DOOR TO NEEDLE TIME OF STREPTOKINASE AND ST SEGMENT RESOLUTION ASSESSING THE EFFICACY OF REPERFUSION THERAPY AT KARACHI INSTITUTE OF HEART DISEASES

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Background: Early start of treatment including coronary revascularisation has been recognised as crucial variable in the outcome of acute ST-segment Elevation Myocardial Infarction (STEMI). Objectives of the study were to determine the magnitude of ST-segment resolution after thrombolytic therapy predicts short- and long-term outcomes in patients with an Acute Myocardial Infarction (AMI). **Methods:** The duration of quasi experimental study was 3 years, from July 2006 to June 2009, conducted at Karachi Institute of Heart Diseases. Total 1,023 patients of STEMI treated with streptokinase (SK) were enrolled in the study. **Result:** Of the total 1023, 689 (67.3%) patients were males and 334 (32.6%) were females. Six hundred and twenty-nine (61.5%) were successfully resolved after thrombolytic therapy while in 395 (38.5%) patients ST-segment could not resolve into 3 conventional ST-segment resolution categories at 60 minute and 90 minute after thrombolysis. Three hundred and twelve (30%) and 444 (43.4%) with complete resolution, 344 (33.62%) and 325 (31.76%) with partial resolution, 367 (35.8%) and 491 (19.29%) were with no resolution at 60 and 90 minutes respectively. **Conclusion:** Shock, congestive heart failure, and recurrent angina and ischemia occurred more often in patients with partial or no ST resolution as compare to complete resolution.

Keywords: myocardial infarction, thrombolysis, ST-segment elevation, congestive heart failure

INTRODUCTION

ST-Elevation Myocardial Infarction (STEMI) is defined as ST elevation on the ECG, which is the electrical manifestation of the pathophysiological changes that follow a thrombotic occlusion of an epicardial coronary artery.[1] Although a single ECG presents about 10 seconds of waveform morphology, acute STEMI displays its dynamic behaviour over time, both spontaneously and in response to therapy.[2] The ST-segment resolution stratified by Schroder into 3 categories (complete resolution, ≥70%; partial resolution, 30–70%; and no resolution, <30%) after reperfusion therapy has been identified as a prognostic indicator for patients with acute myocardial infarction (AMI).[3]

Early resolution of ST-segment elevation has been demonstrated to be a simple and useful predictor of final infarct size, left ventricular function, and clinical outcomes after both thrombolytic and coronary interventional approaches.[4] Thrombolytic therapy for acute myocardial infarction reduces fatality and improves clinical outcomes. However, in 60% of patients the treatment does not restore perfusion in the myocardium at risk and such failure indicates a worse prognosis.[5]

Reperfusion therapy in STEMI is the most important component of treatment, as it strongly influences short- and long-term patient outcome. The main objective of healthcare providers should be to achieve at least 75% of reperfusion therapy applied to patients of STEMI in a timely manner, and preferably within the first 3 hours after onset of symptoms.[6] In the past, reperfusion was commonly assessed in terms of coronary blood flow, achievement of Thrombolytic Induced Myocardial Infarction (TIMI)-3 flow being a favourable sign.[7]

By contrast, ST-segment resolution 60–90 minutes after thrombolysis is an excellent marker of successful myocardial reperfusion. The ischemic time, door-to-balloon time and clinical risk are important determinants of favourable outcome and a strong predictor of survival and preservation of left ventricular function.[8] Longer delays from symptom onset to hospital presentation were associated with reduced likelihood of receiving primary reperfusion therapy, and even among those treated, late presenters had significantly longer door-to-balloon and door-to-drug times.[9]

The aim of our study was to correlate the incidence of complications with ST-segment resolution, thereby reinforcing the role of ST-resolution as a marker of improved clinical outcome in cases of STEMI.

MATERIAL AND METHODS

The duration of quasi experimental study was 3 years from July 2006 to June 2009, conducted at Karachi Institute of Heart Diseases.

Inclusion criterion was age 30–75 years, admission to the coronary care unit with chest pain of ≤4 hour duration, and ECG evidence of transmural ischemia (1–2 mm ST-segment elevation in ≥2 limb leads and/or ≥2 mm ST-segment elevation in ≥2 precordial leads).

