In-Hospital Outcome of Acute Myocardial Infarction in patients receiving Streptokinase

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Objective: To study and compare the in-hospital mortality due to acute myocardial infarction in patients receiving thrombolytic (streptokinase) therapy versus those who were not thrombolysed. **Methods:** This descriptive observational study was conducted at the Coronary care Unit and Cardiology ward of Nishtar Hospital, Multan, from 1st of October 2002 till 30th of April 2003. Four hundred and thirty four patients of acute myocardial infarction who fulfilled WHO criteria of acute myocardial infarction were included in the study. Patients were divided into two groups: patients receiving streptokinase (SK) group and patients not receiving streptokinase (Non-SK) group. In-hospital mortality was our primary endpoint. Mechanical and electrical complications occurring in-hospital after acute myocardial infarction were secondary endpoints. **Results:** Only 47% patients received streptokinase while 53% did not receive it because of delayed presentation or some other contraindication to streptokinase therapy. Mean age of the SK group was 51.58±11.02 years and Non-SK group was 55.78±10 years. In SK group 170(83.3%) patients were males and 34(16.7%) were females. Only 54(26.5%) diabetics and 150(73.5%) non-diabetics received streptokinase. Streptokinase recipients reached the hospital earlier; mean time of onset of symptoms till arrival at the hospital was 4 hours and 25 minutes while non recipients took a longer time in reaching to the hospital. There was no significant difference in the infarct territory between the two groups. The Non-SK group had higher Killip class as compared to SK group on presentation to the hospital. In-hospital mortality was 8.3% in SK group and 24.3% in Non-SK group ($p<0.0001$); left ventricular failure occurred more frequently in Non-SK group and was the most common cause of death in both the groups ($p<0.0001$). Only 4.3% patients in the SK group and 19.6% patients in the Non-SK group died in first 24 hours of hospital admission ($p<0.0001$). Mechanical complications occurred more frequently in Non-SK group ($p<0.008$). There was a statistically non significant difference ($p<0.436$) noted in comparison of electrical complications between the two groups. **Conclusions:** Streptokinase infusion given in the early hours of acute myocardial infarction leads to a significant reduction in in-hospital mortality and mechanical complications like left ventricular failure.

Key words: Acute myocardial infarction; Streptokinase; Mortality; Killip Class.

Every year, more than one million patients in the US have acute myocardial infarction and almost half of these patients have myocardial infarction with ST segment elevation[1]. Despite many therapeutic advances in the treatment of acute myocardial infarction over the past two decades, it continues to be a major public health problem and leading cause of death throughout the industrialized world[2,3].

Myocardial infarction usually occurs when a fissure develops in an atheromatous plaque upon which platelet and fibrin thrombi are formed, leading to occlusion of a coronary artery.[4] Prompt thrombolytic treatment is a well established modality of management of acute myocardial infarction, and mortality is reduced and clinical outcome improved if treatment is started early after the onset of ischemic chest pain[5-9]. The most commonly used fibrinolytic agent in clinical practice world wide is streptokinase.[4,8] A substantial proportion of patients who are eligible for reperfusion therapy still do not receive this treatment , particularly elderly and female patients[10,11].

In Pakistan, in-hospital complications of AMI patients treated with or without streptokinase therapy have been studied in different centers[12-15]. We designed this study to evaluate outcome of AMI patients receiving streptokinase and those not receiving it in Southern Punjab, as no relevant data is available to-date in this region.

Patients and methods

Four hundred and thirty four consecutive patients of acute myocardial infarction hospitalized in coronary care unit and cardiology ward of Nishtar Hospital Multan from 1st of October 2003 till 30th of April 2003 were included in this descriptive observational study.

Patients presenting with acute myocardial infarction were examined by Senior Registrar on call. Patients were included in the study on the basis of WHO criteria of acute myocardial infarction i.e., presence of any two of the following : 1) Chest pain consistent with acute myocardial infarction of less than 24 hours duration. 2) Electrocardiographic changes i.e. ST-Segment elevation >0.2mv in at least two contiguous chest leads or >0.1 mv in at least two contiguous limb leads. 3) New or presumably New Left Bundle Branch Block on electrocardiogram. 4) Raised levels of cardiac enzymes CPK-MB more than double the reference value or Positive Troponin T test done by commercially available Kits of Trop T (Boehringer Mannheim Germany Distributed by Roche Pakistan Pvt. Ltd.). Exclusion criteria were 1) Patients presenting with Non-ST segment elevation

myocardial infarction and 2) Patients who were more than 75 years of age. Patients were divided into two groups.

