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A COMPARATIVE STUDY OF RISK FACTORS, EFFICACY AND COMPLICATIONS OF 7.5 LAKH UNITS VERSUS 1.5 MILLION UNITS OF STREPTOKINASE IN ACUTE MYOCARDIAL INFARCTION IN ELDERLY PATIENTS

Cardiology

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ABSTRACT

Background-As there is increased life expectancy in india, there is increased number of elderly patients having ischemic heart disease are being diagnosed and treated. This study is to evaluate whether half dose (7.5 lakh units) of streptokinase was efficacious as compared to standard dose (15 lakh units) of streptokinase in elderly patient of acute myocardial infarction in achieving reperfusion of the infarct related coronary artery. **Methods-** This study was done in elderly patients having age more than 75 years over a period of one year from may 2022 to may 2023 at kilpauk medical college in chennai. Fifty elderly patients with acute myocardial infarction were enrolled in the study, which presented within 12 hours of onset of symptoms and having no contra-indication to thrombolytic therapy. **Results-** A total of 50 cases included in our study. The mean age of the patients in the study group (cases) was 75.33 ± 5.78 years, while that of control group was 76.00 ± 4.83 years. Majority of the patients (19) were observed to be in the age group of 75-80 years in the study as well as control group. In the study group (cases), 7 (18%) were females and 18 (72%) were males, while in the control group 8 (32%) were females and 17 (68%) were males. **Conclusions-** Half dose (7.5 lakh units) of streptokinase was as effective as the standard dose (15 lakh units) of streptokinase in achieving reperfusion of the infarct related coronary artery, in the elderly patients of acute myocardial infarction

KEYWORDS

Acute Myocardial Infarction, Coronary Artery, Streptokinase, Thrombolysis

INTRODUCTION

Despite advances in the diagnosis and management, STEMI remains a major public health problem in the industrialized world and is on the rise in developing countries.[1] Each year in the United States alone, more than 1 million patients are hospitalized for an MI or coronary heart death. The rate of MI rises sharply in both men and women with increasing age.[1] Of particular concern from a global perspective, the burden of coronary disease in low-and middle-income countries has reached the rate affecting more affluent countries. The limited resources available to treat STEMI in low-and middle-income countries mandate major international efforts to strengthen primary prevention programs. [2]

The overall number of deaths from STEMI has declined steadily over the past 30 years, but it has stabilized over the past decade. Both a decreased incidence of STEMI and a decline in the case-fatality rate after STEMI, which corresponds to greater implementation of guideline-directed care, contributes to this trend. The short-term mortality rate of patients with STEMI ranges from 5% to 6% during the initial hospitalization and from 7% to 18% at 1 year. It accounts for 80% of deaths in the elderly, with 6.8% of the population of India over 65 years.[3] The mortality in elderly is two-times more after AMI as compared to the younger counterparts.[4] In patients aged 65 years or older, the 30-day mortality declined from 20% to 12.4% and the 1-year recurrent MI decreased from 7.1% to 5.1%. Though the traditional dose of streptokinase fixed at 1.5 million units, has been widely accepted, some recent clinical trials have provided non- invasive evidence of reperfusion with half dose streptokinase with comparable results. AMI has been found to be the leading cause of death in elderly over the age of 75 years.

METHODS

This study is a randomized control trial done in elderly patients having age more than 75 years over a period of one year from may 2022 to may 2023. Fifty elderly patients with acute myocardial infarction were enrolled in the study, which presented within 12 hours of onset of symptoms and having no contra-indication to thrombolytic therapy.[5]

Sample size was taken as per convenience of study. The patients were divided 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). Got approval from IEC and consent was taken from all patients.

Statistical Analysis

The data was collected and analysed using standard statistical chi – square test, $P < 0.05$ statistically significant. Data was entered in Microsoft excel and analysis was done using SPSS version 22.

