ORIGINAL ARTICLE

Evaluation of S-T Resolution by Streptokinase Therapy in Patients of Myocardial Infarction among the Age Group of more than 60 Years

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ABSTRACT:

Objective: To evaluate the benefit and efficacy of streptokinase therapy on ST-segment elevation resolution in different types of myocardial infarction in more than 60 years age group.

Materials and Methods: This Hospital based cross sectional study was conducted at National Institute of Cardiovascular Diseases (NICVD) of Karachi, Pakistan. The study included patients more than 60 years of age having different types of myocardial infarction. Fifty patients both male & female fulfilling the inclusion criteria for thrombolytic therapy were included. Baseline ECG was recorded before streptokinase infusion and repeated at completion of infusion, at 90 minutes, day 1 and day 2. Effect of streptokinase therapy (SK) on blood pressure, CKMB, and ST-segment resolution was also evaluated at 90 minutes, day 1, and Day 2.

Results: The mean systolic blood pressure was 138.20±4.57 and 125.20±3.92 pre and post SK therapy reflecting a percentage decrease of 9.40 and highly significant (P<0.001). The Diastolic blood pressure was decrease to 9.52% with a mean value of 84.80± 2.46 and 76.80±1.89 before and after the Streptokinase therapy's, segment resolution at 90 minutes was decreased to 50.69 percent from the baseline and continued to decrease at Day-1 and Day-2 with a percentage reduction of 69.12 and 84.33 % respectively. The P values were highly significant (P<0.001).

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

Keywords: Streptokinase, ECG, ST-elevation, Myocardial infarction, Efficacy

INTRODUCTION:

Myocardial infarction is a key component of the burden of cardiovascular disease. Studying the trends in the incidence and outcome of myocardial infarction and of coronary disease mortality provides crucial insights into the determinants of heart disease which is essential to its treatment and prevention. It is important to recognize that the trends in the incidence and outcome of coronary disease are complex, likely multifactorial and evolve over time.[1]

In developed nations cardiovascular diseases are the leading cause of death and disability and also are increasing rapidly in the developing world. Among 75 years of age and older patients, mortality after acute coronary occlusion approaches 30% at 1 month and exceeds 50% at 1 year. However, despite evidence from several randomized trials that thrombolytic therapy has clear net benefits and is a cost-effective treatment in the elderly.[2]

Intravenous Thrombolysis in Acute Myocardial Infarction "in the Sixth ACCP Consensus Conference on Antithrombotic Therapy" recommended "that patients with ischemic symptoms characteristic of acute myocardial infarction for < 12 h who have ST-segment elevation or left bundle-branch block on the ECG should receive I/V fibrinolytic therapy unless they have contraindications.[3]

Acute myocardial infarction is one of the leading causes of death in the elderly, however clinical data reveals a disproportionately lower use of thrombolytics because of fear of complications especially intracranial hemorrhage. One study has documented that out of one hundred patients 77 (77%) were males and 23 (23%) were females. Mean age was 73.39±5.29 years. No patient developed intracranial hemorrhage. Use of streptokinase for acute myocardial infarction should therefore not be discouraged in the elderly.[4]

Streptokinase is a 1st generation fibrin non-specific thr-

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ombolytic and biochemically a serine protease enzyme derived from certain strains of beta hemolytic streptococci.[5]It consists of a single polypeptide chain containing 414 amino acids. It was first used in 1958 in acute myocardial infarction and since then it has revolutionized the management of acute myocardial infarction.[6]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.[7,8]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.[9]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.[10]

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.[11]

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.[12]

Thrombolytic therapy is that early and sustained re-canalization prevents cell death, reduces infarct size, preserves myocardial function, and reduces early and late mortality.[13]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).

Present study was designed with the objective to observe streptokinase therapy, in ST-segment elevation resolution, in age more than 60 years and in different types of myocardial infarction.Moreover also to observe the toxicity of administered streptokinase therapy.