1. Patients receiving Streptokinase after exclusion of any contraindication to therapy (SK group).
2. Patients not receiving Streptokinase because of presence of any contraindication to therapy (Non-SK group).

A detailed history was recorded particularly age, sex, occupation, address, history of smoking, diabetes mellitus, hypertension, ischemic heart disease and family history of ischemic heart disease. Time from onset of symptoms till arrival at the hospital was noted. Complete physical examination was done with emphasis on pulse, blood pressure, precordial examination and signs of congestive cardiac failure. ECG and X-ray chest was done in all patients. Killip class was taken as a standard to monitor the severity of acute myocardial infarction.[16] Site of myocardial infarction, Killip class and medication given, especially Streptokinase, were noted for all the patients. All patients were treated according to the standard protocol of the Cardiology Unit.[17] Patients were followed up daily and pulse, blood pressure, ECG changes and complications if any were monitored till death or discharge of the patient. Hospital stay of individual patients was also noted.

The primary end point of the study was death. Date and time of death was noted in case of mortality. We also studied mechanical and electrical complications in all surviving patients during their stay in the hospital.

Statistical analysis: All the data was analyzed by SPSS (Statistical Package for Social Sciences) Version 11.0 for Windows. Categorical varialbles were expressed as percentages while continous variables were expressed as mean±SD (Standard deviation). Patient characteristics like time from onset of symptoms till arrival at the hospital, door to needle time, Site of myocardial infarction, Killip class on presentation, in-hospital mortality, cause of death, time of death from admission, mechanical and electrical complications for SK and non-SK groups were compared using Chi-square test. 5% level of significance was used. All tests applied were two tailed.

Results

A total of 434 patients met our inclusion criteria and were studied. Among these only 204 (47%) patients received streptokinase therapy and were included in SK group while 230(53%) patients did not receive streptokinase infusion and were included in Non-SK group. All patients in the study had equal chance of receiving streptokinase ; patients in Non-SK group were those who either presented late or had any contraindication to streptokinase therapy. Among Non-SK group 101(43.9%) patients presented late i.e., after 12 hours of onset of chest pain, 47(20.5%) patients had contraindications like history of recent surgery, cerebro-vascular accident, bleeding peptic ulcer or uncontrolled hypertension (blood pressure more than 180/110 mm of Hg) , 29(12.6%) patients had ECG changes which were considered not suitable for thrombolytic treatment, 14(6%) patients did not have typical chest pain, 19(8%) patients were in cardiogenic shock and 20(8.7%) patients had a history of prolonged CPR so they were not thrombolysed.

Table 1 shows the epidemiological characteristics of the study population. The mean age of study population was 53.68±12.2; mean age of thrombolysed patients was 51.58±11.02 and that of non-thrombolysed group was 55.78±10.69. In order to study the effect of age in both groups we divided age into two groups, <55 years and 55-75 years. In SK group 101(49.5%) patients were less than 55 years and 103(50.5%) were 55-75 years while in Non-SK group 90(39.1%) patients were less than 55 years old and 140(60.9%) were 55-75 years old. Lesser number of female patients 34(16.7%) received streptokinase as compared to male patients 170(83.3%). Only 54(26.5%) patients were diabetic in SK group and 150(73.5%) were non-diabetic. Smokers were 110(53.9%) and non-smokers were 94(46%) in SK group. 67(32.8%) patients were hypertensive in SK group while 76(33%) patients were hypertensive in Non-SK group. History of ischemic heart disease was present in 45(22.1%) patients receiving streptokinase. Family history of ischemic heart disease was present in 33(16.2%) patients in SK group.

