



RESEARCH PAPER

POST-THERAPY OUTCOME AND ECHOCARDIOGRAPHIC ANALYSIS AT THREE WEEKS OF ELDERLY PATIENTS WITH ACUTE MYOCARDIAL INFARCTION FOLLOWING THROMBOLYSIS THERAPY

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ABSTRACT

Introduction: Once severe ischemia has lasted for about 20 minutes, myocardial necrosis ensues, affecting the subendocardium first and then proceeding in a time dependent wave front to reach epicardium about 4 to 6 hours later. Restoration of blood flow before necrosis is transmural, arrests the progression of necrosis and salvages the still viable but ischemic myocardium that would otherwise proceed to necrosis.

Aim: The objective is to assess the occurrence of complications of half dose of streptokinase versus full dose of streptokinase in three weeks follow-up following thrombolysis therapy.

Material and Methods: Sixty elderly patients with acute myocardial infarction were enrolled in the study, presenting within 12 hours of onset of symptoms and having no contra-indication to thrombolytic therapy at GMC, Jammu for a period of one year w.e.f nov.2017 to oct.2018

Results: Out of the total 60 cases included in our study, 30 (50%) were assigned to the study group and 30 (50%) were included in the control group. Overall, 46 (76.7%) males and 14 (23.3%) females were included in the study.

Conclusion: In the present study, we conclude that low dose streptokinase also achieved post-therapy outcome comparable to the standard dose, as assessed clinically and echocardiographically in a short-term follow-up of three weeks.

KEY WORDS : acute myocardial infarction, echocardiography, post-therapy outcome

INTRODUCTION:

Acute myocardial infarction (AMI) has been found to be the leading cause of death in elderly over the age of 65 years. It accounts for 80% of deaths in the elderly, with 6.8% of the population of India over 60 years. The mortality in elderly is two-times more after AMI as compared to the younger counterparts¹. The mortality of infarction increases very steeply with increasing age >65 years with 1-month mortality in the range of 20-30%². Although early studies suggested an increased risk of haemorrhagic complications in the elderly patients receiving thrombolytic therapy^{3,4}, large multicentric trials have shown that this fear is unfounded^{5,6}. However, two recent studies have shown that streptokinase in conventional doses of 1.5 million units was associated with excess of strokes in patients aged more than 70 years⁷. The risk of cerebral haemorrhage following thrombolysis is small, about 1-2 per 1000⁸. Though the traditional dose of streptokinase fixed at 1.5 million units⁹, has been widely accepted, some recent clinical trials have provided non-invasive evidence of reperfusion with half dose streptokinase with comparable results.^{10,11}

MATERIAL AND METHODS:

The present work is a hospital based cross- sectional study for a period of one year from nov.2017 to oct.2018 that included 60 patients of acute myocardial infarction in elderly that presented within 12 hours of onset of symptoms and had no contraindication to administration of streptokinase for thrombolysis. The patients were randomized into two groups: the study group to whom 7.5 lakh units of streptokinase was administered intravenously over 30 minutes, while the control group received the standard dose of 1.5 million units of streptokinase intravenously over one hour. Detailed history was taken and thorough clinical and biochemical profile was done. AMI was diagnosed by criteria defined by World Health Organization (WHO). Electrocardiogram (ECG) was recorded both at baseline and after 3 hours. Echocardiographic analysis of left ventricular function, left ventricular ejection fraction and left ventricular diastolic dysfunction were calculated at three weeks.

RESULTS:

The present study titled "Post-therapy outcome and echocardiographic analysis at three weeks of elderly patients with acute myocardial infarction following thrombolysis therapy" was

conducted in Postgraduate Department of Medicine, Government Medical College Hospital, Jammu from November 2017 to October 2018. All the patients included in the study had presented within 12 hours of onset of symptoms and had no contraindication to administration of streptokinase for thrombolysis. The observations made were considered as follows:

Table 1: Genderwise distribution of cases

Subjects	Gender		Total
	Male No. (%)	Female No. (%)	
Study group	21 (70.0)	9 (30.0)	30 (100.0)
Control group	25 (83.3)	5 (16.7)	30 (100.0)
Total	46 (76.7)	14 (23.3)	60 (100.0)

Table 2: Age wise distribution of cases

Subjects	Age group (in years)				Total No. (%)
	≤ 65 (%)	66-69 (%)	70-75 (%)	> 75 (%)	
Study group	10(33.3)	6(20.0)	10(33.3)	4(13.3)	30(100.0)
Control group	7(23.3)	11(36.7)	9(30.0)	3(10.0)	30(100.0)
Total	17(28.3)	17(28.3)	19(31.7)	7(11.7)	60(100.0)