RESULTS

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:

In the study group, 18 (72.0%) were males and 7(18.0%) were females, while as in control group 17 (68.0%) were males and 8 (32.0%) were females. Overall, 35(75.0%) males and 15(25.0%) females were included in the study. Majority of the patients were in Killip Class I and II at presentation in study as well as control group. None of the patients were having cardiogenic shock at the time of administration of streptokinase. Severity of cardiac dysfunction was similar in both the study and control groups. More than one risk factor was found in cases of both study and control groups. The major risk factor in both study group (60.00%) and control group (52.0%) was smoking, followed by hypertension (56.33% and 48.00% respectively).Both groups were comparable with respect to the distribution of coronary risk factors. Mean therapeutic window in the study group was 5.4 ± 2.1 hours, while in control group was 4.8 ± 1.8 hours. No statistically significant difference was found in the therapeutic windows of both the groups. Mean time to pain relief in the study group was 5.1 ±1.6 hours and in the control group was 5.2 ± 1.8 hours. In the subset of patients having pain relief within 6 hours of completion of streptokinase infusion, the mean time in the study group was 3.9 hours and in control group was 3.5 hours. Applying 't'-test, p-value = 0.22 is statistically non-significant, thus showing no difference in time to pain relief at different doses of streptokinase. Reperfusion occurs if Fc ≥ 0.5 and Fc<0.5 signifies no reperfusion. No statistically significant difference was observed in the reperfusion rates assessed by Fc criterion in the two groups.There was a greater incidence of minor bleed, major bleed and hypotension in the control group (1.5 million units) which was statistically significant.

1.Gender Wise Distribution of Cases

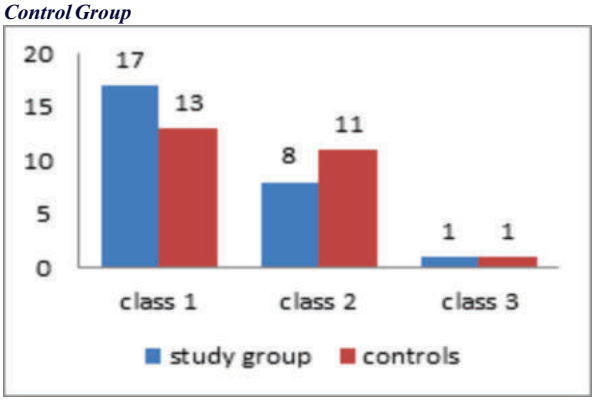
Subjects	Gender		Total
	Male No. (%)	Female No. (%)	
Study group	18 (72.0)	7(18.0)	25 (100.0)
Control group	17 (68.0)	8(32.0)	25 (100.0)
Total	35(75.0)	15(25.0)	50 (100.0)

4.Comparative Evaluation of Therapeutic Window to Thrombolysis and Time to Pain Relief in Study Group and Control Group

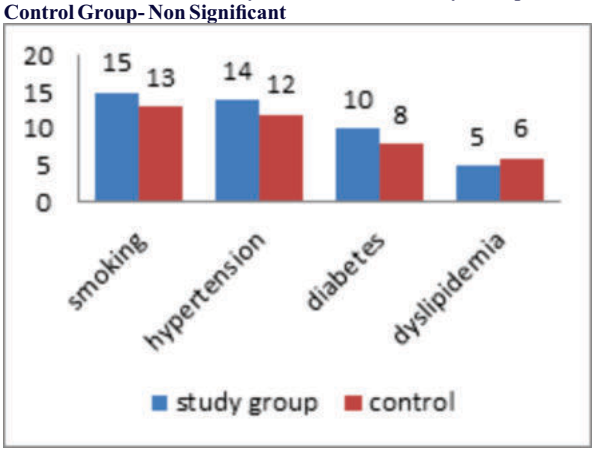
Subjects	Window period(hours)	Time to pain relief after STK (hours)
Study group	5.4±2.1	5.1±1.6

Control group	4.8±1.8	5.2±1.8

2.Distribution of Killip Class at Presentation in Study Group Versus Control Group