Table 1. Epidemiological characteristics of study population

Epidemiological characteristics	SK Group n=204	Non- SK Group n=230
Age (Mean years)	51.58±8.04	55.78±10.13
<55 years	101(49.5%)	90(39.1%)
55-75 years	103(50.5%)	140(60.9%)
Female	34(16.7%)	55(23.9%)
Male	170(83.3%)	175(76.1%)
Diabetes mellitus	54(26.5%)	64(27.8%)
Smokers	110(53.9%)	108(47%)
Nonsmokers	94(46.5%)	122(53%)
Hypertension	67(32.8%)	76(33%)
H/O IHD	45(22.1%)	62(27.0%)
Family H/O IHD	33(8.2%)	28(12.2%)

Table 2 shows the presentation characteristics of study population. The mean time of onset of symptoms till arrival at the hospital was 4 hours and 25 minutes in SK group and 9 hours and 40 minutes in Non-SK group. In SK group 64(31.4%), 109(53.4%) and 31(15.2%) patients reached the hospital in <3 hours, 3-6 hours and 6-12 hours respectively. It was noted that most patients, i.e., 109(53.4%) , took 3-6 hours in reaching the hospital after the onset of symptoms. Regarding ECG on presentation , there was no significant difference between different groups in site of myocardial infarction. One hundred and twenty one (59.3%) patients in streptokinase group and 129(56.1%) patients in non streptokinase group had anterior wall myocardial infarction. Only 4(2%) patients in Killip class IV were thrombolysed while 13(5.7%) patients were not thrombolysed. More patients in Non-SK group

were in advanced Killip class on presentation as compared to SK group patients.

Fig. 1. Comparison of primary and secondary end points in SK and Non SK groups

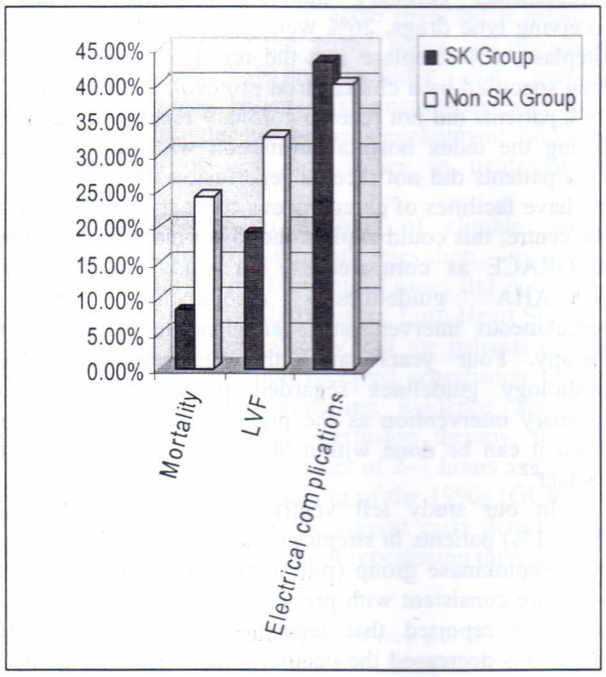

Table 2. Presentation characteristics of study population

Presentation characteristics	SK Group n=204	Non-SK group n=230
Time from onset of symptoms till arrival at the hospital Mean hours		
Mean hours	4.45±1.02 hors	9.60±2.16 hours
<3 hours	64(31.4%)	7(3%)
3-6 hours	109(53.4%)	55(23.9%)
6-12 hours	31(15.2%)	67(29.1%)
12-24 hours	0	101(43.9%)
Door to needle time		
Mean minutes	102.13±66.8	----
Within 30 minutes	33(16.2%)	----
30 min-1 hour	50(24.5%)	----
1-2 hours	71(34.8%)	----
>2 hours	50(24.5%)	----
ECG		
Anterior wall MI	121(59.35)	129(56.1%)
Inferior wall MI	72(35.3%)	84(36.5%)
Lateral wall MI	6(2.950	4(1.7%)
Posterior wall MI	5(2.5%)	2(0.9%)
Left bundle branch block	0	11(4.8%)
Killip Class		
I	29(14.2%)	68(29.6%)
II	9(4.4%)	16(7%)
III	2(1%)	7(3%)
IV	4(2%)	13(5.7%)