Exclusion criteria were past Q-wave myocardial infarction, severe cardiac failure, systolic blood pressure <90 mm Hg, AMI within the preceding 7 days, moderate to severe valvular heart disease, known allergy to any of the protocol medications, and contraindications to use of SK (streptokinase administration within the previous 6 months, allergy to the drug, surgery or cerebrovascular accident within previous 6 weeks, warfarin therapy, active peptic ulcer disease, bleeding disorders, uncontrolled hypertension).

The study population was divided into 3 groups at 60 minutes and 90 minutes after administration of streptokinase.

1: Patients with complete (>70%) ST-segment resolution
2: Patients with partial (30–70%) ST-resolution, and
3: Patients with no ST-segment resolution.

The endpoint was a composite of recurrent ischemic chest pain, Heart failure, arrhythmia or death. ST elevation was recorded in millimetres from the lead in which maximum elevation was observed. Repeat ECG was performed after 60 and 90 minutes of administration of Streptokinase. Follow-up was conducted for each patient throughout his or her hospital stay.

RESULTS

Total 1023 patients of STEMI treated with streptokinase were enrolled in our study. Six hundred and eighty-nine (67.3%) were males and 334 (32.6%) were females. Six hundred and twenty-nine (61.5%) were successfully resolved after thrombolytic therapy while in 395 (38.5%) patients ST-segment could not resolved.

Table-1 shows smoking/tobacco chewing habits, history of diabetes, hypertension, hypercholesterolemia, peripheral vascular diseases, previous history of Unstable Angina (USA), myocardial infarction and revascularisation. Among the patients who reached early to hospital and received streptokinase 587 (88.57%) showed successful resolution of ST-segment, only in 76 (11.46%) thrombolysis failed because of reasons like severe hypotension, bleeding from different sites, anaphylactic reactions during infusion of streptokinase, and not getting full dose of thrombolytic therapy.

Anterior wall myocardial infarction was seen in 690 (67.44%) patients, 429 (62%) had good results while 261 (37.8%) failed to resolve ST segment. Lateral wall MI was present in 178 (17.39%) patients. Among them 112 (63%) successfully resolved ST-segment while 66 (37%) failed to resolve. Inferior MI was evident in 145 (14%) of patients. Here 103 (71%) had good results and 42 (29%) had failure to resolve. Ten (1%) patients were with posterior MI, among them 8 (0.8%) had ST-segment resolution and 2 (0.2%) failed to resolve ST-segment. Thirty-eight (3.7%) patients developed pulmonary oedema, 18.42% had successful thrombolysis and 21 (55.26%) could not resolve ST-segment.

Table-2 stratifies patients into 3 conventional ST segment resolution categories at 60 minute and 90 minute after thrombolysis. Three hundred and twelve (30%) and 444 (43.4%) patients were with complete resolution, 344 (33.62%) and 325 (31.76%) were with partial resolution, and 367 (35.8%) and 491 (19.29%) were with no resolution respectively. Frequency of stroke, shock, re-ischemia, re-infarction, congestive heart failure and death were more with persistent elevation of ST-segment as compare to complete resolution.

Table-1:- Patients' characteristics in relation to ST-segment resolution (Success) and non-resolution (Failure)

