity and 97% positive and 42% negative predictive value regarding prediction of
coronary artery patency. The half dose (750,000 units) regimen of streptokinase therapy used in the
present study is supported by another study, where it was concluded that if sufficient streptokinase is
given to produce a systemic fibrinolytic state, smaller doses (500,000 and 750,000 units) are as
effective as larger ones (1.5 million units) in inducing coronary reperfusion. This is a small pilot trial
done in local patients, using previously validated non-invasive markers of coronary reperfusion against
the gold standard of coronary angiography. Patients were not randomized with standard and half dose
SK regimens. Before the half dose SK regimen can be recommended on routine basis, large
randomized trials comparing the standard and half dose groups mortality would be required.

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