Table 3. In-hospital outcome of study population

Outcome measure	SK Group n=204	Non-SK Group n=230	p value
In-hospital mortality	17(8.3%)	56(24.3%)	<0.0001
Cause of death			
LVF	8(3.9%)	32(13.9%)	<0.
VT,VF	1(0.5%)	5(2.2%)	00
CHB	2(1%)	14(6.1%)	01
Asystole	6(2.9%)	5(2.2%)	
Time of death after admission			
1st 24 hours	10(4.9%)	45(19.6%)	<0.0001
24-48 hours	0	3(1.3%0	
>48 hours	7(3.4%)	8(3.5%)	
Mechanical complications			
LVF	39(19.1%)	5(32.6%)	<0.008
MR	0	2(0.9%)	
Electrical complications			
1st degree AVB	10(4.9%)	5(2.2%)	<0.436
2nd degree	3(1.5%)	3(1.3%)	
AVB	3(1.5%)	1(0.4%)	
Atrial	1(0.5%)	2(0.9%)	
Fibrillation	4(2%)	7(3%)	
AIVR	33(16.2%)	24(10.4%)	
APCS	4(2%)	5(2.2%)	
PVCS	8(3.9%)	17(7.4%)	
Asystole	4(2%)	3(1.3%)	
CHB	8(3.9%)	10(4.3%)	
VF	2(1%)	1(0.4%)	
VT	4(2%)	6(2.6%)	
LBBB	2(1%)	4(1.7%)	
RBBB	2(1%)	4(1.7%)	
RBBB+LAH			
RBBB+LPH			
Other complications			
Post MI	2(1%)	9(3.9%)	<0.
Angina	2(1%)	3(1.3%)	00
Reinfarction	0	2(0.9%)	8
CVA			

LVF=Left ventricular failure; MR=Mitral regurgitation; AVB=Atrioventricular block; AIVR=Accelerated idioventricular rhythm; APCS=Atrial premature contractions; PVCS=Premature ventricular contractions; CHB=Complete heart block; VT=Ventricular tachycardia; VF=Ventricular fibrillation; LBBB=Left bundlebranch block; RBBB=Right bundle branch block; LAH=left anterior hemiblock; LPH=left posterior hemiblock; CVA=Cerebrovascular accident.

Table 3 shows the in-hospital outcome of the study population. Figure 1 shows the comparison of primary and secondary end points of the study population. Total in hospital mortality was 73(16.8%). In-hospital mortality was 17(8.3%) in SK Group while it was significantly higher 56(24.3%) in Non-SK group ($p<0.0001$). Left ventricular failure was the major cause of death in both groups and was present in 8(3.9%) in SK Group and 32(13.9%) in Non-SK ($p<0.0001$). We also observed that most mortalities occurred during the first 24 hours after admission to the hospital i.e. 10(4.9%) patients in SK group and 45(19.6%) in Non-SK group died in first 24 hours ($p<0.0001$). Mechanical complications included left ventricular failure which occurred in 30(19.1%) patients in

SK group and 75(32.6%) patients in Non-SK group ($p<0.0001$). Premature ventricular contractions occurred in 33(16.2%) patients in SK group and 24(10.4%) in Non-SK group while complete heart block occurred in 8(3.9%) patients in SK group and 17(7.4%) patients in the Non-SK group ($p<0.436$). Post MI angina occurred in 9(3.9%) and re-infarction in 3(1.3%) patients in SK group ($p<0.008$). Mean hospital stay was 4.39±1.83 days in SK group and 5.89±2.66 days in Non-SK group ($p<0.0001$).

Discussion

Acute myocardial infarction is the leading cause of death throughout the world despite latest therapeutic advances in treatment. Thrombolytic treatment has a well established role in the management of acute myocardial infarction, mortality is reduced and clinical outcome improved if treatment is started early after the onset of ischemic chest pain. The most commonly used fibrinolytic agent is streptokinase. Increasing age and female gender have somewhat limited the use of thrombolytic therapy although there is evidence of benefit in both groups.

In the present study we noted that the in-hospital mortality in thrombolysed patients was 8.3% while it was 24.3% in non thrombolysed patients ($p<0.0001$). Our results are consistent with previous studies[9,12,13,18]. Data from the Fibrinolytic Therapy Trialists (FTT) collaborative group[18] shows that streptokinase saves around 30 lives per 1000 patients treated. They have reported a higher mortality in non-thrombolysed patients. Mahon et al[9] from Ireland have reported a mortality of 14% in thrombolysed patients and 22.4% in non-thrombolysed patients; thirty percent of their patients were above 75 years with a mean age of 67.0, while we studied only those patients who were less than 75 years of age and the mean age of our study population was 53.68±12.2 years. Chaudhrey et al[12] from Faisalabad have reported a mortality of 4.2% in thrombolysed group and 29.8% in non-thrombolysed groups. They reported a lower mortality in streptokinase group probably because their sample size was smaller. They studied only 102 patients. Several multicentre trials have shown a mortality of 8-9% in streptokinase treated patients[19,20]. Gardezi et al[13] from Lahore have reported a lower mortality in streptokinase group as compared to Non-SK group, they studied 664 patients admitted over a period of 12 months. In our study, the in-hospital mortality in streptokinase recipients is similar to several International trials[19-21]. GUSTO-I[21] compared front-loaded Alteplase, aspirin and infusion heparin with streptokinase and reported 6.3% mortality in Alteplase group and 7.3% mortality in streptokinase group. ISIS-3[20] compared Anistreplase with streptokinase and reported a mortality of 10.5% and 10.4% in Anistreplase and streptokinase groups respectively. INJECT trail[19] reported a mortality of 9.5% in streptokinase group and 9.0% in Reteplase group.

