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Original Research Article

Observational Study on Failure of Thrombolysis with Streptokinase in Acute Myocardial Infarction Using ECG Criteria

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Abstract:

Background: The primary treatment for acute myocardial infarction (AMI), which is a growing concern in developing countries, is thrombolysis. Patients with a poor prognosis are those who fail to achieve effective reperfusion, which occurs in 25–50% of cases. Since there are other options for reperfusion, it's critical to recognize them. Aim of this study to failure of thrombolysis with streptokinase in acute myocardial infarction using E.C.G criteria.

Methods: A prospective study of patients presenting with acute myocardial infarction in Department of Medicine, Darbhanga Medical College and Hospital, Laheriasarai, Bihar for a period of one year from September 2020 to August 2021. A total of 220 patients who presented with acute myocardial infarction were included in the study.

Results: Out of 220 patients 193(87.7%) males and 27 (12.3%) females participated in the study. All the patients underwent thrombolysis with streptokinase. Out of 220 patients who were being thrombolysed with streptokinase, most of them (97; 41.1%) were in the age group of 56-65 years. Out of all the patients who underwent thrombolysis (n=220), thrombolytic failure was observed in 121 (55%) patients. Failure rate was significantly higher in the age group of 56-65 years (88; 72.7%). Significantly higher prevalence of thrombolytic failure with streptokinase was observed among diabetic patients (65.2%) as compared to non-diabetics (52.3%).

Keywords: Thrombolysis, Streptokinase, Acute Myocardial Infarction.

Introduction

The acute coronary syndromes include unstable angina, ST segment elevation myocardial infarction (STEMI), non-ST segment elevation myocardial infarction (NSTEMI). [1] Worldwide around 7 million people suffer myocardial infarctions per year (White et al., 2008). Around one third of these patients having acute myocardial infarction (AMI) die within the first hour of having symptoms usually due to fatal arrhythmia.

Characteristic ST Segment elevation in the 12-lead electrocardiogram (ECG) accompanied by clinical symptoms of chest pain provide the most rapid way to diagnose those patients who should receive thrombolysis to help dissolve thrombus and restore blood flow.

Thrombolysis has been the cornerstone of treatment for patients having STEMI by improving outcomes and preserving left ventricular function. [2] Analysis of ST segment resolution on ECG, after fibrinolytic therapy, in cases of STEMI offers an attractive and cost-effective solution to assess coronary reperfusion. [3] Although successful recanalization of the epicardial vessel is a necessary condition, it is the microvascular flow that most strongly correlates with outcome.

Patients with AMI experience sudden cardiac death due to ventricular tachycardia and fibrillation (VT/VF). These complications occur more in patients with failed thrombolysis in STEMI. ST segment changes reflect myocardial rather than epicardial flow and hence yield prognostic information beyond that provided by coronary angiogram alone. [4]

Since there is paucity of data on the use of streptokinase as a thrombolytic agent in AMI in our region, this study was conducted to determine the failure rate of thrombolysis with streptokinase in AMI using ECG criteria.

Material and Methods

This prospective study was conducted in the Department of Medicine, Darbhanga Medical College and Hospital, Laheriasarai, Bihar for a period of one year from September 2020 to August 2021. All cases of AMI with the diagnosis on WHO criteria i.e. presence of any two of the following were included: (i) Chest pain consistent with acute myocardial infarction of <12 hours duration; (ii) Electrocardiography changes i.e. ST segment elevation >0.2 mv in at least two contiguous chest leads or >0.1 mv in at least two contiguous limb leads; (iii) New or presumably new left bundle branch block on electrocardiogram; and (iv) Raised levels of cardiac enzymes (CPK-MB more than double of the reference value or positive troponin I/T test).

Exclusion criteria included patients with non-ST elevation myocardial infarction (NSTEMI), subjects who were not given streptokinase due to contraindication to the therapy, streptokinase given in other hospitals, previous streptokinase use (5 days to 2 years), symptom-to-needle time of more than 24 hours and patients who had undergone primary angioplasty and fully evolved cases with pathological Q wave.

