EARLY IN-HOSPITAL RE-INFARCTION AFTER THROMBOLYSIS FOR ACUTE MYOCARDIAL INFARCTION (AMI) IN AFIC/NIHD RAWALPINDI

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ABSTRACT

This study was designed to determine the frequency and variables of in-hospital re-infarction after streptokinase in patients with first acute ST segment elevation myocardial infarction (AMI), hospitalized in CCU of AFIC/NIHD from Feb 2002 to July 2002. Of 200 consecutive patients of AMI who received streptokinase, 73% (n = 146) were males and 27% (n = 54) were females, mean age was 55.5 years (29-81). Frequency of in-hospital re-infarction documented in this study was 6.5% (n = 13) a median time of 2.5 days (1-6) after thrombolysis. Patients with re-infarction had higher in-hospital mortality within ten days of hospitalization (30.77% versus 7.5% without re-infarction; P = .01). Median time to death after re-infarction was 3 days (2 - 10) with 50% of deaths occurring within 48 hours of re-infarction. Rates are comparable with previously conducted large-scale studies (GUSTO I/III and TAMI study). Advanced age, diabetes mellitus, hypertension, increasing killip class > at the time of admission, fluctuation in heart rate and hyperilipidaemias were the most important predictors /variables associated with higher in-hospital re-infarction and subsequent increased morbidity and mortality. Improved treatment, preventive strategies and early detection of re-infarction should be an important goal of AMI management. Repeat thrombolysis and early revascularization where possible in selected cases can decrease the cardiac mortality and morbidity.

Keywords: Acute myocardial infarction (AMI), streptokinase (SK), re-infarction, predictors

INTRODUCTION

Ischaemic Heart Disease (IHD) is the major cause of morbidity and mortality all over the world [1]. Dispite of multiple therapeutic advances in treatment of acute myocardial infarction over the past two decades, it continues to be a major public health problem and a leading cause of death through out the Industrialized world [2]. It is usually attributable to atherosclerotic obstruction of coronary vessels and clinically presents as a spectrum of sign and symptoms ranging from angina pectoris to acute myocardial infarction most aptly termed as acute coronary syndrome [3, 4]. Myocardial infarction generally occurs when there is an abrupt cessation in coronary blood flow following a thrombotic occlusion of a coronary artery previously narrowed by atherosclerosis. Fuster et al., (1992) has shown that Myocardial Infarction, ischaemic events and cardiac necrosis can result from the irregularity, fissured or rupture of atherosclerotic plaques [4]. Plaques instability has also been associated with systemic factors such as infection, involvement of a genetic predisposition, autoimmunity. Alternatively, rupture may result from iatrogenic causes such as coronary artery bypass, catheter-based vascularization or local factors such as

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coronary artery artheroma or superimposed thrombus or plaque haemorrhage [4,5].

Thrombolytic therapy has been major advance in the management of acute myocardial infarction. Although the mortality rate following AMI has declined by 23-30% over the last two decades after advent of streptokinase but is still high in elderly diabetics as compared to young patients [6,7]. Streptokinase works by lysing infarct artery thrombi and achieving reperfusion, thereby reducing infarct size, preserving left ventricular functions and improving survival. The greatest benefit occurs if treatment initiated within first 6 hours when 50% or greater reduction in mortality rate can be achieved [5,6,7]. Because of potential antigenicity it is not recommended for use in those with recent streptococcal throat infection or readministration to those who have had previous use in the prior 12 months. In these individuals, the use of a nonantigenic thrombolytic agent, such as t-PA, is recommended [7,8].

Early re-infarction occurs infrequently after streptokinase therapy but confers increased risk of morbidity and mortality [9]. Re-occlusion of infarct artery after successful thrombolytic therapy is demonstrated in 5-30% of patients, but clinical re-infarction occurs in only 4% of patients and most of the re-occlusion (78%) is not associated with clinically overt symptoms or apparent re-infarction [10,11]. On the average the maximum number of re-infarction occurs between 2-6 days, median 3.8 days after initiation of thrombolysis [11,12,13].

