

Streptokinase in STEMI: ninety minute ECG for ST resolution; experience in an acute medical unit

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Abstract

Streptokinase is the main thrombolytic used for the management of ST Elevated Myocardial Infarctions (STEMI) in Sri Lanka. We assessed the efficacy of streptokinase in restoring myocardial perfusion following acute STEMI. One hundred and eight patients were studied. Sixty eight (56%) patients responded to streptokinase. Forty five (41.7%) had anterior STEMI and 20 (44.4%) responded ($p < 0.001$). Forty four had inferior STEMI and 32 (72.7%) responded ($p = 0.007$). Fifteen had antero-lateral STEMI and 13.3% responded. Time from the onset of pain to arrival at hospital was 137 in responders and 339 minutes in non responders ($p = 0.004$). Eight (11.8%) responders and four (10%) non responders were on aspirin. Thirty two (47.1%) responders and 16 (40%) non responders were smokers. Twenty (29.4%) responders and 9 (22.5%) non responders were having diabetes mellitus. Considerably higher percentage responded to streptokinase. Inferior myocardial infarctions have significantly high reperfusion rates. Delayed hospital admission had a major impact in the non responders.

Introduction

Fibrinolytic agents are the mainstay to attain reperfusion following ST-elevation myocardial infarction. They provide rapid, complete and sustained restoration of normal flow in the Infarct Related Artery (IRA) which results in reduced morbidity and mortality. Two techniques have been deployed to assess the myocardial reperfusion. The angiographic method is invasive and is not readily available at many centers in the world¹. Demonstration of the resolution of ST

elevation on the surface electrocardiogram (ECG) following coronary reperfusion is easy to and is vastly available due to its simplicity and the low cost². The angiogram measures epicardial blood flow in contrast to micro vascular circulation that reflects myocardial perfusion measured by the electrocardiographic changes^{3,4,5,6}. Furthermore, ST resolution has been found to be correlated strongly with myocardial contrast echocardiography findings⁶. Therefore, ST resolution is associated with prognostic implications in patients either receiving fibrinolytic agents or undergoing primary coronary angioplasty following STEMI^{7,8,9,10,11,12,13}.

Streptokinase revolutionized the management of myocardial infarction¹⁴. GISSI trial established the benefits of streptokinase in reducing both morbidity and mortality following acute myocardial infarction¹⁵. Streptokinase still holds its position as one of the most widely used drugs in the management of acute myocardial infarction in many parts of the world including Sri Lanka. Streptokinase is being used in Sri Lanka for the management of STEMI since the mid 1980s¹⁶. However, the safety and the efficacy of streptokinase in acute myocardial infarction have not been assessed on Sri Lankan population to date. We sought to determine the efficacy of streptokinase in restoring myocardial perfusion following acute myocardial infarction. We assessed myocardial reperfusion by analysing 60-minute ST resolution on surface ECG, and sought to identify the predictors of ST resolution.

Methods

We conducted a prospective study on consecutive patients admitted to the Professorial Medical Unit, Colombo South Teaching Hospital from 1st November 2008 to 31st October 2009 with a diagnosis of STEMI. Acute myocardial infarction was diagnosed by ischaemic chest discomfort ≥ 30 minutes in duration and ST segment elevation ≥ 0.1 mV in two contiguous limb leads or ≥ 0.2 mV in two contiguous precordial leads. We limited the analysis to cases in which 1.5 million units of streptokinase were given and 12-lead ECGs before and 90 minutes after the administration of streptokinase were recorded.

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ECG Analysis

ECGs of patients were analyzed by the Medical Registrar of the ward. The magnitude of ST segment elevation was measured manually 20ms after the end of the QRS complex from leads I, aVL and V1 to V6 for anterior and antero lateral MI and leads II, III, aVF for inferior MI. Reciprocal ST depression ≥ 0.1 mV in leads II, III and aVF for anterior MI and in leads V1 to V4 for inferior MI were included. The sum of ST deviation was calculated at baseline and 90 minutes after initiation of streptokinase. The percent resolution of ST deviation was calculated and categorised into two groups; resolution ($\geq 50\%$) and no resolution (0% to $<50\%$).