A detailed history was taken, particularly of age, sex, occupation, and other risk factors like smoking, diabetes mellitus, hypertension, family history of ischaemic heart disease, etc. Complete physical examination of patients was done upon presentation in the emergency department and important parameters such as pulse, blood pressure, respiratory rate, pallor, cyanosis, JVP, pedal edema, LAP, icterus, clubbing were noted. Time from onset of chest pain to presentation of patient in emergency was noted through the history. The first ECG was recorded prior to starting streptokinase, and the second ECG was recorded after completion of streptokinase infusion. This was done after 90 minutes, but a time window of 2 to 4 hours was allowed. Vertical height of ST segment elevation in the lead with the maximum segment elevation (worst infarct lead) before and after streptokinase was measured using a standard ruler in millimeter. The ST segment was measured 80 milliseconds from J point, which corresponds to the peak of ST elevation. J point was defined as the first turning point in the ST segment on ECG. Failure of thrombolysis with streptokinase was defined as <50% reduction in ST segment elevation after 90 minutes (time window 2 to 4 hours) in the worst infarct lead with no idioventricular rhythm. Streptokinase was given intravenously to each patient at a dose of 1.5 million units, diluted in 100 ml of normal saline, over one hour.

All data was analyzed using the Statistical Package for Social Sciences (SPSS). Numerical data was recorded as mean and standard deviation, and categorical data as frequency and percentages. A p-value of <0.05 was considered significant association with thrombolysis failure using streptokinase. Univariate analysis using chi-square test for categorical data and student's t-test for numerical data was used to compare the association of variables.

Results

A total of 220 patients, 193 (87.7%) males and 27 (12.3%) females were included in the study. Most of the patients 97 (41.1%) were in the age group of 56-65 years, followed by 86 (39.1%) in the age group of 46-55 years, 25 (11.4%) in <45 years and 12 (5.4%) in the age group of 66-75 years. Thrombolytic failure rate was observed in 121 (55%) patients, significantly more in the age group of 56-65 years (88; 72.7%). Mean age (59.5 years) in thrombolytic failure group was 10 years higher than success group. Failure rate was more in females (18/27; 66.7%) compared with males (103/193; 53.4%).

Relationship of thrombolytic failure with location of myocardial infarction, symptom-to-needle time, KILLIP class, smoking, diabetes mellitus and hypertension respectively is given in Table 1. Mean (± standard deviation) values of total leukocyte count (TLC), vital signs, duration of door-to-needle time in thrombolytic failure and success groups is given in Table 2. Medication used in thrombolytic failure and success groups is given in Table 3.

Table 1: Relationship of Thrombolytic Failure with Different Parameters

Parameters		Failure Group n (%)	Success Groupn (%)	p-value
Location	Anterior Inferior	99(75) 22(25)	33(25) 66(75)	0.00
Symptom-to needle time	≤6 hours >6 hours	56(45.2) 65(67.7)	68(54.8) 31(32.3)	0.00
KILLIP class	Class I Class II-IV	65(56) 56(53.8)	51(44) 48(46.2)	0.74
Habit	Non-smoker Smoker	26(61.9) 95(53.4)	16(38.1) 83(46.6)	0.31
Diabetes status	Diabetic	30(65.2)	16(34.8)	0.11

	Non-diabetic	91(52.3)	83(47.7)	
Hypertension status	Hypertensive Non-Hypertensive	55(64.7) 66(48.9)	30(35.3) 69(51.1)	0.02

Table 2: Mean (± standard deviation) values of Thrombolytic Failure and Success Groups

Parameters	Failure Group Mean (±SD)	Success Group Mean (±SD)
Total Leukocyte count (mm^3)	13.8 (±4.3)	13.3 (±3.7)
Heart Rate (bpm)	81 (±18.5)	74 (±16.6)
SBP (mmHg)	134.8 (±26.9)	125.1 (±23.2)
DBP (mmHg)	84.2 (±19.6)	76.5 (±14.3)
Door-to-needle time (minutes)	116 (±83.5)	91 (±47.5)

Table 3: Medication Used in Thrombolytic Failure and Success Groups

Medication	Failure Group n (%)	Success Group n (%)	Total n (%)	p-value
Beta Blocker	84(60)	56(40)	140(63.6)	0.33
ACE inhibitor	90(54.5)	75(45.5)	165(75)	

Discussion

In the present study, the failure rate of thrombolysis with streptokinase was 55% in STEMI, using the ECG criteria. These results are in concordance with the multicentre GUSTO-I trial which compared different thrombolytic strategies, where streptokinase was shown to have 54% arterial patency rate after 90 min. [5]

Patients with anterior location of infarct had a worse clinical outcome, as compared to inferior infarct in the present study. This was related to a larger final infarct size and a lower subsequent left ventricular ejection fraction. [6] These results are in contrast to the observation of large clinical trials, including GUSTO-I, which showed that thrombolysis with streptokinase in patients with anterior infarct was associated with lower mortality and morbidity. [5] However, our results are in concordance with subsequent studies including INJECT, which showed that patients with anterior infarct achieved less reperfusion success compared to inferior infarct when given thrombolytic agent. [3] Our study has shown that thrombolytic failure with streptokinase was significantly higher (p=0.00) with anterior wall MI (75%) as compared to inferior wall MI (25%).