Third world countries have scarce resources, which demand optimal utilization. No much data is available from Pakistan, which has assessed the frequency of in-hospital re-infarction after streptokinase administration in AMI patients. We conducted this study in AFIC/NIHD Rawalpindi spanning over a period of six months between Feb to Jul 2002 in order to document frequency and variables of in-hospital re-infarction after streptokinase. The data collected may guide us in our future management strategies and judicious use of resources.

PATIENTS AND METHODS

The proposed study was an observational comprising of 200 consecutive patients of first acute ST segment elevation myocardial infarction (AMI) who received Streptokinase and hospitalized in CCU of AFIC/NIHD Rawalpindi between Feb 2002 to Jul 2002.

Diagnosis of AMI was made on a gold standard triad of ischaemic chest pain suggestive of cardiac disease, characteristic ECG changes of AMI (ST elevation > .2MV in at least two contiguous chest leads or > .1MV in two contiguous limb leads) and cardiac specific biochemical markers exceeding the standard reference ranges. Patients with chronic heart failure, valvular heart diseases, coronary artery bypass surgery and congenital heart diseases were excluded. Adult male or female patients, age more than 20 years, with first ST segment elevation acute myocardial infarction who received Streptokinase were the subject of this study.

Patients were assessed clinically with special emphasis on history of chest pain, dyspnoae and physical examination including pulse, Blood pressure, cardiovascular and respiratory system. Investigations like electrocardiogram (ECG), serum cardiac enzymes level and coagulation profile (PT/PTTK) was performed daily. Baseline blood complete picture, urine routine examination, chest radiograph, serum lipid profile, blood glucose levels and echocardiography were done in all cases. Patients remained hospitalized and observed for a minimum period of 10 days after initiation of streptokinase. Diagnosis of re-infarction if any was made by presence of any two of the following [11].

(a) Recurrent ischaemic symptoms lasting greater than 15 minutes after resolution of symptoms of index infarct.

(b) Occurrence of new ST waves changes or appearance of new Q waves.

(c) Appearance of new left bundle branch block.

(d) Second elevation of creatine kinase (CK-MB) to above the upper limit of normal and increased by greater than 50% over the previous value. The total CK measurement has to be either re-elevated to at least twice the upper limit of normal and increased by at least 25% or re-elevated to 200 units/litre over the previous value.

(e) Angiographic re-occlusion of previously documented patent infarct related artery.

Data was entered and processed on SPSS 10 software. All categorical variables are described as percentages and continuous variables as mean with standard deviations. The variables considered alongwith age were gender, Diabetes mellitus, hypertension, killip class, smoking, heart rate, AMI location and hyperlipidaemias. Influence of various confounding risk factors/variable on re-infarction was determined using chi-square (X2) and all P Values less than .05 were considered statistically significant.

RESULTS

Of 200 consecutive patients with first acute ST segment elevation myocardial infarction (AMI) hospitalized in CCU of AFIC/NIHD Rawalpindi from Feb 2002 to July 2002, 73% (n = 146) were males and 27% (n = 54) were females, mean age was 55.5 years (29-81). Characteristics of the patients with AMI and re-infarction are shown in (table-1). Frequency of in-hospital re-infarction documented in current study was 6.5% (n = 13). Median time to re-infarction after initiation of streptokinase was 2.5 days (1-6). Patients with re-infarction had higher in-hospital mortality within ten days of hospitalization (30.77% versus 7.5% without re-infarction; P = .01) (table-2). Median time to death after re-infarction was 3 days (2-10) with 50% deaths occurring within 48 hours of re-infarction.

Early re-infarction was significantly higher in patients with advanced age, male gender, diabetes mellitus, hypertension and hyperlipidaemia. Mean age of the patients with re-infarction was 65.7 years + 12.5 with maximum rate of re-infarction above 60 years of age (fig. 1). Re-infarction was four times higher in patients with diabetes mellitus (14.03% versus 3.49% in non diabetic; P = .059). Similar increased frequency of re-infarction was observed in patients with anterior MI (9.5% versus 4.55% with interior MI) (fig. 2). Increased killip class > I at the time of admission was associated with increase rate of re-infarction; 4.5%, 8.1%, 10.34% and 30.77% for killip class I, II, III and IV respectively (table-3). Re-infarction rate did not differ significantly by smoking status (7.58% versus 5.97% in non smoker; P = .098). Relation of heart rate to re-infarction was j-shaped with nidar in frequency in 60bpm, modest increase at lower rate less than 60 bpm, reduce re-infarction rate from 60 to 100bpm and marked increase in patient with heart rate greater than 100 bpm (fig. 3).

