Original Article

Streptokinase Study on ST Segment Resolution in Patients age Less Than 40 Years with Myocardial Infarction

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ABSTRACT

Background: Thrombolytic therapy for Acute Myocardial Infarction has been one of the most potent treatment ever developed for condition that kill more patients worldwide than any other.

Objective: To evaluate the benefit and efficacy or observational studies of streptokinase therapy on ST-segment elevation resolution in different types of myocardial infarction that focus especially on the younger age group less than forty years.

Study design: To observe the streptokinase therapy, in ST-segment elevation resolution, in age less than 40 years and in different types of myocardial infarction.

Place and Duration of Study: The study was conducted at national institute of cardiovascular diseases (NICVD) of Pakistan, Karachi.

Materials and Methods: All patients fulfilling the inclusion criteria for thrombolytic therapy were included. Baseline ECG recorded before streptokinase infusion and repeated at completion of infusion i.e. 90 minutes, day 1 and day 2.

Results: Streptokinase therapy on blood pressure, CKMB, and ST-segment resolution at 90 minutes, day 1, and Day2 in less than 40-year of age patient. The mean systolic blood pressure was 124$\pm$ 3.32 and 112$\pm$3.00 pre and post SK therapy reflecting a percentage decrease of 6.67 and highly significant ($P<0.001$). The Diastolic blood pressure was decrease to 6.25% with a mean value of 76.80$\pm$ 2.70 and 72$\pm$1.91 before and after the Streptokinase therapy's, segment resolution at 90 minutes was decreased to 52.01 percent from the baseline and continued to decrease at Day-1 and Day-2 with a percentage reduction of 70.65 and 83.69 % respectively. The P values were highly significant ($P<0.001$).

Conclusion: Thrombolysis improves survival when given within 12 hours of the onset of symptoms. The magnitude of benefit is greatest when reperfusion is established early. Age itself should not be considered a contraindication for fibronolysis

Key Words: Streptokinase, ECG, ST-Elevation, Myocardial infarction.

INTRODUCTION

Cardiovascular diseases (VCD) are the leading cause of death and disability in developed nations and are increasing rapidly in the developing world.

Coronary atherosclerosis is by far the most frequent cause of ischemic heart disease and plaque disruption with superimposed thrombosis is the main cause of acute coronary syndrome of unstable angina, myocardial infarction and sudden death[1, 2].The true frequency of atherosclerosis is difficult, if not possible to accurately determine because it is a predominantly asymptomatic condition. More advanced lesions begin to develop when individuals are aged approximately 25 years.

Plaque rupture is probably the most important mechanism underlying the unpredictable rapid progression of coronary lesions[3].The role of platelets in acute coronary syndromes begins with the exposure of the sub-endothelium after plaque rapture. Thrombosis develops on a plaque either because the plaque tear open (rupture) exposing the highly thrombogenic core to blood in arterial lumen [4].

ST-segment elevation is an excellent marker of acute coronary occlusion in which reperfusion therapy is needed. Patient with non ST elevation of myocardial infarction have a thrombotic stenosis in the affected artery but the artery is usually patent ,in contrast ST-elevation myocardial infarction the artery is occluded and at base line flow cannot be worsen, it can only improve [5].

The most frequently use electrocardiographic criteria for identifying acute myocardial infarction is ST-segment elevation where ST-segments are (re) emerging as a clinical tool of great importance. Evaluating the response to thrombolytic therapy that early resolution of ST-segment elevation is a useful mean of assessing perfusion [6].

Thrombolytic therapy is that early and sustained recanalization prevents cell death, reduces infarct size, preserves myocardial function, and reduces early and late mortality [7]

Purpose of study: The current evidences indicate that early thrombolytic therapy can limit extent of myocardial necrosis in evolving myocardial infarction may be early restoration of coronary blood flow, preserve left ventricular function and reduce mortality in patients with acute myocardial infarction (AMI)

Primary Objective: To observe the streptokinase therapy, in ST-segment elevation resolution, in age less than 40 years and in different types of myocardial infarction.

Secondary Objective: To observe the toxicity of streptokinase.

MATERIALS AND METHODS

The study was conducted in the Department of Pharmacology and therapeutics, Basic Medical Sciences Institute Jinnah Post-graduate Medical Centre in collaboration with National Institute of Cardiovascular diseases (NICVD) of Pakistan, Karachi. The study was approved by the postgraduate committee at NICVD. Informed consent for administration of thrombolytic drug was obtained from each patient.

Inclusion criteria: Less than 40 years.
Chest pain suggestive of myocardial infarction
ECG findings of ST-Segments elevations.