Variables	Total	Success	Failure	*p*
Total patients given Streptokinase	1023	629 (61.5%)	394 (38.5%)	
Male	689 (67.3%)	418 (60.66%)	271 (39.33%)	0.440
Female	334 (32.6%)	211 (63%)	123 (36.8%)	
Smoker/tobacco chewer	766 (74.8%)	525 (83.4%)	241 (61%)	<0.001
Diabetes	435 (42.5%)	298 (68.5%)	137 (31.49%)	<0.001
Hypertension	640 (62.56%)	515 (80.46%)	125 (19.53%)	<0.001
Hypercholesterolemia	488 (47.7%)	390 (80%)	98 (20%)	<0.001
Peripheral vascular disease	15 (1.46%)	11 (73.3%)	4 (26.6%)	0.07
Previous angina	658 (64.3%)	550 (83.58%)	108 (16.4%)	<0.001
Previous myocardial infarction	440 (43%)	339 (77%)	101 (23%)	<0.001
Previous revascularization	55 (5.37%)	32 (58%)	23 (41.8%)	0.600
Door to needle time within 1-hour	663 (64.8%)	587 (88.53%)	76 (11.46%)	<0.001
Anterior infarct	690 (67.44%)	429 (62%)	261 (37.8%)	0.510
Lateral infract	178 (17.39%)	112 (63%)	66 (37%)	0.660
Inferior infarct	145 (14%)	103 (71%)	42 (29%)	0.010
Posterior infarct	10 (1%)	8 (0.8%)	2 (0.2%)	0.220
Heart rate (bpm) Mean (Range)	72 (60–84)	73 (63– 85)	74 (64–86)	
Systolic blood pressure Mean (Range)	132 (118–150)	135 (120–150)	135 (120–150)	
Killip class >I	38 (3.7%)	7 (1%)	21 (5.3%)	<0.001
Peak creatine kinase MB ≥5 UNL	897 (87.63%)	722 (80%)	175 (19.50%)	<0.001

Table-2: Baseline characteristics and clinical outcome after 6-weeks according to ST-segment resolution category after 60 and 90 minute

Outcome	ST- Resolution			
	Complete (≥70%)	Partial (30 to <70%)	None (<30%)	
Patients with 60 min ST-resolution	**312 (30%)**	**344 (33.62%)**	**367 (35.8%)**	*p*
Shock	15 (4.8%)	19 (5.5%)	27 (7.35%)	0.340
Stroke	3 (1%)	5 (1.4%)	8 (2.17%)	0.430
Re-Ischemia	44 (14%)	58 (16.8%)	63 (17%)	0.500
Re-Infarction	13 (4.16)	33 (10.57%)	48 (15.38%)	*0.003*
Death	5 (1.6%)	9 (2.6%)	12 (3.2%)	0.380
CCF	36 (11.53%)	65 (18.9%)	98 (26.7%)	<0.001
Patients with 90 min ST-resolution	**444 (43.4%)**	**325 (31.76%)**	**254 (24.8%)**	
Shock	39 (8.78%)	44 (13.53%)	49 (19.29)	<0.001
Stroke	9 (2%)	11 (3%)	15 (6%)	0.020
Re-Ischemia	48 (10.81%)	55 (16.9%)	59 (23.2%)	<0.001
Re-infarction	29 (6.53%)	32 (9.84%)	46 (18%)	<0.001
Death	12 (2.70%)	18 (5.53%)	29 (11.41%)	<0.001
CCF	59 (13.28%)	65 (20%)	72 (28.34%)	<0.001

Table-3 demonstrates Thrombolysis in Myocardial Infarction (TIMI) flow grading after angiography. Three hundred and twenty-six patients presented with Left Anterior Descending Artery (LAD) artery lesions among them 20 patients in TIMI 0/1, 57 with TIMI 2 and 77 with TIMI 3 flow in patients with resolving ST-segment, while 85, 54, and 33 with TIMI I, II, and III flow respectively in non-resolve ST-segment. Left Circumflex Artery (LCX) lesions in 188 patients 15, 14, and 56 with TIMI I, II, and III respectively, 50, 36 and 17 in non-resolving ST-segment. One hundred forty-eight patients with Right Coronary Artery (RCA) stenosis here 8, 26, 33 patients were showing TIMI I, II, and III respectively while 25, 18, and 38 showing TIMI I, II, and III respectively in persistent ST-elevation. This indicates TIMI scoring improved with resolving ST- segment. Our study proved as ejection fraction also improved with resolving ST elevation.