MATERIALS AND METHODS:

This hospital based cross sectional study was carried out in 2005 for a total duration of 6 months. 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 and BASR of Karachi University. Informed consent for administration of thrombolytic drug was obtained from each patient. Inclusion criteria was patients diagnosed with myocardial infarction,more than 60 years of age ,with chest pain suggestive of myocardial infarction, ECG findings of ST-Segments elevations.Exclusion Criteria was patients with myocardial infarction havingactive internal bleeding,cerebro-vascular accident, blood pressure> 200/100 mmHg, pregnancy, allergic reaction to streptokinase, previous coronary artery bypass Graft. Streptokinase (Streptofactor Hakimsons/Eskinase, Medinet), 1500000 units was used

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 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 μg/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 exhibited that there were 44 (88%) males and 6(12%) 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 those patients (Table 1).

The mean systolic blood pressure was 138.20±4.57 and 125.20±3.92 pre and post SK therapy reflecting a percentage decrease of 9.40 and high significant ($P<0.001$). The Diastolic blood pressure was decrease to 9.52% with a mean value of 84.80± 2.46 and 76.80±1.89 before and after the Streptokinase therapy. ST-segment resolution at 90 minutes was decreased to

50.69 percent from the baseline and continued to decrease at Day-1 and Day-2 with a percentage reduction of 69.12 and 84.33 % respectively. The P values were highly significant (P<0.001) (Table 2)

There were 30 patients out of 50 with anterior wall Myocardial Infarction. The mean value of Systolic Blood Pressure (SBP) before therapy was 146.43± 4.98 and was decreased to 132.86±4.11 after therapy with Streptokinase. The Diastolic Blood Pressure (DBP) was decreased to 10.32 percent post Streptokinase therapy. The ST segment shows a resolution of 62.45% 69.99 and 87.14% at 90 minutes, day-1 and day-2 respectively. Figure-1 The P value for SBP, DBP and ST-segment resolution was highly significant (P<0.001).(Table 3a)

Twenty patients had inferior wall infarction in more than 60-years.(Table-3b)There was highly significant value of SBP, DBP and ST-segment resolution. The mean Systolic Blood Pressure value was 127.73±7.30 before therapy and decrease to 115.45±6.23 post streptokinase therapy which shows a percentage decrease of 9.61. The Diastolic Blood pressure showed a percentage decrease of 8.13. The ST elevation before therapy was 1.40± 0.16, which was resolved to 0.70± 0.13, 0.50 ± 0.13 and 0.33± 0.14 at 90-minutes, day-1 and day-2, showing a percentage decrease of 50.57, 64.28 and 76.92 respectively (Figure-2). The P value was also highly significant (P<0.001).

Table: 1
Gender, site of myocardial infarction & mortality in age group of > 60 Years

Variables	Age group >60 years n= 50	Total %
Male	44	88%
Female	06	12%
Anterior Wall MI	30	60%
Inferior Wall MI	20	40%
Latral Wall MI	--	--
Death	2	4%

Table: 2
Percentage changes from Pre to Post Streptokinase (SK) therapy

Variables	No of Observation	(Mean ± SEM)		% change	p-Value
		Pre SK Therapy	Post SK Therapy	Pre to Post	
SBP (mmHg)	48	138.20 ± 4.57	125.20 ± 3,92	(-) 9.40	0.001***
DBP (mmHg)	48	84.80 ± 2.46	76.80 ± 1.89	(-) 9.52	0.001***
CKMB (IU)	48	50.92 ± 1.82	154.80 ± 4.25	204.00	0.001***
ST Resolution 90 min	48	2.17± 0.18	1.07± 0.12	(-) 50.69	0.001***
ST Resolution day 1	48	2.17± 0.18	0.67 ± 0.08	(-) 69.12	0.001***
ST Resolution day 2	48	2.17± 0.18	0.34 ± 0.08	(-) 84.33	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: 3a
Effects of Streptokinase (SK) therapy according to the site of anterior wall myocardial infarction in >60 year of age
There were 30 patients out of 50 with anterior wall Myocardial Infraction

Variables	No of Observation	(Mean ± SEM)		% change	p-Value
		Pre SK Therapy	Post SK Therapy	Pre to Post	
SBP (mmHg)	30	146.43± 4.98	132.86± 4.11	(-) 9.26	0.001 ***
DBP (mmHg)	30	90.00± 4.11	80.71± 2.21	(-) 10.32	0.001 ***
CKMB (IU)	30	54.36 ± 2.51	154.00 ± 7.04	183.29	0.001 ***
ST Resolution 90 min	30	2.69 ± 0.17	1.01 ± 0.12	(-) 62.45	0.001 ***
ST Resolution day 1	28	2.69 ± 0.17	0.80 ± 0.10	(-) 69.99	0.001 ***
ST Resolution day 2	28	2.69 ± 0.17	0.35 ± 0.10	(-) 87.14	0.001 ***