3. Distribution Of Coronary Risk Factors In Study Group Versus Control Group- Non Significant



5.Comparative Evaluation of Reperfusion Using Single Non-Invasive Criterion- Fractional Change on ECG in Study Group Versus Control Group- not significant

Fractional ecg change	Study group N=25	Control group N=25	p'-Value (χ^2 - test)
0.5	19	17	0.23(not significant)
0.5	6	8	0.23(not significant)

6.Comparison Between Complications Following Streptokinase Infusion in Study and Control Groups

Complications	Study group	Control group	p-Value (Z-test)
Minor bleed	0	2	0.016
Major bleed	0	1	0.021
Hypotension	0	1	0.018

DISCUSSION

This study is titled as "Comparative efficacy of 7.5 lakhs units vs 15 lakh units of streptokinase in acute myocardial infarction in elderly patients was conducted in a prospective manner in kilpauk medical college, chennai over a period of one year. 50 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 - 25 patients in the study (Cases) group were thrombolysed with 7.5 lakh units of streptokinase (Half dose) over thirty minutes while the rest 25 patients in the control group were administered 15 lakh units of streptokinase (Conventional full dose) over one hour.

Mean therapeutic window in the study group was 5.4 ± 2.1 hours, while in control group was 4.8 ± 1.8 hours. No statistically significant difference was found in the therapeutic windows of both the groups. Mean time to pain relief in the study group was 5.1 ±1.6 hours and in the control group was 5.2 ± 1.8 hours. 72% (18) of patients had complete pain relief within 6 hours of completion of streptokinase infusion in the study group (cases), 68% (17) of the patients had complete pain relief within 6 hours of completion of streptokinase therapy in the control group. There was no statistically significant difference between the two groups by Z-test (p = 0.219). In the subset of patients having pain relief within 6 hours of completion of streptokinase infusion, the mean time in the study group (Cases) was 4.142 hours compared with 4.24 hours in the control group, the difference of which was not significant. This was comparable with the studies of Sivan et al.[8] and Ahmed et al[6] Reperfusion is characterized by a rapid progressive decrease in pain intensity within 30 minutes of onset of its abatement (Shah et al).[9] 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 68.0% (17) and 72% (18) 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 re-perfused if Fc ≥ 0.5 and not re-perfused if Fc < 0.5. A fractional change value of Fc ≥ 0.5 had been found to 67%) specific and 93% sensitive for predicting a patent artery (Hogg et al).[10]

The study has shown that in a dose-related comparison of thrombolytic therapy, there was no significant difference in the number of patients re-perfused by non-invasive criteria, singly and in combination between the group receiving 7.5 lakh units of streptokinase (Study group) and 1.5 million units of streptokinase (Control group). Dose ranging studies of thrombolysis and streptokinase have yielded similar comparable results using variable criteria for assessing reperfusion (Gottlich et al,[11] Six et al,[13] Ahmed et al,[6] Bose et al.[7])

The results of our study also corroborate with those of Sivan et al[8] who analysed the efficacy and safety of streptokinase in full conventional dose (15 lakh units), half dose (7.5 lakh units) 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 compared to full dose (15 lakh units) streptokinase. Of all the 50 patients, 34(68.0%) patients re-perfused by Fc criterion had therapeutic window less than 6 hours as compared with 16 (32%) patients having therapeutic window of 6-12 hours. According to AHA/ACC guidelines for management of acute myocardial infarction, therapeutic window should be less than 12 hours (Ryan et al),[15] though the rates of reperfusion was 60-70% in studies that delayed treatment for more than 6 hours after onset of chest pain (Anderson et al 1984. This is also validated and supported by studies that have shown that older thrombi are more resistant to lysis (Karsch et al).[14]

CONCLUSIONS

Low dose (7.5 lakh units) of streptokinase was as effective as the standard dose (15 lakh units) of streptokinase in achieving reperfusion of the infarct related coronary artery in elderly patients of acute myocardial infarction. Also, low dose streptokinase (7.5 lakh units) infusion was found to be associated with a lower incidence of haemorrhagic complications as compared to 15 lakh units of streptokinase infusion.

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