ORIGINAL ARTICLE

Diversity in Response to Thrombolysis with Streptokinase in Patients Presenting With Acute Myocardial Infarction

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ABSTRACT

Background: A plethora of literature is available on therapeutic implications of thrombolytic therapy with Streptokinase but the variations in response to thrombolysis of different ethnic and racial classes has been overlooked in the past. The rationale of our study is to evaluate the patterns of response to Streptokinase in different subsets of patients not evaluated in the previous literature.
Aim: To evaluate various parameters of diversity in response to thrombolysis with streptokinase in patients presenting with acute Myocardial Infarction in various subsets of our general population..
Methods: This quasi experimental study was conducted in the emergency department of Punjab Institute of Cardiology Lahore from December 2011 to January 2013. We enrolled 300 Patients of both genders presenting with acute myocardial infarction and thrombolyzed all of them with streptokinase. The primary end point was evaluation of diversity in response to thrombolysis and duration of this response. Secondary end points included the analysis of relationship between streptokinase therapy and various demographic parameters and clinical factors in the population under study.
Results: The data collected from 189 Males and 111 Females (n=300) was analyzed on SPSS version 16 for diversity and duration of response to thrombolysis with streptokinase..
Conclusion: The overall survey of 300 patients under study that there is a significant variation in response and duration of response to thrombolysis with streptokinase in various ethnic, racial and clinical subsets of patients.
Keywords: Acute Myocardial Infarction (AMI) , Streptokinase(SK), Thrombolysis, Diversity, Response, Percutaneous Coronary Intervention (PCI), Coronary Artery Bypass Grafting (CABG)

INTRODUCTION

Acute Myocardial Infarction is one of the leading causes of death globally. The pathogenesis of acute Myocardial Infarction involves rupture of a pre existing plaque and formation of an occlusive thrombus resulting in Coronary Thrombosis and acute episode of MI. Since the inception of Coronary care units worldwide there has been a dramatic decrease in mortality due to AMI from 30 to 15% and a further reduction of 5-7% by the use of Thromoblytics like Streptokinase and other agents. Streptokinase is a first generation fibrinolytic agent isolated from haemolytic streptococci and produced from bacterial cultures and is primarily the original thrombolytic agent. It has no direct effect on plasminogen and acts by binding with plasminogen to form a 1:1 complex that becomes an active enzyme to convert plasminogen to plasmin. These Streptokinase plasminogen complexes are thus converted to Streptokinase plasmin complexes known as Ogen complexes[1]**.** These complexes activate circulating and fibrin bound plasminogen producing a systemic lytic state. Moreover Streptokinase may increase circulating levels of activated Protein C which further enhances clot lysis[2] It results in substantial systemic fibrinogenolysis, fibrinoginaemia and elevation of fibrin degradation products (FDPs) on account of its non fibrin specificity and capability of lysing circulating and clot bound plasminogen to plasmin[3]**.**.

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MATERIAL AND METHODS

This study was conducted at the emergency department of Punjab Institute of Cardiology Lahore from December 2011 to January 2013. Three hundred diagnosed patients of acute ST segment elevation Myocardial Infarction from both genders presenting within twelve hours of the onset of symptoms and also those patients who presented after twelve hours of the onset of symptoms with persistent chest pain were included in this study. (AHA guidelines for thrombolysis with SK II a). The diagnosis of ST segment elevation Myocardial Infarction was established on the basis of WHO criteria i.e., history of typical chest pain, ST-T segment elevation or more than 1 mm in two or more consecutive ECG leads and elevation of Biochemical