Two patients died because of ventricular fibrillation *** Highly Significant(-) Shows decrease from pre to post streptokinase therapy

Table: 3b
Effects of Streptokinase (SK) therapy according to the site of
Inferior wall Myocardial Infarction in < 60 year of age
There were 20 patients out of 50 with inferior wall myocardial Infarction

Variables	No of Observation	(Mean ± SEM) Pre SK Therapy	Post SK Therapy	% change Pre to Post	p-Value
SBP (mmHg)	20	127.73 ± 7.30	115.45±6.23	(-) 9.61	0.001 ***
DBP (mmHg)	20	78.18 ± 3.77	71.82 ± 2.63	(-) 8.13	0.001 ***
CKMB (IU)	20	46.55 ± 2.05	155.82±4.01	234.76	0.001 ***
ST Resolution 90 min	20	1.40 ± 0.16	0.70 ± 0.13	(-) 50.57	0.001 ***
ST Resolution day 1	20	1.40 ± 0.16	0.50 ± 0.13	(-) 64.28	0.001 ***
ST Resolution day 2	20	1.40 ± 0.18	0.33 ± 0.14	(-) 76.92	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

Comparative percentage change in the >60 age according to the site of myocardial infarction group, with anterior wall infarction showed a percentage change of 9.26, 10.32, 183.29 and 87.14 of SBP, DBP, CKMB and ST-segment resolution at day2, as compared to a percentage decrease of 9.61, 8.13, 60.4, 234.73, and 76.92 in patients with inferior wall myocardial Infarction at day-2(Table 4a) The mean duration of chest pain was 4.89± 0.28 hours. The minimum chest pain duration was 2 hours and maximum it was 12 hour. The mean stay at hospitals was at hospital was 5.03± 0.24 from a period of 5-days to 15-days (Table 4b)

The complications of Streptokinase therapy in more than 60 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.

ST-Resolution at Day-1 and Day-2, pre and post SK-therapy according to site of M-1 are mentioned in Figure 2 and 3.

Table: 4a
Pharmacological action of Streptokinase therapy on blood pressure, CKMB and
ST-Segment elevation resolution

GROUP	Site of MI	SBP mmHg	DBP mmHg	CKMB IU	ST Resolution 90-Mints	Day-1	Day-2
More than 60 years	Anterior Wall	(-) 9.26	(-) 10.32	183.29	(-) 62.45	(-) 69.99	(-) 87.14
	Inferior Wall	(-) 9.61	(-) 8.13	234.73	(-) 50.57	(-) 64.28	(-) 76.92

(-) sign shows decrease from pre to post SK-therapy

Table: 4b
Duration of chest pain, Cholesterol, Random blood sugar and duration of patients stay at hospital

Group		Duration Chest Pain Hours	Cholesterol (mg/dl)	RBS (mg/dl)	Hospital stay days
More than 60 years	n	50	50	50	48
	Mean ± SEM	4.89±0.28	218.84±8.67	132.16±13.82	5.03±0.24
	Range	2-12	132-290	59-392	4-15

Figure: 1
ST- Resolution according to site of myocardial infarction in more than 60 years age Patients