The overall in-hospital mortality in our study population was 16.8% which is similar to several other studies[9,11,12,15]. GRACE investigators[10] have reported a mortality of 6% which is considerably lower than our study ; the reason could be that in their study 43% patients received lytic alone, 6% received a lytic and underwent percutaneous coronary intervention. Among patients receiving lytic drugs, 26% were given streptokinase, 21% alteplase, 6% reteplase and the rest (15%) another lytic drug specified by a clinical trial protocol. In this trial only 38% patients did not receive coronary reperfusion therapy during the index hospital admission while in our study 53% patients did not receive reperfusion therapy. We did not have facilities of percutaneous coronary intervention at our centre; this could explain the lower mortality observed in GRACE as compared to our study. In 1999, the ACC/AHA guidelines[17] recommended primary percutaneous intervention as an alternate to fibrinolytic therapy. Four years later, the European society of cardiology guidelines regarded primary percutaneous coronary intervention as the preferred therapeutic option when it can be done within 90 minutes of first medical contact[22].

In our study left ventricular failure occurred in 39(19.1%) patients in streptokinase group and 75(32%) in non-streptokinase group ($p<0.008$). Other findings in our study are consistent with previous studies.[9,23] Hasdai D et al[23] have reported that reperfusion with thrombolytic agents has decreased the occurrence of cardiogenic shock in patients with persistent ST segment elevation myocardial infarction. Left ventricular failure was the cause of death in 3.9% patients in streptokinase group and 13.9% in Non-streptokinase group ($p<0.0001$)[9,23,24]. All these studies reported a higher incidence of left ventricular failure in non-thrombolysed patients. However GISSI-I[25] workers reported that 69.9% of shock patients died in streptokinase group as compared to 70.1% in control group; the lack of benefit of thrombolytic agents in treating cardiogenic shock may be attributed to decreased coronary thrombolysis in states of low perfusion pressure[23]. Barakat et al[24] have reported that left ventricular failure was the strongest predictor of death within one year of infarction. They have reported lesser incidence of left ventricular failure in young age group.

In our study complete heart block occurred in 3.9% patients in SK group and 7.4% patients in Non-SK group while premature ventricular contractions occurred in 16.2% patients in streptokinase group and 10.4% in control group ; however there was a non-significant association observed ($p<0.436$). Chaudhery et al[12] have reported that rhythm disturbances were more common in streptokinase group.

In our study all patients had equal chance of receiving streptokinase; patients in Non-SK group were those who either presented late or had any contraindication to Streptokinase therapy. Patients in the SK group were younger and in lower Killip class than patients in Non-SK group; this was merely a coincidence although studies

have shown that older patients present late and in advanced Killip class than younger patients[26,27].

Conclusion

Our study confirms the findings of previous studies that streptokinase therapy reduces in-hospital mortality and improves clinical outcome of acute myocardial infarction patients if started in the early hours of myocardial infarction. With the understanding that coronary atherosclerosis may be an inflammatory disease, future research should concentrate on development and wide implementation of new approaches in treatment and prevention.

In GRACE up to a third of eligible patients presenting with ST-segment elevation myocardial infarction within 12 h of symptom onset did not receive reperfusion therapy. Similarly, in the Euro Heart Survey of acute coronary syndromes, only half the patients enrolled with ST-segment elevation received reperfusion therapy. And finally, despite compelling evidence about the importance of very early reperfusion therapy, the time from symptom onset to treatment of 2–7 hours as recorded in clinical trials in the beginning of the 1990s (GUSTO-1) has remained unchanged. We suggest early detection and treatment for optimal benefits of reperfusion therapy.

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