DISCUSSION

Atherosclerotic cardiovascular diseases account for about half of all premature deaths in developed as well as in developing countries [1]. Thrombolysis reduces mortality in patients with Acute Myocardial infarction (AMI) as shown conclusively in trials of thousands of patients [5, 6,7]. These studies have characterized the frequency, timings and clinical predictors of death after ST elevation AMI in fibrinolytic era but less attention has been focused on incidence and predictors of early re-infarction after thrombolysis. Re-occlusion of infarct related artery after successesful thrombolytic therapy in patients with Acute Myocardial infarction (AMI) is associate with adverse outcome [10,12]. Re-occlusion has been demonstrated in 5 – 30% patients after successful thrombolysis but clinical re-infarction is documented in only on

Table-1: Base line characteristics

Variables	AMI Patients (n=200)	Re-infarction n(%) =13 (6.5)	P. Value
Age, y ± SD	55.5 (29-81)	65.7 ± 12.5	.001
Gender Male	146 (73)	11 (7.53)	0.813
Female	54 (27)	2 (3.7)	
Days from thrombolysis to re-infarction	-	2.5 (1-6)	-
Diabetes Mellitus	57 (28.5)	8 (14.03)	0.058
Hypertension	60 (30)	6 (10)	0.631
Hyperlipidaemia	47 (23.5)	4 (8.5)	0.938
Smoking	66 (33)	5 (6.09)	0.98
ST Elevation MI Site			0.796
Ant. Wall MI	84 (42)	8 (9.52)	
Inf. Wall MI	110 (55)	5 (4.54)	
Others (Lat+ RV infarct)	6 (3)	0	
Cardiogenic Shock	13 (6.5)	4 (30.77)	0.004

4% of patients and most of reocclusions are not associated with clinically overt symptoms or apparent re-infarction [11,12,13].

In the current study the chief finding is in-hospital re-infarction rate (6.5%) after thrombolysis with streptokinase, although an uncommon complication is associated with four to five time increased in mortality versus those without re-infarction or recurrent ischaemia. Significant multivariate variables/predictors of in-hospital death or re-infarction included advanced age, male gender, diabetes mellitus, hypertension Increased killip class > I and anterior MI at the time of admission [12,14]. Our data is consistent with previous large-scale fibrinolytic trials reporting 2.1% to 6.1% of re-infarction rate after thrombolytics, although occurs in frequently but confers increased risk of cardiac mortality [9,11,15]. This strong association and most predictive value for re-infarction and mortality affirm their powerful role in risk stratification after AMI [12,16].

Re-infarction was associated with increased in-hospital complications and subsequent deaths. Nearly 1 in 6 re-infarction went into cardiogenic shock and one-third developed chronic heart failure. Major causes of death observed were anterior MI with re-infarction, cardiognic shock and cardiac arrythmias. Pooled data from Thrombolysis and Angioplasty in Myocardial Infarction (TAMI) and re-current ischaemia in GUSTO trials indicate that patients with re-infarction have significantly higher rates of death and heart failure than patients without recurrent ischaemic events [12,13,16].

Table-2: Effect of Re-infarction on mortality

Patient Status	No. of Patients	Deaths	%age Mortality	P-value
Total AMI Patients	200	15	30.77	.013
Re-infarctions	13	4	7.5	

Table-3: Relationship of killip class with re-infarction

Killip class	No. of Patients	Re-infarction	Percentage
I	111	5	4.5
II	37	3	8.1
III	29	3	10.34
IV	13	4	30.77