In the present study, 67.7% of the patients with symptom-to-needle time >6 hours had failed thrombolysis with streptokinase as compared to 45.2% failure rate in those with symptom-to-needle time <6 hours (p=0.00). This observation is in concordance with Kharash et al. [7] who concluded that shorter the time lag between onset of pain and treatment the better are the results.

This study was not intended to look into the causes of longer symptom-to-needle time, but a search through the records had identified possible reasons which included inappropriate initial triage, delay in transport, missed initial diagnosis and delay in starting treatment. Being a "myocardial infarction equivalent", history of diabetes mellitus had strongly predicted subsequent episode of cardiac event as well as mortality. As shown by Maket al., diabetic cohorts in a GUSTO-I trial (n = 5,944) had a higher mortality rate at 30 days with OR 1.77 and this risk was maintained after one year. [5] Although only 20.9% of the study cohorts were diabetic patients in the present study, 65.2% of the diabetic patients did not achieve successful thrombolysis as compared to non-diabetic in whom failure was seen in 52.3% (p=0.11). Our observation is in concordance with that of Chowdhury et al., who concluded from their study that reperfusion failed in 67.2% of diabetic patients with STEMI in comparison with 19.8% in non-diabetic group. [8]

The reasons for the higher risk of failure were the diffuse and multiple small vessel diseases in diabetic patients, which did not respond well to streptokinase. Diabetic patients usually present to the hospital later, due to their impaired sensation in myocardial ischaemic pain. In addition, diabetic patients have a lower ejection fraction.

Hypertension is a known risk factor for higher mortality in patients who have AMI, and it is additive to other known risk factors, as shown in the Framingham study. [9] Large international trials have shown that hypertension was an important predictor of mortality in the thrombolysis era, including GUSTO-I and GISSI-2. [10] A total of 38.6% patients were hypertensive in our study. Most of the hypertensive patients (64.7%) did not achieve successful thrombolysis with streptokinase in comparison to 48.9% failure rate in normotensive patients (p=0.02). This is in concordance with the observation of Lee et al., who reported failure in 66.2% of patients with hypertension in comparison to 51.2% in normotensive patients. Possible reasons for the higher failure rate were poorly-controlled hypertension, high-risk nature of hypertension and possible accelerated atherosclerosis associated with endothelial dysfunction. [11] In our present study, failure rate was higher in females (66.7%) as compared to males (53.4%) (p=0.19). Our results are in contrast to the observation of Sultana et al., who found that thrombolytic failure with streptokinase was higher in males (39.3%) as compared to females (36.8%). [12] In our study, 80.9% patients were smokers. Thrombolytic failure was seen in 53.4% of smokers as compared to 61.9% in non-smokers (p=0.31). This is in contrast with the observation of Sultana et al., who reported thrombolytic failure in 61% of smokers. [12] In our study, mean age in thrombolytic failure group was 59.5 years as compared to 49.4 years in successful thrombolysis group. Maximum patients were in the age group of 56-65 years (n=97; 44.1%), with thrombolytic failure being maximum in the same age group (n=88) (p=0.00).

In our study, the failure rate of thrombolysis was higher in patients with Killip Class I (56%) as compared to patients with Killip Class II-IV (53.8%) (p=0.74). Streptokinase is the first generation thrombolytic agent. It acts by complexing with plasminogen and it is not fibrin specific. Eventually there is depletion of plasminogen, known as "plasminogen steal", which will limit the fibrinolytic action accounting partly for the thrombolysis failure. [13] Late presentation is an important risk factor for failed thrombolysis in AMI. Persistence of chest pain and non-resolution of reciprocal ST depression are significantly associated with failed thrombolysis. [14]

Conclusion

Since streptokinase has a high failure rate of thrombolysis among AMI patients, other reperfusion strategies should be considered, especially in the high-risk patients. Newer generation thrombolytic agents include the tissue plasminogen activators (tPA) (e.g. alteplase and reteplase). These are associated with a better thrombolysis outcome compared to streptokinase. However, these agents are expensive and not always available in resource-poor areas. Another strategy is PCI, which in many prospective trials have shown better mortality outcome compared to thrombolytic agents.

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