Exclusion Criteria: Active internal bleeding
Cerebro-vascular accident
Blood pressure>200/100 mmHg
Pregnancy
Allergic reaction to streptokinase
Previous Coronary Artery bypass Graft

Materials: Streptokinase (Streptofactor, Hakimsons/ Eskinase, Medinet), 1500000 units.
Sphygmomanometers, Cardiac monitor,
Electrocardiograph,

Methods:

Criteria of ST-segment resolution: A positive ST-marker was defined as a reduction in ST-segment elevation of more than 50% within 90 minutes after the start of thrombolytic therapy.

Treatment of Plan:

- All patients fulfilling the inclusion criteria for thrombolytic therapy were included and admitted to either coronary care unit or place in the ward with and continuously monitored for arrhythmias.
- Baseline 12 lead electrocardiogram was taken
- Two intravenous lines were maintained, one in each arm. One I/V line used for medication and another for collection of blood samples.
- Blood sample for complete blood count, erythrocyte sedimentation rate, urea creatinine, blood glucose, cardiac enzymes and lipid profile, activated partial thromboplatin time.
- Tablet aspirin 150 mg was given once for 24 hours.
- Isosorbide dinitrate I/V infusion 10-20 ug/min followed by oral nitrates
- Streptokinase 1.5 million units dissolved in 100 ml 5% dextrose water infused in 60 minutes.
- Vital signs 10 minutes during the infusion.
- The 12 lead electrocardiograms were recorded
- Baseline ECG recorded before streptokinase infusion and repeated at completion of infusion i.e. 90 minutes, day 1 and day 2.

RESULTS

During the four months study period 50 patients were included in the study after fulfilling the inclusion criteria for thrombolytic therapy.

Demography of patients with acute myocardial infarction exhibits that there were 46 (92%) males and 4 (8%) females, of these 50 patients 30 (60%) had an anterior wall infarction, while 20 (40%) suffered from an inferior wall infarction. No patient had a lateral wall acute myocardial infarction. Two patients died and cause of death was ventricular fibrillation in this patient.

Table-1 shows the effects of streptokinase therapy on blood pressure, CKMB, and ST-segment resolution at 90 minutes, day-1, and Day-2 in less than 40-year of age patient. The mean systolic blood pressure was 124$\pm$ 3.32 and 112$\pm$3.00 pre and post SK therapy reflecting a percentage decrease of 6.67 and high significant ($P<0.001$). The Diastolic blood pressure was decrease to 6.25% with a mean value of 76.80$\pm$ 2.70 and 72$\pm$1.91 before and after the Streptokinsae therapy. ST-segment resolution at 90 minutes was decreased to 52.01 percent from the baseline and continued to decrease at Day-1 and Day-2 with a percentage reduction of 70.65 and 83.69 % respectively. The P values were highly significant ($P<0.001$).

Table-2 shows the effects of Streptokinase therapy according to the site of Myocardial Infarction in less than 40-years of age. There were 30 patients out of 50 with anterior wall Myocardial Infarction. The mean value of Systolic Blood Pressure (SBP) before therapy was 120.67$\pm$ 4.08 and was decreased to 108.67$\pm$3.22 after therapy with Streptokinase. The Diastolic Blood Pressure (DBP) was decreased to 4.47 percent post Streptokinase therapy. The ST segment shows a resolution of 51.6% 72.3% and 83.07% at 90 minutes, day-1 and day-2 respectively. The P value for SBP, DBP and ST-segment resolution was highly significant ($P<0.001$).

Table-3 includes patients with inferior wall infarction in less than 40-years. Twenty patients present with this type of infarction. Two patients died because of

ventricular fibrillation within one hour of infusion. There was highly significant value of for SBP, DBP and ST-segment resolution. The mean Systolic Blood Pressure value was 129.00 ±5.47 before therapy and decrease to 117.00± 5.59 post Streptokinase therapy which shows a percentage decrease of 9.30.

Table No.1: Myocardial infarction patients of less than 40-years of age Percentage changes from Pre to Post Streptokinase therapy

Variables	No of observation	(Mean ± SEM) Pre SK Therapy	(Mean ± SEM) Post SK Therapy	% change Pre to Post	p-Value
SBP (mmHg)	48	124.00 ± 3.32	112.00 ± 3.00	(-) 9.67	0.001***
DBP (mmHg)	48	76.80 ± 2.70	72.00 ± 1.91	(-) 6.25	0.001***
CKMB (IU)	48	52.64 ± 2.49	150.52 ± 6.69	185.94	0.001***
ST Resolution 90 min	48	1.92 ± 0.15	0.92 ± 0.20	(-) 52.01	0.001***
ST Resolution day 1	48	1.92 ± 0.15	0.56 ± 0.08	(-) 70.65	0.001***
ST Resolution day 2	48	1.92 ± 0.15	0.31 ± 0.08	(-) 83.69	0.001***

Pharmacological action of Streptokinase therapy on blood pressure, CKMB and ST-Segment elevation resolution
*** Highly Significant
(-) Shows decrease from pre to post streptokinase therapy

Table No.2: The effects of Streptokinase therapy according to the site of Anterior wall Myocardial Infarction in >40 year of age

There were 30 patients out of 50 with anterior wall MI.