	Pre-SK Therapy	Post-SK Therapy
Anterior wall	2.69	0.35
Inferior wall	I.40	0.33

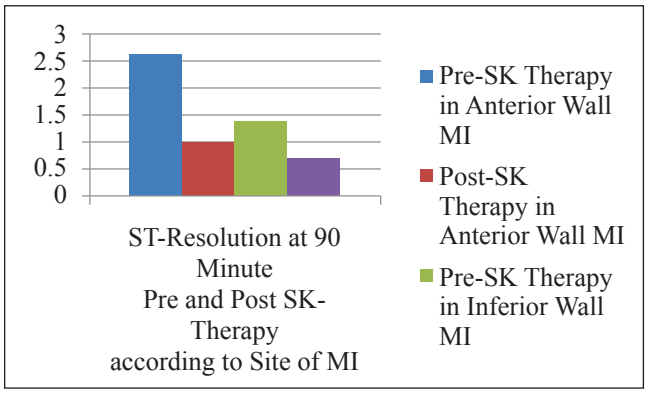


Figure: 2

	Pre-SK Therapy	Post-SK Therapy
Anterior wall	2.69	0.80
Inferior wall	I.40	0.50

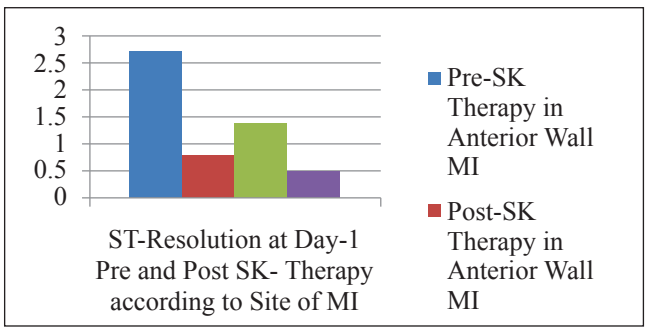
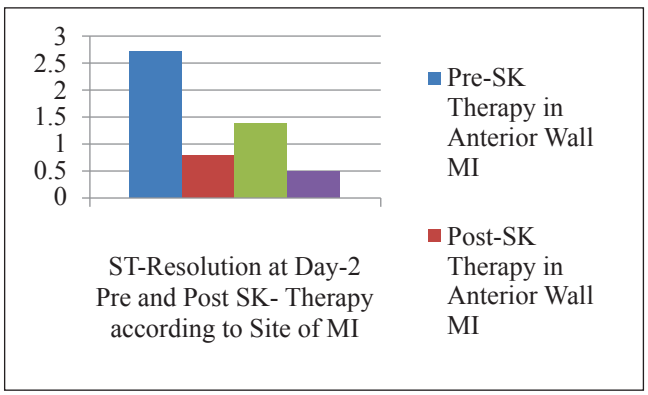


Figure: 3

	Pre-SK Therapy	Post-SK Therapy
Anterior wall	2.69	0.35
Inferior wall	I.40	0.33



DISCUSSION:

The best reperfusion treatment is one that achieves the highest rate of early, complete, and sustained infarct-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.Medical therapy alone is the preferred treatment in older patients after myocardial infarction. Indications of revascularization in older patients after myocardial infarction are prolongation of life and relief of unacceptable symptoms despite optimal medical management.[14]

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 decreases with increased age, but should not be considered a contraindication.[15]This study was conducted to observe the efficacy and complication of streptokinase therapy in more than 60 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[16] 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[17] in which hospital mortality was 2 to 9 percent for patients 61 to 70 years old as compared to younger patients. In our study the in- hospital mortality was 4 percent in patients more than 60 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[18], 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[19], the data of the study do not provide evidence from withholdingfibrinolytic 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.

In patients with acute myocardial infarction, quick initiation of thrombolytic therapy is the best strategy for improvement of survival and reduction of morbidity. Since advanced age by itself is certainly not a contraindication to thrombolytic therapy, and because reinfarction occurs frequently, the benefit-risk ratio of reexposure to streptokinase or its derivative is decreased in the elderly who present with reinfarction.[20]Our study did match with the study of, [21] thrombolytic therapy with streptokinase was found to be a beneficial and cost-effective treatment for suspected acute myocardial infarction in elderly patients in a wide variety of clinical circumstances.Acute myocardial infarction is one of the leading causes of death in the elderly, however clinical data reveals a limited use of thrombolytic because of fear of complications especially intracranial hemorrhage. Use of streptokinase for acute myocardial infarction should not be discouraged in the elderly.[22]This decade has witnessed the establishment of thrombolysis, the most widely available therapeutic intervention that specifically treats the direct cause of myocardial infarction and leads to biologically and clinically compelling patient outcome benefits.[23,24,25]

CONCLUSION:

Thrombolytic therapy with streptokinase is found to be a beneficial and cost-effective option for patients having suspected acute myocardial infarction.Thrombolysis when given within 12 hours of the onset of symptoms, improved survival, is beneficial and cost effective. Present study has demonstrated rapid restoration of coronary blood flow in patients with evolving myocardial infarction and the magnitude of benefit is greatest when reperfusion is established early. Age itself should not be considered a contraindication for fibronolysis. 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.

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