Table 3: Comparative evaluation of mean values of hemodynamic parameters of study group and control group

Subjects	Pulse (min)	Mean ± Standard Deviation	
		Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)
Study group	83.07 ± 13.80	125.13 ± 19.66	77.47 ± 11.78
Control group	76.67 ± 11.90	133.40 ± 25.51	83.00 ± 12.36

Table 4: Distribution of myocardial infarction sites in study group versus control group

Site of myocardial infarction (MI)	Study group No. (%)	Control group No. (%)	Total No. (%)
Antero-inferior MI	1 (3.3)	—	1 (1.7)
Antero-lateral	1 (3.3)	—	1 (1.7)
Antero-lateral MI	1 (3.3)	—	1 (1.7)

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Antero-septal MI	1 (3.3)	—	1 (1-7)
AWMI	18 (60.0)	14(46.7)	32 (53.3)
Infero-lateral MI	1 (3.3)	1 (3.3)	2 (3.3)
IWMI	7(23.3)	15 (50.0)	22 (36.7)
Total	30 (100.0)	30 (100.0)	60(100.0)

Table 5: Distribution of Killip Class at presentation in the study group versus control group

Subjects	Killip Class			Total
	Class I	Class II	Class III	
Study group	23 (76.7)	7(23.3)	-	30 (100.0)
Control group	10(33.3)	18 (60.0)	2 (6.7)	30 (100.0)
Total	33 (55.0)	25 (41.7)	2 (3.3)	60(100.0)

Table 6: Distribution of coronary risk factors in study group versus control group

Risk factors	Study group (n = 30) No. (%)	Control group (n = 30) No. (%)	'p'-value (z-test)
Smoking	18 (60.0)	20 (66.67)	0.352 NS
Hypertension	16 (53.33)	14 (46.67)	0.358 NS
Diabetes	8 (26.67)	4(13.33)	0.180NS
Family H/o CAD	6 (20.0)	8 (26.67)	0.333 NS
Hyperlipidemia	4(13.33)	12 (40.0)	0.493 NS

NS Non-significant

Table 7: Comparative evaluation of therapeutic window to thrombolysis and time to pain relief in study group and control group

Subjects	Mean ± Standard Deviation	
	Therapeutic window (hours)	Time to pain relief after STK (hours)
Study group	6.32 ± 2.23	5.90 ±4.76
Control group	4.90 ± 1.96	5.61 ± 3.36

Table 8: Comparison between reperfusion by combined criteria -fractional change and time from STK to peak CPK-MB in study group versus control group

Time from STK to peak CPK-MB (hours)	Study group (n = 30)		Control group (n = 30)		'p'- value (test)
	Fc≥ 0.5 No. (%)	Fc < 0.05 No. (%)	Fc≥ 0.5 No. (%)	Fc < 0.05 No. (%)	
0 to < 12	22 (73.3)	-	16 (53.3)	2 (6.7)	0.13 NS
12 to 24	4 (3.3)	4(13.3)	8 (26.7)	4(13.3)	

NS = Non-significant

Post-therapy outcome

- 1.Clinical
- 2.Byechocardiography

Among clinical criteria to assess post-therapy outcome, the criteria included were minor bleed, major bleed, anaphylaxis and hypotension.

Table 9: Comparison between complications following streptokinase infusion in study and control groups

Complications	Study group (n = 30) No. (%)	Control group (n = 30) No. (%)	p-value (Z-test)
Minor bleed	-	2 (6.6)	0.016
Major bleed	-	-	-
Anaphylaxis	-	-	-
Hypotension	-	-	-

Table 10: Comparison between occurrence of post-myocardial infarction (MI) angina in study group versus control group

Subjects	Post MI angina		Total No. (%)
	Negative No. (%)	Positive No. (%)	
Subject group	28 (93.3)	2 (6.7)	30(100.0)
Control group	30(100.0)	—	30(100.0)
Total	58 (96.7)	2 (3.3)	60 (100.0)

Table 11: Comparison of mean left ventricular ejection fraction (LVEF) by echocardiography between study group and control group at three weeks

Subjects	Mean ± Standard Deviation
Study group	50.33 ± 3.93
Control group	49.87 ±4.95

Table 12: Comparison of left ventricular diastolic dysfunction (LVDD) by echocardiography between study group versus control group at three weeks

