EFFICACY OF THROMBOLYTIC THERAPY IN PRESERVING LEFT VENTRICULAR FUNCTION FOLLOWING ACUTE MYOCARDIAL INFARCTION

ABID AMIN KHAN, NOOR AHMED, MAIMOONA INAYAT

SUMMARY

This study is a prospective study to determine the value of thrombolytic agents in restoring patency in the infarct related artery and its consequent effect on left ventricular function. At total of 48 patients were investigated, all presenting with symptoms of chest pain. Clinical, electrocardiography and echocardiographic criteria were used to document myocardial infarction. 2-D and M-mode echocardiography was used to detect abnormalities of contraction and relaxation of myocardium. Two group of patients were formed giving thrombolytic and non thrombolytic therapy.

Echocardiography was done on admission, discharge and three weeks after discharge from hospital. Patients in both group were evaluated for clinical signs of left ventricular dysfunction according to Killip criteria. The study showed a better left ventricular function in group receiving thrombolytic therapy. Patients who could not be given thrombolytic therapy showed deteriorating left ventricular function which progressed even after one week.

It is concluded that addition of thrombolytic therapy definitely improves left ventricular function by restoring patency of infarct related artery, and thereby improving perfusion of ischemic myocardium.

INTRODUCTION

Acute myocardial infarction constitutes one of the most important causes of death of cardiovascular diseases[1]. The commonest causes are due to potential complications like asystole, arrhythmias, and sudden cardiac death. The most important pathogenetic mechanism is disruption of intimal atherosclerotic plaque with superimposed fresh thrombus and vasospasm leading to total occlusion of a previously[2] partially occluded artery. The usual outcome is myocardial necrosis in the area supplied by the occluded artery. Risk factors associated with this fatal outcome are obesity, hypertension, hyperlipidemias, smoking, diabetes and family history. Myocardial infarction can lead to a variety of complications including arrhythmias papillary muscle dysfunction, ventricular aneurysm and cardiac rupture. Ventricular remodeling and dysfunction are most important late complication associated with large number late post myocardial infarct deaths. The prognosis of majority of patients who go on to develop such complications is exceptionally grave and therefore early intervention is always recommended[4]. Amongst many strategies employed principally aspirin, beta blockers, and thrombolytic therapy is recommended to ensure adequate reperfusion[5]. This study was designed to determine the efficacy of streptokinase to prevent left ventricular dysfunction after myocardial infarction as compared to patients to patients receiving aspirin, beta blockers, nitrates or ACE inhibitors only.

METHODS

48 patients with first episode of acute myocardial infarction were included in the study. The age group was 30-80 years and the mean age was 55 years.

The diagnosis of acute myocardial infarction was documented in each case by a typical history of chest pain, serial ECG changes and cardiac enzyme elevation.

* *Department of Cardiology, Bolan Medical Complex Hospital Quetta.*

The electrocardiographic criteria for the diagnosis of acute myocardial infarction was appearance of Q waves greater than 0.04 seconds or tall R waves in V1 with R/S ratio more than 1 and transient ST elevation (> 2mm). 12 lead ECG was performed on admission, 12 hours and then daily for three days.

Patients were treated by aspirin, morphine, nitrates, beta blockers etc. Those who had no contraindications (> 70s, >9hours chest pain, peptic ulcer and bleeding disorders) were also given thrombolytic therapy and heparin. Those patient who had history of bleeding disorders e.g peptic ulcer, documented recent streptococcal infection or other contraindications, were not given thrombolytic therapy. Both groups (thrombolytic & non thrombolytic) were evaluated for clinical signs on left ventricular dysfunction and classified according to Killip.

2 dimensional and M-mode echocardiographic studies were performed on phased array sector scanner of Toshiba SSH-140A coloured Doppler. The scan probe contained 3.75 and 2.5 MHz transducers driven through a 90 degrees sector arc. Studies were recorded on a VHS cassette. Images were then available for redisplay and evaluation in real time, slow motion and single frame format. The examinations were performed in supine or 30 degrees left lateral position. Cross sectional images of left ventricle were obtained at short and long axis through basal, mid ventricular and apical areas. Basal region was the short axis through the left ventricular cavity at mitral, mid ventricular at papillary muscle and apical area at the apex. Basal and mid ventricular regions were divided in eight segments both and the apical area in four segments thus the whole myocardium consisted of 20 segments[6]. Each segment was examined for akinesia, hypokinesia, dyskinesia, and normal movement. Care was taken to ensure to examine the entire circumference of left ventricle at basal, mid and apical regions. Ejection fraction more than 55% was considered normal. Echocardiographic examinations were performed on admission, discharge and a month after discharge.