markers like cardiac enzymes and Troponin T. All patients were thrombolyzed with Streptokinase. Response and duration of this response to Streptokinase and its diversity in various subsets of patients was thoroughly investigated and evaluated. Duration and diversity of response to Streptokinase were our primary end points while relationship of this response with other variables was our secondary end point. Response to Streptokinase was monitored according to the established guidelines of resolution of ST segment elevations and relief of chest pain. Similarly duration of response to Streptokinase was investigated on the basis of time interval from the onset of symptoms to the injection of Streptokinase. The dead line for inclusion criteria with ST segment elevations and chest pain was a duration of twelve hours from the onset of symptoms. Patients were thrombolyzed with Streptokinase in the emergency room and were observed for successful thrombolysis as per electrocardiographic and clinical criteria i.e resolution of ST segments and relief of chest pain and were classified as early, late and non responders. Those responding in less than 30 minutes were early, within 30 minutes as normal and more than 30 minutes and later responders. Whole data was analyzed on SPSS for windows version 16 and results compiled were tabulated to finally evaluate the relationship of various parameters relating to response to thrombolysis with SK and its duration..

RESULTS

Out of 300 patients 189(63%) were Male and 111(37%) were Female. Mean age of the patients was 50.2±14.3 years. It was found that 240(80%) patients were from the province of Punjab, 23(7.6%) were from Sindh, 19.4(6.4%) from Balochistan and 18(06%) from Khyberpakhtoonkhwa. 03(01%) were foreigners while 297 (99%) were Asians. 63(21%) cases had fair complexion, 83(27.7%) were dark in colour and 154(19.3) had normal or wheatish complexion. Married cases were 242(80.7%) while 58 (19.3%) were single. About 143(47.7%) belonged to educated class and 157(52.3%) were uneducated. Business executives were 68(22.7%) while 88(29.3%) were professionals. Sedentary life style was seen in 242(80.7%) cases and 58 (19.3%) belonged to exercising group of people who had active life style. One hundred fifty seven (52.3%) were diagnosed cases of anxiety neuroses. Out of 111 females 10(3.3%) patients were pregnant and 07(2.3%) had menstruation when they sustained acute MI. Evaluation of this study population for risk factors revealed 167(55.7%) smokers, 130(43.3%) obese, 183(61%) diabetics, 179(59.7%) hypertensives, 164(54.7%) hyperlipidaemia cases, 101(33.7%) alcoholics, 41(13.7%) drug addicts of various classes and 202(67.3%) patients had a strong family history of Ischaemic Heart Disease. Elevation of cardiac enzymes was seen in 268(89.3%) cases while Troponin T elevation was noticed in 286(95.3%) patients after 8-10 hours of symptom onset. 157(52.3%) cases were already on antiplatelet therapy with Aspirin and 115 (38.3%) with Clopidogrel. 106(35.3%) patients were on Low Molecular Weight or Unfractionated Heparin due to some other reason before sustaining acute MI. 92(30.7%) patients gave history of previous thrombolysis with Streptokinase. Door to Needle Time was less than 30 minutes in 295(98.3%) patients while it was more than 30 minutes in 05(1.7%) cases. Previous history of Percutaneous Coronary Intervention (PCI) was present in 36(12%) cases while 31(10.3%) cases had undergone coronary artery bypass grafting (CABG) in past. 133(44.3%) patients had history of CVA or Stroke . About 18(06%) patients already had double vessel coronary artery disease while 27(09%) had triple vessel coronary artery disease previously. Other characteristics of population under study included 84(28%) anaemic, 40(13.3)% uraemic, 29(9.7%) hyperthyroid and 45(15%) hypothyroid subjects . 88(29.3%) were already using beta blockers for hypertension or other reasons, 115(38.3%) were on ACE inhibitors while 109(36.3%) were on calcium channel blockers. 277(92.3%) presented to emergency ward with chest pain, 153(51%) with sudden onset of breathlessness (SOB), 127(42.3%) with palpitations while 103(34.3%) presented with dizziness or vertigo. Previous congenital heart disease was present in 19(6.3%) while valvular heart disease was seen in 55(18.3%). Out of 300 patients 165(55%) had Anterior Wall MI , 118(39.3%) had anterolateral wall MI, 73(24.3%) had Inferior Wall MI and 28(93%) had inferior wall plus right ventricular MI. It was observed that 85(28.3%) patients suffered from atrial fibrillation during thrombolysis with SK, 19(6.3%) had ventricular tachycardia, 46(15.3%) exhibited accelerated idioventricular rhythm (AIVR), 79(26.3%) had Sinus Tachycardia, 32(10.7%) had Sinus Bradycardia while 21(07%) had complete heart block during thrombolysis. It was found that 270 (90%) patients arrived in the emergency ward within 12 hours duration of the onset of symptoms while 30 (10%) patients reported after 12 hours. All patients were thrombolyzed with Streptokinase. Out of 300 patients, 252 (84%) had ST elevation Myocardial Infarction changes in ECG while 48 (16%) patients arrived with evolving changes towards ST segment elevation.