Subjects	LVDD		Total No. (%)
	Negative No. (%)	Positive No. (%)	
Subject group	8 (26.7)	22 (73.3)	30 (100.0)
Control group	6 (20.0)	24 (80.0)	30 (100.0)
Total	14 (23.3)	46 (76.7)	60 (100.0)

Table 13: Comparison of infarction location (post-therapy) by echocardiography between study group and control group at three weeks

Subjects	Infarction location		Total No. (%)
	Anterior wall No. (%)	Inferior wall No. (%)	
Subject group	22 (73.3)	8 (26.7)	30 (100.0)
Control group	14 (46.7)	16(53.3)	30 (100.0)
Total	36 (60.0)	24 (40.0)	60 (100.0)

DISCUSSION:

Sixty elderly patients with acute myocardial infarction were enrolled in the study, presenting within 12 hours of onset of symptoms and having no contra-indication to thrombolytic therapy. The patients included in the study were randomized into two groups - 30 patients in the study (cases) group were thrombolysed with 7.5 lakh units of streptokinase (half dose) over thirty minutes while the rest 30 patients in the control group were administered 1.5 million units of streptokinase (conventional full dose) over one hour. Post-therapy outcome and echocardiographic analysis at three weeks of patients with acute myocardial infarction following thrombolysis therapy were done.

Baseline characteristics:

Both, the study and the control groups were matched for age and gender. The mean age of the patients in the study group (cases) was 69.33 ± 5.78 years, while that of control group was 69.00 ± 4.83 years. Majority of the patients (19) were observed to be in the age group of 70-75 years in the study as well as control group. In the study group (cases), 9 (30%) were females and 21 (70%) were males, while as in control group 5 (16.7%) were females and 25 (83.3%) were males. Overall, 14 (23.3%) females and 46 (76.7%) males were included in the study. Four and three patients were aged more than 75 years in the study and control groups, respectively. Both the groups were matched for gender and age. This was comparable with the age and gender groups of other studies.

Mean pulse rate of patients in the study group (cases) was 86.07 ± 13.08 per minute while as those of the control group was 76.67 ± 11.90 per minute. Mean systolic blood pressure of patients in the study group (cases) was 125.13 ± 19.65 mmHg and in the control group was 133.40 ± 25.50 mmHg, respectively. Mean diastolic blood pressure of patients in the study group (cases) was 77.47 ± 11.77 mmHg and 83.00 ± 12.36 mmHg in the Control group.

Majority of the patients in the study as well as control group had anterior wall myocardial infarction (53.3%) followed by inferior wall myocardial infarction (36.7%). Both the study and control groups were matched for distribution of infarct sites.

Most of the patients were in Killip class I and II at presentation in the study (cases) as well as the control group. Twenty-three in the study group and 10 in the control group were in Killip class I, while 7 in the study and 18 in the control group were in Killip class II. None of the patients in the study group were in Killip Class III, while as 2 patients

in the control group were in Killip class III. None of the patients were having cardiogenic shock at the time of presentation when administered streptokinase. Severity of cardiac dysfunction was similar in both the study and the control group.

Both the groups were matched with respect to Killip class at presentation. The major risk factor in both the groups was smoking, accounting for 60% (18 cases) and 66.67% (20 cases) in the study and the control group, respectively. This was followed by hypertension as a risk factor, comprising 53.33% (16 cases) and 46.67% (14) in the study and the control groups, respectively. No statistically significant difference was found between study and control groups regarding distribution of risk factors.

As per the study protocol, only those patients coming within 12 hours of onset of typical symptoms of acute myocardial infarction were included in the study. The mean therapeutic window (*i.e.* time from onset of cardiac pain to administration of streptokinase) in the study group was 6.32 ± 2.23 hours while as those in the control group was 4.90 ± 1.95 hours. No statistically significant difference was found in the therapeutic window of both the groups.

The mean time to pain relief from streptokinase infusion in the study group (cases) was 5.90 ± 4.75 hours compared to 5.61 ± 3.22 hours in the entire control group. 73.33% (22) of patients had complete pain relief within 6 hours of completion of streptokinase infusion in the study group (cases), 60% (18) of the patients had complete pain relief within 6 hours of completion of streptokinase therapy in the control group. This was comparable with the studies of **Sivan *et al.* (2003)**¹¹ and **Ahmed *et al.* (1992)**⁹. Reperfusion is characterized by a rapid progressive decrease in pain intensity within 30 minutes of onset of its abatement (**Shah *et al.* 1993**)¹². However, this is a subjective phenomenon and no definite time period has been documented to signify reperfusion.