RESULTS

48 Patients were both male and female with an age raging from 47 to 65 were include in the study. Both groups consisted of 24 patients. Time from onset of chest pain to the initiation of thrombolytic therapy was 4-9 hours. 45 % of patients in thrombolytic group were in Killip I, 37.5 % in II, 16.5 % in III and non in Killip IV. In non thrombolytic group 16.5 % in I, 25 % in II, 34 % in III and 25 % in Killip IV. (table 2).

Post MI angina.

The incidence of post myocardial infarction angina was 67 % in group receiving thrombolytic therapy and it was 12.5 % in non thrombolytic group (table 3) while in hospital.

Left ventricular Function.

11 (45 %) patients of group A (thrombolytic) had normal left ventricular function on admission. This figure raised to 18 (75%) one week after discharge. In group B (non thrombolytic) number of patients with normal left ventricular function was 19 (79%) on admission and 5 (20%) on final echocardiographic evaluation (table 2 and figures 1 and 2).

DISCUSSION:

Acute myocardial infarction can lead to a variety of morbid complications prominent among which is left ventricular dysfunction. The underlying cause of acute myocardial infarction is thrombotic occlusion of coronary artery supplying a particular area of myocardium, leading eventually to necrosis. This invites several other complications in its wake, specifically ventricular rupture, asystole, ventricular arrhythmias and sudden death.

Table 1

MI site	Group A	Group B
Anterior	14	15
Inferior	10	9

Table 2
No. of patients with left Ventricular dysfunction detected by Killip classification.

Group	Class I	Class II	Class III	Class IV
A	11(45)	9(37.5)	4(16.5)	Nil
B	4 (16.5)	6(25)	8(34)	6(25)

Figures in parenthesis are percent values

Table 3
No. of patients with post myocardial infarction angina.

A	16(67%)
B	3(12.5%)

Table 4
No. of patients having Ejection fraction calculated on three echocardiographic studies in GROUP A

Ejection Fraction	On Admission	On Discharge	1week after
40-45%	2(8)	1 (1)	2(8)
45-50%	4(16)	5(20)	3(12.5)
50-55%	7(29)	7(29)	1 (1)
55-60%	7(29)	3(12.5)	9(37)
60 and above	14(16)	18(33)	9(37)

Figures in parenthesis are percent values.

Table 5
No. of patients having Ejection fraction in Group B

Ejection Fraction	On Admission	On Discharge	1week after
40-45%	1(4)	5(20)	5(20)
45-50%	1(4)	5(20)	7(29)
50-55%	3(12.5)	3(12.5)	7(29)
55-60%	5(20)	4(16)	2(8)
60 and above	14(58)	7(29)	3(12.5)

Figures in parenthesis are percent values.