Variables	No of observation	(Mean ± SEM) Pre SK Therapy	(Mean ± SEM) Post SK Therapy	% change Pre to Post	p-Value
SBP (mmHg)	30	120.67 ± 4.08	108.67 ± 3.22	(-) 9.94	0.001 ***
DBP (mmHg)	30	74.67 ± 1.65	71.33 ± 1.92	(-) 4.47	0.001 ***
CKMB (IU)	30	52.13 ± 2.90	152.6 ± 9.00	192.86	0.001 ***
ST Resolution 90 min	30	2.17 ± 0.19	1.05 ± 0.29	(-) 51.6	0.001 ***
ST Resolution day 1	30	2.17 ± 0.19	0.60 ± 0.01	(-) 72.3	0.001 ***
ST Resolution day 2	30	2.17 ± 0.19	0.37 ± 0.11	(-) 83.07	0.001 ***

Pharmacological action of Streptokinase therapy on blood pressure, CKMB and ST-Segment elevation resolution
*** Highly Significant
(-) Shows decrease from pre to post streptokinase therapy.

Table No.3: The effects of Streptokinase therapy according to the site of Inferior wall Myocardial Infarction in >40 year of age

There were 20 patients out of 50 with inferior wall MI.
Two patients died because of ventricular fibrillation within one hour of infusion

Variables	No of observation	(Mean ± SEM) Pre SK Therapy	(Mean ± SEM) Post SK Therapy	% change Pre to Post	p-Value
SBP (mmHg)	18	129.00 ± 5.47	117.67 ± 5.59	(-) 9.30	0.001 ***
DBP (mmHg)	18	80.00 ± 3.33	73.00 ± 3.96	(-) 8.75	0.001 ***
CKMB (IU)	18	53.40 ± 4.64	147.30 ± 11.52	175.84	0.001 ***
ST Resolution 90 min	18	1.50 ± 0.17	0.59 ± 0.12	(-) 60.44	0.001 ***
ST Resolution day 1	18	1.50 ± 0.17	0.50 ± 0.14	(-) 66.66	0.001 ***
ST Resolution day 2	18	1.50 ± 0.17	0.22 ± 0.09	(-) 85.18	0.001 ***

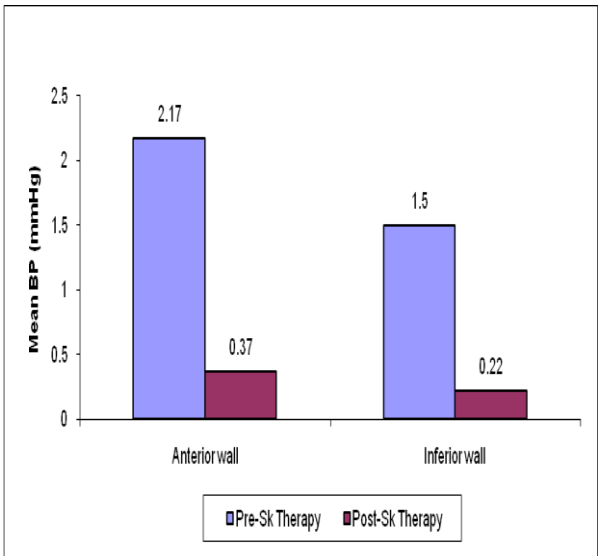
Pharmacological action of Streptokinase therapy on blood pressure, CKMB and ST-Segment elevation resolution
*** Highly Significant
(-) Shows decrease from pre to post streptokinase therapy

Table No.4: Duration of chest pain, Cholesterol, Random blood sugar and duration of patients stay at hospital

Group		Duration Chest Pain	Cholesterol	RBS	Hospital stay
		Hours	(mg/dl)	(mg/dl)	Days
Less than 40 years	n	50	50	50	48
	Mean ± SEM	4.56±0.54	218.84±8.67	132.16±13.82	5.29±0.47
	Range	2-12	132-290	59-392	4-15

Figure No.1:

	Pre-SK Therapy	Post-SK Therapy
Anterior wall	2.17	0.37
Inferior wall	1.5	0.22



ST- Resolution according to site of myocardial infarction in less than 40 years age Patients

The Diastolic Blood Pressure showed a percentage decrease of 8.75. The ST elevation before therapy was 1.50± 0.17, which was resolved to 0.59± 0.12, 0.50 ± 0.14 and 0.22± 0.09 at 90-minutes, day-1 and day-2, showing a percentage decrease of 60.44, 66.66 and 85.18 respectively. The P value was also highly significant (P<0.001).