Statistical Analysis

Continuous variables were expressed as mean \pm SD and 95% confidence interval where appropriate. Categorical variables were compared using Pearson Chi square tests or Fisher's exact test where appropriate. Continuous variables were compared using one-way analysis of variance (ANOVA) (F tests). A logistic regression analysis using forward technique was employed to determine significant independent predictors of complete ST resolution. A significant level was defined when $p < 0.05$. Data were analysed using the SPSS 16 software package SPSS Inc., Prentice Hall, New Jersey

Results

Our study group consisted of 83 male and 25 female patients. The clinical characteristics of the

patients are summarized in the Table 1. The mean age of the group was 58.5 years. Sixty eight (56%) patients (52 (60%) males and 16 (61%) females) responded with more than 50% reduction in the ST segment following streptokinase. Forty five (41.7%) patients had anterior STEMI and 20 (44.4%) responded to streptokinase. There were 44 patients with inferior STEMI and 32 (72.7%) patients responded to streptokinase. Eight responders (11.8%) and four (10%) non responders were on aspirin and, two responders were on clopidogrel. Seven (10.3%) responders and six (15%) non responders were on statins. 32 (47.1%) responders and 16 (40%) non responders were smokers. 20 (29.4%) responders and 9 (22.5%) non responders were having diabetes mellitus. There were 10 (14.7%) and 7 (17.5%) hypertensive patients in the responders and non responders respectively.

There was a higher response in ECGs from those with ST elevation in the inferior leads II, III, aVF ($p=0.007$). The response rate to streptokinase in relation to the pattern of ST elevation is given in Tables 2 and 3. The time from the onset of pain to arrival at the hospital was 137 in responders and 339 minutes in the non responders. The time difference was statistically significant between the responders and non responders. ($p=0.004$). The door to needle time was 102 in responders and 89 minutes in the non responders. 26 (38.2%) responders and 11 (27.5%) non responders developed complications following myocardial infarction. The summary of complications is given in Table 4. Left ventricular failure (LVF) was reported in 11 (16.2%) patients who responded to streptokinase.

Table 1. Clinical characteristics of the patients treated with streptokinase

	<i>Number of responders</i>	<i>Number of non responders</i>	<i>Total</i>
Mean age	58.1	59.2	58.5
Male	52	31	83
Female	16	9	25
Diabetes mellitus	20	9	29
History of smoking	32	16	48
History of hypertension	10	7	17
Prior thrombolysis	1	1	2
Previous aspirin therapy	8	4	12
Previous statin therapy	7	6	13
Previous clopidogrel therapy	2	0	2
Door to needle time	102	89	97
Onset of pain to hospital	137	339	210

Table 2. Distribution of STEMI according to the area of myocardium involved

<i>Type of STEMI</i>	<i>Responders Number</i>	<i>Non responders Number</i>	<i>Total No of patients (%)</i>	<i>Significance P value</i>
Anterior	20	25	45 (41.7%)	< 0.05
Antero inferior	1	1	2 (1.8%)	>0.05
Posterior	0	1	1 (0.9%)	> 0.05
Inferior	32	12	44 (40.7%)	< 0.05
Antero lateral	2	13	15 (13.9%)	> 0.05
Anterior + Antero lateral	22	38	60 (55.6%)	>0.05

Table 3. Statistical significance of ST resolution following streptokinase therapy according to the area of myocardium involved

<i>Type of STEMI</i>	<i>Positive responders (%)</i>	<i>P value</i>
Anterior vs Inferior	44.4 / 72.7	0.007
Anterior vs Antero lateral	44.4 / 13.3	<0.001
Anterior vs Anterior + Antero lateral	44.4 / 36.7	0.284
Antero lateral vs Inferior	13.3 / 72.7	<0.001
Anterior + Antero lateral vs Inferior	36.7 / 72.7	0.065