Figure - 1
Comparison on echocardiography done on in both groups

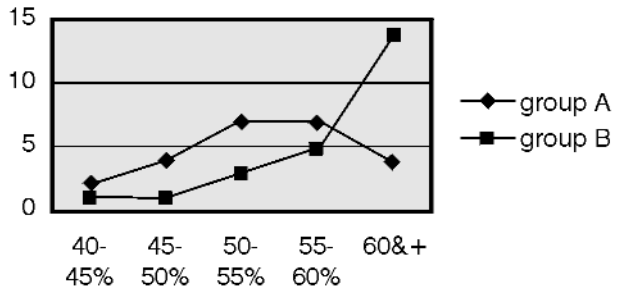


Figure - 2
Comparison of ejection fraction compared on discharge

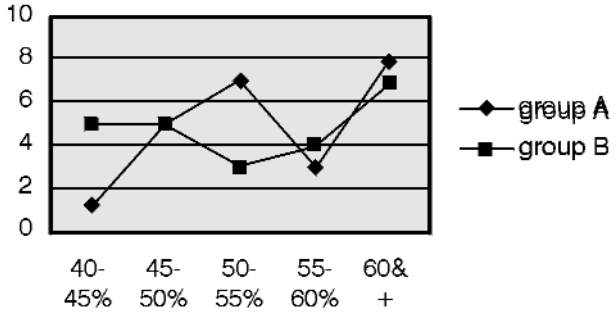
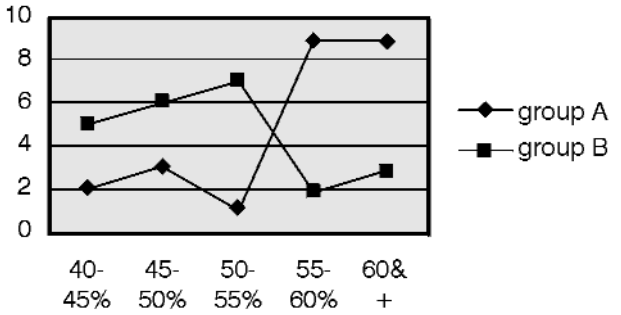


Figure - 3
Ejection fraction compared in both groups one week after discharge



The acute episode is usually triggered by disruption of a plaque with superimposed thrombosis and vasospasm. Thrombosis follows as a result of subendothelial collagen being exposed to blood components leading to activation of platelets and their adherence to the ruptured plaque. This is why early thrombolysis has beneficial effect on complication of acute myocardial infarction[7]. The time interval for thrombolytic therapy is ideally 4-9 hours, as was in this study, but late thrombolysis has been shown to have positive long term benefits. This is related to the benefit conferred by patency of infarct related artery[8].

The beneficial effects are further potentiated when an effective antithrombolytic regimen like antiplatelet and anticoagulant therapy is added[9,10,11]. This is because the site of occlusion remains highly thrombogenic due to residual fibrin and this thrombogenic state is counter acted by antiplatelets and anticoagulants effectively.

The ejection fraction of patients receiving thrombolytic therapy in the study was higher then

those who did not. This can partially be explained by the ability of the streptokinase to forestall the wave of infarction spreading from the infarct area 12, 13. . by salvaging the ischemic myocardium in the vicinity of infarct area, thrombolytic therapy can improve left ventricular function. Variouse other studies have shown streptokinase to have clear benefit in complications after acute myocardial infarction then those who did not. Anistreplase, Alteplase and rTPA have also been evaluated in several studies documenting improvement in left ventricular function after myocardial infarction14,15,16 .

Frank left ventricular dysfunction after myocardial infarction results when atleast 40% of the functioning myocardium is lost17 . This complication can lead to cardiogenic shock with a fatal outcome18,19. Killip grading is most useful to detect left ventricular dysfunction at bedside. Echocardiography give valuable information regarding wall motion and ejection and was therefore used as a major investigation to detect left ventricular dysfunction in this study. Measurement of CK-BM has also been used to detect patency of the infarct related artery20.21.

Left ventricular dysfunction after myocardial infarction can be effectively treated by ACE inhibitors22, 23, and 24.

Many clinicians initially feared that the wide spread use of thrombolytic therapy would create an increased demand for follow up procedures including surgical revascularization. The higher incidence (67%) of post myocardial infarct angina in this study confirms theses doubts, raising the need for intervention in all patients receiving thrombolytic therapy.

CONCLUSION:

Thrombolytic therapy with streptokinase has shown to have positive effects over ventricular performance affected adversely by acute myocardial infarction. This study highlights the beneficial effects of thrombolytic therapy given along anti platelets and anticoagulants in preserving left ventricular function after myocardial infarction in local population at Quetta.

REFERENCES

1. Gruppo Italiano per lo studio della streptochinasi nell' Infarto Miocardico (GISSI). Effectiveness of intravenous thrombolytic treatment in acute mycoardial infarction.Lancet 1986;1:397-401.

2. DeWood MA, Spores J,Notske R, et al. Prevalence of total coronary occlusion during the early hours of transmural myocardial infarction N Engl J;Med 1980 ;303:897-902.

3. Nicolosi GL'Latini R, Marino P,et al. prognostic value of predischarge quantitative two dimensional echocardiographic measurements and the effects of early lisinopril treatment on left ventricular structure and function after acute myocardial infarction in the GISSI-3 trial eur Heart J 1996;11:1646-1656.

4. Fibrinolytic therapy trails (FTT) Collaborative Group. Stress ECG and Coronary angiography for any possible intervention like PTCA and CABG. Lancet 1994; 343:311-322.