Table A: Demographic and salient clinical data (n=300)

Variables	**n**
7Male	189(63%)
Female	111(37%)
Punjab	240 (80%)
Sindh	23 (7.6%)
Balochistan	19 (6.4%)
Khyber Pakhtoonkhwa	18 (6%)
Foreigners	03 (1%)
Asians	297 (99%)
Smoking	167(55.7%)
Obesity	130(43.3%)
Family History of Ischaemic Heart Disease	202(67.3%)
Hyperlipidaemia	164(54.7%)
Diabetes Mellitus	183 (61%)
Hypertension	179(59.7%)
Duration of symptoms	
<12 hours	270(90%)`
≥12 hours	30 (10%)
Cardiac Enzymes Elevation	268(89.3%)
Troponin T	286(95.3%)
Prior treatment with Streptokinase	92 (30.7%)
Door to needle time	
<30 minutes	295(98.3%)
≥30 minutes	05(1.7%)
Age in years	
Mean ±SD	50.2±14.3
Min – Max	(18 – 87)
Chest Pain	277(92.3%)
Sudden onset of Breathlessness SOB	153(51%)
Palpitations	127(42.3%)
Vertigo/ Dizziness	103(34.3%)
Anterior Wall MI	165(55%)
Anterolateral Wall MI	118(39.3%)
Inferior Wall MI	73 (24.3%)
Inferior wall plus right Ventricular Infarct	28(9.3%)
Atrial Fibrillation	85 (28.3%)
Ventricular Tachycardia	19 (6.3%)
Accelerated Idioventricular Rhythm AIVR	46 (15.3%)
ECG Changes on presentation	
ST-T Segment Elevation	252 (84%)
Evolving Changes	48 (16%)
Relief of Chest Pain	
Not Relieved	281(93.7%)
Not relieved	19(6.3%)
Duration of Response to Streptokinase	
>30 minutes	89 (29.7%)
≤30 minutes	52 (17.3%)
Within 30 minutes	12 (43%)
No Response	30 (10%)
Resolution of ST-T Changes	
Resolved	267 (89%)
Not Resolved	33 (11%)

Chest pain was relieved in 281(93.7%) patients while 19(6.3%) had persistent chest pain after thrombolysis. ST-T changes resolved in 267(89%) pts while in 33(11%) cases resolution of ST-T changes was not seen. Total 52(17.3%) cases responded to Streptokinase in less than half an hour (30 minutes) fulfilling the above cited criteria of successful thrombolysis. 129(43%) pts responded to SK within 30 minutes while 89(29.7%) patients responded in more than half an hour and 30(10%) pts did not respond to Streptokinase at all.