P – Value .021

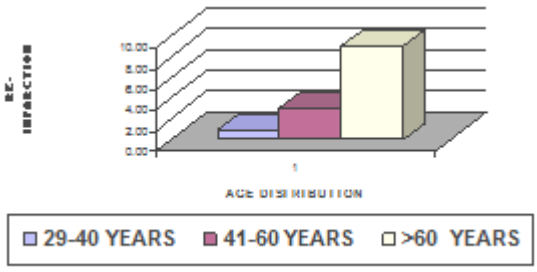

Fig.1: Age influence on re-infarction

Frequency of re-infarction did not differ significantly between smokers and non-smokers. Influence of smoking on re-infarction was also examined in the International Tissue Plasminogen activator-streptokinase mortality trial. Barbash and colleagues [17] reported that active smokers had significantly lower rates of in-hospital re-infarction compared with ex-smoker and nonsmoker (2.7%, 5.0% and 4.7% respectively; P<0.001). Similarly, TIMI II investigators have shown paradoxical; benefit of smoking on survival after MI. However this "protective" effect of smoking may be lost quickly Our study was not designed to capture post discharge re-infarction events but other investigators have shown four fold rise in re-infarction rate at one year in patients who continue to smoke versus those who stop smoking [12 & 18].

Despite the fact that 6.5% of patients treated with streptokinase for acute mycordial infarction experienced in-hospital clinical re-infarction with an associated increased in mortality, few reports describe or evalauate the treatment strategies used in this population. The relative advantages and disadvantages of interventional revascularization compared with repeat thrombolysis for re-infarction have not been quantified. Both treatments are available in many hospitals, but coronary intervention procedures are usually associated with at least 1 to 3 hours of logistic delay, especially after working hours [19, 20,21]. The GUSTO 1 and ASSENT 2 databases gave us a unique opportunity to review the worldwide changes in practice over the last 10 years in the treatment of re-infarction after thrombolysis. Repeat thrombolytic therapy should be considered especially where and when timely cardiac catheterization and interventional capabilities are not readily available. However the risk of repeat thrombolysis is to be weighed carefully with the improved mortality gained at likely risk of increased bleeding, as shown in ASSENT 2 [19].

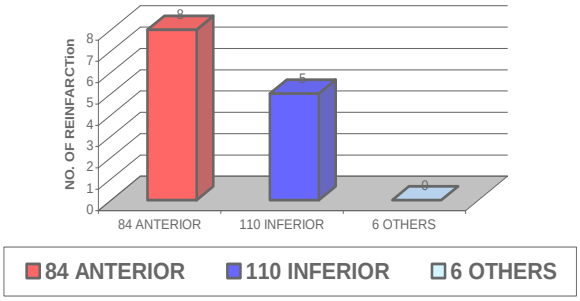

Fig.2: Effect of MI location on re-infarction

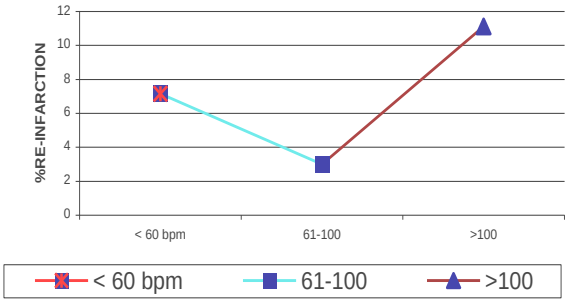

Fig.3: Relation ship of heart rate with re-infarction

By showing that re-infarction is strong independent predictor of in-hospital death after acute MI, our analysis supports ongoing clinical trials of strategies to prevent early re-infarction [22]. The higher associated mortality and narrow therapeutic window suggest that prevention of re-infarction should be an important goal of MI management [23,24,25].

Important limitations of this study were inability to capture unrecognized re-infarction in patients who died early, median time to death was 3 days with maximum death within 48 hours of re-infarction. Some patient's probably died from re-infarction be fore confirmatory enzyme or ECG data became available or before serum cardiac markers could become elevated. These patients were not classified as re-infarction.

CONCLUSION

In the current study 6.5% of the patients who underwent thrombolysis for AMI suffered in-hospital re-infarction, associated with reduced survival. Cardiac Mortality was five times higher in patients with re-infarction

during initial hospitalization than patients without re-infarction or recurrent ishaemia. The findings and predictors discussed will raise awareness of this post-infarction complication and lead more clinicians to consider aggressive therapies. Further studies should be carried out to assess the results of early re-vascularization in the form of PCI (Percutaneous Coronary Intervention), CABAG, use of newer thrombolytic agents, oral / iv antiplatelet and new antithrombin regimens in prevention / treatment of re-infarction and with a hope for a better survival in our patients population.

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