5. ISIS-2 (Second International Study of infarct Survival collaborative group randomized trail of intravenous streptokinase, oral aspirin, both, or neither among 17,187cases if suspected acute myocardial infarction :ISIS-2, Lancet 1988;2:349-360.

6. Report of the American Association of echocardiogram on nomenclatures and standards. Identification of myocardial wall segments Nov.82 (Quoted Harvey Feigenbaum, echocardiogram in coronary artery disease edited by himself).

7. The GUSTO angiographic investing the effects of tissue plasminogen activator, streptokinase, or both on coronary-artery patency, ventricular function, and survival after acute myocardial infarction. N Engl JMed. 1993;329:1619-1622.

8. Sherry S, Marder VJ. Streptokinase and recombinant tissue plasminogen activator (r-tPA) are equally effective intreating acute myocardial infarction. am Int Med. 1991;114:417-423.

9. Giugliano RP.Mc Cabe CH, Antman EM , et al. the thrombolysis in myocardial infarction (TIMI) investigators. Lower dose heparin with fibrinolysis is associate with lower rates of intracranial hemorrhage. Am Heart J 2001;141:742750.

10. Gruppo Italiano per lo studio della sopravvivenza nelPingarto miocardico. GISSI-2: Factorial randomised trial of alteplase versus streptokinase and heparin versus no heparin among 12,490 patients with acute myocardial infarction. Lancet 1990;336:65-71.

11. Mc Mohan S,Collins R, Knitght C, Yusuf S, Peto R.Reduction of major morbidity and mortality with heparin in acute myocardial infarction . Criculation1988;78,Suppl 11:1119 (abs).

12. Reimer KA, Jennings RB. The "wavefront phenomenon" of myocardial ischaemic death. Transmural progression of mecrosis within the framework of ischaemic bed size (myocardium at risk) and collateral flow. Lab Invest 1979:40:633-644.

13. Goa K-L, Henwood JM,Stolz JF5 et al Intravenous streptokinase:A reappraisal of it's Therapeutical use in Acute Myocardial Intarction. Drugs 1990;39(5):693-719.

14. The GUSTO investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. N Engl J Med 1993;329:673-682.

15. Lee KL, Califf RM, Simes J, et al. Holding GUSTO up to light:Gl9obal Utilization of streptokinase and Tissue Plasminogen activator for Occluded Coronary Arteries. Ann intern Med. 1994;120:876-881.

16. Verstraete M. Third generation thrombolytic drugs.Am J Med.2000;109:52-58.

17. L. David Hillis, Richard A Lange, Michael D Winniford, Richard L. Page, thrombolytic therapy of myocardial infarction . Manual of clinical problems in cardiology, lippincott & Williams 2003;39:168-171.

18. Goldberg w, Gore M. Thompson CA, et al Recent magnitude of and temporal trends (1994-1997) in the incidence an Hospital death rates of cardiogenic shock complicating acute myocardial infarction: the second national registry of myocardial infarction Am Heart J 2001;141:65-72.

19. Page M, Caulfield JB, Kastor JA, et al Myocardial changes associated with cardiogenic shock. N Engl J Med . 1971;285:133-137.

20. Tanasijevic W, Cannon CP. Antman EM, et al. Myoglobin , creatinime kinase-MB and cardiac troponin-160 minute ratios predict infarct related artery patency after thrombolysis for acute myocardial infraction: result from the thrombolysis in myocardial infarction study (TIMI) 1 10B. J Am Coll Cardiol 1999;34:739-747.

21. Lewis BS, Ganz W, Laramee P et al (1988) Usefulness of a rapid initial increase in plasma creatine kinase activity as a marker of reperfusion during thrombolytic therapy for acute myocardial infarction. Am. J Cardiol.,62:20-4.

22. ISIS-4 collaborative group. A randomized trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. Lancet 1995;345:669-685.

23. Kober L, Torp-Pederson C, Carlsen JE, etal. A clinical trial of the angiotensinonverting-enzyme inhibitor trandolapril in patients with left ventricular dysfunction after myocardial infarction. N Engl JMed. 1995;333:16701676.

24. The Acute Infarction Ramipril Efficacy (AIRE) Study investigators. Effect of Ramipril on mortality and mortality and morbidity of survivors of acute myocardial infarction with clinical evidence of heart failure. Lancet 1993;342-828.