DISCUSSION

Although the efficacy of streptokinase has been mentioned in studies analyzing its therapeutic benefits and complication rates. This study reports the diversity in response to streptokinase therapy and its duration in different clinical subsets of patients. A study conducted on 1023 patients over a period of three years revealed that the complications of shock, congestive cardiac failure and recurrent angina occurred more often in patients who had partial or no resolution of ST-T segments after thrombolysis with Streptokinase[4].·The influence of Door to Needle time on myocardial salvage is dependent upon timely thrombolysis[5]. The analysis of our data clearly endorses the results of both above mentioned studies. In our study population a Door to Needle Time of less than 30 minutes revealed miraculous results and successful thrombolysis fulfilling electrocardiographic as well as clinical criteria as compared to late arrivals. Thrombolysis in patients more than 75 years of age presenting with Acute Myocardial Infarction has been evaluated in a study and they have found that it is unlikely to confer a survival benefit in old age[6]. In more than 75 years old patients with Acute Myocardial Infarction there were fewer in hospital complications with overall reduction in 30 day and one year mortality[7]. A recent meta analysis of 3322 patients aged 75 years and older presenting with acute ST elevation Myocardial Infarction within 6 hours of the symptom onset, thrombolytic therapy with Streptokinase was associated with an absolute mortality reduction of 3.4% which is similar to that seen in young patients[8]. Another study conducted at University of Alabama Birmingham has compared and evaluated the response to thrombolysis in white and Hispanic races and found a better are early response to thrombolysis in Blacks[9]. Among the females ten patients were pregnant in our study group . Women exhibit worst 30 day in hospital mortality but not after one year in Anterior wall Myocardial Infarction after thrombolysis. This difference in 30 day mortality outcome is influenced by different therapeutic options including thrombolysis with Streptokinase[10]. A study group at Harvard Medical School has reported similar relative and greater absolute risk reductions than men treated with Enoxaprin (Low Molecular Weight Heparin) or Unfractionated Heparin as an adjunctive therapy with thrombolysis with SK**[11].** Daniel T Quinlan and associates conducted a study on patients presenting with Acute Myocardial Infarction who were given Low molecular weight or Unfractionated Heparin as an adjunct to thrombolytic therapy and they found that there is not benefit of unfractionated Heparin in this group but those patients who were given Low molecular weight Heparin had a significant reduction

in reinfarction rate by a quarter and overall mortality by 10%[12]. Michael Eldar and associates concluded that those patients with AMI who develop paroxysmal atrial fibrillation have worst short and long term prognosis as compared to those without atrial fibrillation[13]. Ventricular Tachycardia was seen in 19 patients and all these patients were those who responded to Streptokinase in less than half an hour. Brad G Angeja and associates have investigated and concluded in a large cohort that impaired epicardial and microvascular flow in diabetic patients impedes and hampers the responses to thrombolytic agents[14]**.** Ventricular Fibrillation was more commonly seen in early hours of Myocardial Infarction with or without thrombolysis while Ventricular Tachycardia was more common during thrombolysis[15]. Ventricular Tachycardia in our group was more common in Diabetic patients and they were all late responders to Streptokinase. Severity of symptoms and clinical presentation instead of underlying risk factors determines early mortality within 24 hours of thrombolysis with Streptokinase[16]**.** Marino Labinaz MD and associates have reported high 30 day mortality in patients receiving thrombolytic therapy after AMI who had undergone prior Coronary Artery Bypass Grafting (CABG) as compared to those without CABG[17]. We had 167 smokers in our study population Younger smokers exhibited an early response to streptokinase as compared to older cases of (60-70) years. Smokers have a better hospital and six month outcome as compared to non smokers or ex smokers[18]. Kalman Kafetz and Robert Luder from North Middle sex hospital London have concluded that Streptokinase was safely used in 73 patients aged > 75 years with complete freedom from all side effects and a good response[19]**.** Our old > 75 year patients responded to SK within half an hour time frame (P<0.001).

CONCLUSION

Here we conclude that there is a significant variation in response of various demographic and clinical subsets of patients presenting with Acute Myocardial Infarction to Streptokinase therapy in terms of time duration. Myocardium salvage is our main goal because ***"Minutes Means Myocardium".***

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