Table-3 shows the comparative percentage change in the <40 age according to the site if myocardial Infarction group with anterior wall infarction there was a percentage change of 9.94, 4.47, 72.3 and 83.07 of SBP, DBP and ST-segment resolution at 90 minutes, day1, and day2, as compared to a percentage decrease of 9.30, 8.75, 60.4, 66.6, and 85.18 in patients with inferior wall myocardial Infarction

Table-4 shows the mean value of other variables in the less than 40 years age patient. The mean duration of chest pain was 4.56± 0.54 hours. The minimum chest pain duration was 2 hours and maximum it was 12 hour. The mean stay at hospitals was at hospital was 5.29 ± 0.47from a period of 5-days to 15-days.

The complications of Streptokinase therapy in less than 40 years age patients was, that out of 50 patients two died because of ventricular fibrillation, which could have been due to reperfusion arrhythmias or the arrhythmias as a normal cardiac event in Myocardial Infarction.

DISCUSSION

The best reperfusion treatment is one that achieves the highest rate of early, complete, and sustained infract-related artery patency in the largest number of patients, but with the lowest rate of undesirable effects.

Emergency management of acute myocardial infarction is evolving at an extremely rapid pace. What nearly all mortality reducing strategies have in common is, prompt restoration of blood flow to ischemic myocardium that has been compromised by intra-coronary thrombosis. Three clinical criteria have been proposed as markers for myocardial perfusion is reduction of chest discomfort (pain), improvement of electrocardiographic ST-segment elevation, and reperfusion arrhythmias. These clinical signs have been shown to be related to coronary artery recanalization and prognosis. Resolution of chest pain is very subjective and may frequently be related to analgesic medicine, cardiac arrhythmia could be a part of arrhythmias complicating acute myocardial infarction Resolution of ST-segment elevation has been shown to be a simple and useful predictor of final infarct size, left ventricular function and clinical outcome after thrombolytic therapy.

Though the use of thrombolytic therapy decrease with increased age, but should not be considered a contraindication [8]. This study was conducted to observe the efficacy and complication of streptokinase therapy in young less than 40 years age patient.

The results of the present study suggest that streptokinase is effective and reduces the percentage resolution of ST-segment elevation. It is also suggested this therapy should be offered to all patients presenting with ST-segment elevation of acute myocardial infarction.

Our study matches with the study of Laurie.A.Otto [9] which provided careful and detailed analysis of trial with specific regard to beneficial-to risk ratio for patients.

Our study matches with the GISSI-study [10] in hospital mortality was 2 to 9 percent for patients 61 to 70 years old as compared with younger patients. In our study the in hospital mortality was 4 percent in patients younger than 40 years.

Present study has demonstrated rapid restoration of coronary blood flow in patients with evolving myocardial infarction. Our study matches with the study of Schroder R[11] .who performed short term infusion of streptokinase in 93 patients within six hours after the onset of acute myocardial infarction.

Our study matches with Fibrinolytic Therapy Trials Collaborative (FTT) group study[12]. The data of the study do not provide evidence from withholding fibrinolytic therapy from patients on the basis of age. The excess of death in this study on day 0 to 1 increased with age but so did the reduction in death during days 2 to 35. The absolute mortality reduction seems much the same among younger and older patients. We do have early death in our study, two patients died within twelve hours of the start of therapy, whereas the patients discharged continue to do well

Our study did match with the study of Thiemann et al [13]. This study reported an analysis of 7864 patients treated with thrombolytic therapy. After thrombolysis there was survival benefit in younger patients. The complications rates were up to 16 percent in old age but were of minor nature.

CONCLUSION

The present study has demonstrated rapid restoration of coronary blood flow in patients with evolving myocardial infarction. Although intra-coronary application may be somewhat more effective, the advantage of intravenous administration is striking.

Considering the experience of others we concluded that I/V short term infusion of streptokinase can be performed safely in patients with evolving myocardial infarction.

One limitation of the administration of an intravenous infusion of streptokinase is that it can cause a significant fall in systemic blood pressure and rapid infusion of high dose intravenous streptokinase frequently causes transient and sometimes severe fall in blood pressure, the magnitude of which is directly related to the rate of infusion of streptokinase.

The clinical results are encouraging. Yet, to ascertain the true impact on short and long term morbidity and mortality from acute myocardial infarction.

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