Table-3: Baseline characteristics according to TIMI flow grade categories after angiography

Group/ Variable	Total	TIMI 0/1 ST-Resolved	TIMI 0/1 ST-Persisted	TIMI 2 ST-Resolved	TIMI 2 ST-Persisted	TIMI 3 ST-Resolved	TIMI 3 ST-Persisted	
Total	**678**	**45**	**165**	**99**	**132**	**168**	**69**	*p*
LAD	326	20 (6%)	85 (26%)	57 (17.5%)	54 (16.56%)	77 (23.6%)	33 (10%)	0.170
LCX	188	15 (8%)	50 (26.5%)	14 (7.44%)	36 (19%)	56 (29.8%)	17 (9%)	*0.020*
RCA	148	8 (5.4%)	25 (17%)	26 (17.56%)	38 (25.67%)	33 (22.29%)	18 (12%)	0.050
Others	16	2 (12.5%)	5 (31%)	2 (12.5%)	4 (25%)	2 (12.5%)	1 (6.25%)	0.740
Ejection Fraction		30–35%	25–30%	35–40%	35–40%	>45%	>45%	

DISCUSSION

This study comparatively assesses the predictive accuracy of early (60 minute and 90 minutes) standard 12-lead ECG against post-infarction clinical endpoints and later ECGs. Patients with AMI arrive at our hospital relatively rapidly due to its central location and most of the patients could utilise maximum benefit of thrombolytic therapy because streptokinase (SK) was provided by government free of cost. Several modes of reperfusion therapy for evolving Myocardial Infarction (MI) have been developed which differ in terms of effectiveness, complexity and cost.[10] Currently, the most relevant treatment options are: SK (1.5 MU over 1 hour), reteplase (2 boluses of 10 MU), and alteplase (tissue plasminogen activator, t-PA, 100 mg over 1.5 hour) and immediate angioplasty.[11] Streptokinase is the least costly treatment option while direct angioplasty is expensive and complex.[12] We used SK due to cost effectiveness. Treatment of acute STEMI with thrombolytic therapy showed greater mortality reduction.[13,14] Thrombolytic therapy with SK and other agents reduces mortality and is now well accepted as the mainstay of revascularisation options for most patients after an acute myocardial infarction.[15]

Streptokinase is as efficacious as alteplase (recombinant tissue plasminogen activator; Rt-PA), anistreplase, reteplase and saruplase in reducing mortality.[16] Enoxaparin is superior to unfractionated heparin, it also proved as fibrinolytic therapy with combination of SK and the potent anticoagulant agent resulted in similar adjusted outcomes compared with more costly regimens utilising a fibrin-specific lytic.[17] Thrombotic coronary artery occlusion is now recognised as the usual cause of acute myocardial infarction. Following coronary occlusion, myocardial necrosis begins within 40 minutes in the subendocardium and progresses outward toward the epicardium over the next several hours. The intracoronary infusion of SK will produce lysis of the occluding thrombus in up to 80% of patients.[18] The SK regimen (1.5 MU/60 minutes) has remained unchanged for the past 20 years in patients with STEMI due to fear of hypotension (a specific effect of this thrombolytic agent) and of haemorrhagic complications.[19] Restoration of infarct vessel patency has become one of the cornerstones of treatment for acute ST-elevation (Q wave) myocardial infarction.[20] Intravenous fibrinolytic agents are the most widely used means for acute reestablishment of vessel patency, and their use has become routine as large clinical trials have shown their unequivocal benefit.[21] Risk assessment based on clinical information, exercise stress testing, and an estimate of left ventricular function contribute with prognostic information in thrombolysed MI patients.[22] We perform coronary angiogram and assess TIMI flow as well as ejection fraction of left ventricle, showed improvement of TIMI flow and ejection

fraction in patients with resolve ST-segment after thrombolytic therapy. Thrombolytic therapy with SK is most effective if given within the first 1.5 hours after the onset of symptoms of acute myocardial infarction.[23] Determination of ST-segment resolution 60 minutes after the administration of thrombolytic therapy allows accurate risk stratification for mortality and congestive heart failure.[24] Although primary angioplasty should be the preferred treatment strategy when inter-hospital transfer can be completed within 2 hours.[25] Our results showed 2.7% mortality in complete resolution while 11.4% with no resolution of ST-segment.

CONCLUSIONS

Thrombolytic therapy initiated within 1 hour of a patient presenting to a hospital with AMI reduces the mortality rates. Using simple measurements of ST-segment elevation high and low risk groups of patients can be identified as early as 60 and 90 minutes after initiating thrombolysis after AMI. Patients with failure of ST-segment resolution after thrombolytic therapy or who re-infarct after early ST-segment resolution warrant aggressive treatment.

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