Table 4. Complications following STEMI treated with streptokinase

<i>Type of complication</i>	<i>Number of patients</i>	
	<i>Responders</i>	<i>Non responders</i>
Low blood pressure 2	0	
Angina	3	0
Bleeding	4	0
Deaths	0	1
Left ventricular failure	12	4
Cardiac shock	2	2
Ventricular fibrillation	2	3
Ventricular tachycardia	1	1
Total	26	11

Discussion

This is the first study in Sri Lanka to our knowledge that analyzed myocardial reperfusion following thrombolytic therapy for myocardial infarctions, using ST resolution at 90 minutes. European studies have shown a 50% complete resolution at 180 minutes in Caucasian patients⁷. In an Asian population complete resolution at 60 minutes was found in only 24%². Our results have shown a much improved value (63%) at 90 minutes.

The time from onset of pain to arrival at the hospital is considerably longer in the non responders compared to the responders. Although not statistically significant ($p > 0.05$), the door to needle time is prolonged in the latter group. The total time duration from onset of pain to the initiation of streptokinase is longer in the non responders. Responders have arrived at the hospital without delay which could have contributed to the higher response rate in that group. Delayed hospital admission may have been one of the reasons for the lower response rate in the other group. However, the door to needle time in both groups is alarmingly prolonged. It is a vital area to improve in achieving a better outcome in the management of acute myocardial infarction. Delay in taking ECGs in these patients was identified as one of the reasons for treatment delay. Providing ECG apparatus to all the medical wards with adequate training to the nursing staff and the junior doctors would eliminate a major constraint in the management of acute myocardial infarctions.

The percentage of 90 minute ST Resolution (STR) in our cohort is considerably higher than previous studies. However, the mean age of our study population is relatively lower and older patients in those studies may have responded poorly to the streptokinase therapy. There is no significant difference in the response to streptokinase between males and females ($p > 0.05$).

The success rate with streptokinase is significantly higher in the patients with inferior myocardial infarctions ($p < 0.05$). Patients with anterior myocardial infarctions had a less success with streptokinase therapy ($p > 0.05$). However, the patients with anterior MIs had significantly higher success with streptokinase therapy when compared with antero lateral and antero inferior myocardial infarctions. It would emphasize that the success of thrombolytic activity of streptokinase is significant when the extent of infarction is confined to a smaller area of the heart. However, it is noteworthy to mention that the successful thrombolysis against anterior myocardial infarctions is clinically important because anterior myocardial infarctions carry a higher

mortality. It also reiterates the necessity of coronary interventions in patients with extensive myocardial ischemia with more than single vessel disease.

A sub analysis of GUSTO 111 confirmed that ninety minute STR is correlated with STR at 180 minutes and, therefore low rate of mortality at 30 days and at one year¹⁸. Nevertheless, the effects of early STR against long term mortality in our patients remained to be found. A significantly higher success with early STR at ninety minutes compared to the other studies make it interesting to find whether it is really correlate with angiographic evidence.

In addition, the reperfusion is a dynamic process and, some cardiologist advocate for continuous ECG monitoring to elucidate dynamic ST segment recovery. Although early STR has found to correlate with the long term mortality, the prognostic implications of ST segment fluctuations have not been studied in depth. Fortunately, an early variability of STR has played only a minor role in the quality of outcome¹⁷. Therefore, it is unclear whether our patients with very high early STR are showing a real and persisting coronary patency following thrombolysis.

The influence of prior anti platelet therapy with both aspirin and clopidogrel were found to be not statistically significant ($p > 0.05$). Prior use of statins, smoking, diabetes, and hypertension did not show any significant association with regards to response to SK. But, our numbers in these categories were small in each arm and this would be a possible explanation.

As with most studies, we used the resolution of the sum of ST-segment elevation (sum STR) after reperfusion therapy. Implications of sum STR has been valued because it is used to predict infarct size, left ventricular function, epicardial vessel patency, and mortality^{5,7,13,19,20}. Although time consuming, measuring ST-segment elevations from all leads relate to infarct location and size which could be used to compare with angiographic evidence later. However, some authors prefer to use single lead STR claiming the simplicity and relatively higher predictive accuracy²¹.

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