Reperfusion using the criterion of fractional change (Fc) on ECG was achieved in 86.67% (26) and 80% (24) of the patients in the study and the control group, respectively. The difference between the two groups by chi-square test was $p = 0.2$, which is not statistically significant. According to fractional change, the patients were said to be reperfused if $Fc \geq 0.5$ and not reperfused if $Fc < 0.5$. A fractional change value of $Fc \geq 0.5$ had been found to 67% specific and 93% sensitive for predicting a patent artery (**Hogg *et al.* 1988**)¹³.

In a study taking time from streptokinase infusion to peak CPK as a criterion for reperfusion, it was found that peaking of CPK occurred at 9.7 ± 6.3 and 12.3 ± 4.8 hours in those receiving 7.5 lakh units and 1.5 million units of streptokinase, respectively (difference not statistically significant) (**Gottlich *et al.* 1988**)¹⁴. In this study, in the group receiving, 7,50,000 IU of streptokinase, 89% patients showed peaking of CPK-MB within 12 hours, while 67% of patients did so in the group given 1,500,000 IU. This compares well with the data of the present study.

The results of our study also corroborate with those of **Sivan *et al.* (2003)**¹¹ who analyzed the efficacy and safety of streptokinase in full conventional dose (15 million units), half dose (7.5 lakh) and no thrombolysis in the elderly population (> 75 years). Successful thrombolysis in their study was defined as ST-segment resolution of 50% or more. They concluded that half dose (7.5 lakh units) streptokinase has equal efficacy, better clinical outcome, and reduced rate of complications as compared to full dose of streptokinase.

Post-therapy outcome:

Considering the complication rate, the criteria to assess post-therapy outcome/complications clinically included any minor bleed, major bleed, anaphylaxis and haemorrhage. In our study, there was a greater incidence of minor bleed in the control group (patients receiving 1.5 million units of streptokinase) which was statistically significant. However, no major bleed or any other

complication was encountered either in the study group (cases) or the control group following thrombolytic therapy. Thus, 7.5 lakh units of streptokinase was safer in elderly patients as compared to 1.5 million units in terms of minor bleeding complications.

However, post-myocardial infarction angina occurred in 2 (6.7%) cases among the study group while as no such event occurred in the control group.

Echocardiographic analysis at three weeks:

The results obtained on echocardiographic analysis of patients at 3 weeks after acute myocardial infarction showed that the left ventricular ejection fraction (LVEF) ranged from 44 to 59% in the study group (cases) and 41 to 57% in the control group. Mean LVEF in the study group (cases) was 50.33 ± 3.92 while in the control group was 49.87 ± 4.94 , there was no statistically significant difference of left ventricular ejection fraction at 3 weeks in the two groups as assessed by t-test ($p = 0.687$). On correlating the echo evaluated LVEF at 3 weeks in patients with reperfusion by fractional change, it was found that the mean LVEF in those reperfused by Fc criterion was 51.82% and 53.10% in the study and control groups, respectively. The t-test for significance gave p-value of 0.375 (not statistically significant). Thus, thrombolysis with either low (7.5 lakh units) or standard dose (1.5 million units) produces similar variation in left ventricular ejection fraction (LVEF).

In a study, the global ejection fraction at 3 months using radionuclide ventriculography was 50 ± 14 and 45 ± 16 in low and standard dose streptokinase, respectively (**Six *et al.* 1990**)¹⁵.

Left ventricular diastolic dysfunction (LVDD) assessed by echo at the end of three weeks post-myocardial infarction was present in 22 (73.3%) patients among the study group (cases) and 24 (80.0%) patients among the control group. Two-tailed significance (chi-square test) for both the groups came to be 0.761, which was statistically not significant implying that low and standard dose of streptokinase do not alter the post-myocardial infarction outcome in terms of left ventricular diastolic dysfunction.

Reperfusion leads to better left ventricular ejection fraction and less ventricular diastolic dysfunction in the post-myocardial infarction period as documented by other studies (**White *et al.* 1987**)¹⁶.

Conclusion : In the present study, we conclude that low dose streptokinase also achieved post-therapy outcome comparable to the standard dose, as assessed clinically and echocardiographically in a short-term follow-up of three weeks. Also, low dose streptokinase (7.5 lakh units) infusion was found to be associated with a lower incidence of haemorrhagic complications as compared to conventional full dose (1.5 million units) of streptokinase infusion.

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