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A Study On Factors Influencing The Outcome Of Thrombolysis In Acute Myocardial Infarction.

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ABSTRACT

Coronary Heart disease has been defined as impairment of heart function due to inadequate blood flow to the heart compared to its needs caused by obstructive changes in the coronary circulation to the heart. Thrombolytic therapy has been consistently proven to reduce mortality and morbidity. Despite this, it has been recognized that thrombolytic therapy has failed in a significant population. There is a lot of room for improvement. We need to identify the factors that are responsible for the failure of thrombolysis. To find out the overall success rate of thrombolysis in the coronary care unit of Department Of General Medicine, Government Mohan Kumara Mangalam Medical College, Salem, Tamil Nadu, India. This observational prospective cohort study was conducted at Government Dharmapuri Medical College And Hospital, Dharmapuri, Tamil Nadu, India in the year September 2022.84 patients were included in the study. All patients received streptokinase 1.5 million units in 100 ml of normal saline over 60 minutes. Aspirin was given to all patients. The use of heparin, Beta-blockers, and ACE inhibitors was according to CCU protocols which were in the accordance with ACC/AHA recommendations. Patients were analyzed for the success of thrombolytic therapy 90 minutes after initiation of thrombolytic therapy, applying the above-mentioned criteria. Those who underwent successful thrombolysis were grouped into groups A. Those with failed thrombolysis were grouped into group B. A total of 83 patients were studied. Their age ranged from 34 – to 76 years (mean 55.03 yrs).68 of them were males (82%) and 15 females (18%)20 of them were hypertensives (24%) .44 people were smokers (53%) and 29(59%) consumed alcohol. 23 patients experienced preinfarction angina (28%). 50 patients had anterior wall infarction (60%) and 33 patients (40%)had inferior infarction. Alcohol consumption has influenced the outcome of thrombolytic therapy favorably. Univariate analysis revealed a success rate of 69% in the drinkers versus 44% in non-drinkers. (p=0.03, odds ratio=2.78). In this study, the overall success rate of thrombolysis was 54%. Inferior wall myocardial infarctions had a better success rate than anterior wall myocardial infarctions and it was statistically significant. Smokers had a lesser success rate than nonsmokers, but it did not reach statistical significance. Alcohol intake was associated with a better success rate even though statistically not significant. Hypertensives didn't show any difference in the success rate. Diabetics do not differ from nondiabetics concerning the success rate of thrombolysis. There was a trend towards a worse outcome in those aged more than 60 years. But it was not statistically significant. Gender was not found to influence the success rate of thrombolysis. Pre infarction angina did not affect the success rate of thrombolysis.

Keywords: Myocardial Infraction, Thrombolysis, Hypertension, Diabetes Mellitus

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INTRODUCTION

Coronary heart disease (CHD) is a worldwide health epidemic. In the United States, for example, it is estimated that 13.7 million Americans have CHD, including more than 7.2 million individuals who already have had a myocardial infarction. From the 1960s to 1990 the CAD prevalence increased two-fold (from 2% to 4%) in rural India and threefold (from 3.45to 9.45%) in Urban India.[1] The prevalence is even higher in South India (13% urban and 7% rural). In 1990, 25% of deaths in India were attributable to cardiovascular disease compared to diarrheal disease,12% due to respiratory infections, and 5% due to tuberculosis. In the group of persons older than 30 years of age, 213 per 100,000 individuals have CHD. [2] Although age-specific events related to CHD have fallen dramatically in the last few decades, the overall prevalence has risen as populations age and patients survive the initial coronary or cardiovascular event. Worldwide 30 percent of all deaths can be attributed to cardiovascular disease of which more than half are caused by CAD.[3] coronary heart disease has been defined as impairment of heart function due to inadequate blood flow to the heart compared to its needs caused by obstructive changes in the coronary circulation to the heart. It is the cause of 25- 30% of deaths in most industrialized countries.[4] In India also it is a major public health problem. It is aptly called by WHO the modern epidemic. The increasing incidence of coronary heart disease may be a reflection of increased longevity, adoption of a high- fatdiet based on meats decreased exercise made possible by increasing affluence. [5] It is not surprising to note that sir William Osler devoted only a few pages in his textbook of Medicine published in 1892 to the discussion of Acute myocardial infarction. It was the brilliant work of Herrick 1912 who performed an autopsy on acute myocardial infarction patients that put forward the new concept of thrombotic occlusion of the coronary artery as the cause of downstream necrosis of the heart muscle. [6] Thrombolytic therapy has been consistently proven to reduce mortality and morbidity. Despite this, it has been recognized that thrombolytic therapy has failed in a significant population. There is a lot ofroom for improvement. We need to identify the factors that are responsiblefor the failure of thrombolysis.[7]

METHODS

This observational prospective cohort study was conducted at Department Of General Medicine, Government Mohan Kumara Mangalam Medical College, Salem, Tamil Nadu, India in the year 2021-2022 over 12 months 84 patients were included in the study. All patients received streptokinase 1.5 million units in 100 ml of normal saline over 60 minutes. Aspirin was given to all patients. The use of heparin, Beta-blockers, and ACE inhibitors was according to CCU protocols which were in the accordance with ACC/AHA recommendations. Patients were analyzed for the success of thrombolytic therapy 90 minutes after initiation of thrombolytic therapy, applying the above-mentioned criteria. Those who underwent successful thrombolysis were grouped into groups A. Those with failed thrombolysis were grouped into group B. Inclusion criteria. Presence of typical chest pain suggestive of Acute myocardial infarction along with ECG evidence of acute myocardial infarction. Criteria for thrombolysis being 2mm or more ST elevation in two contiguous limb leads. Time window of 12 hrs from the onset of pain to the initiation of thrombolysis. Exclusion criteria: Late thrombolysis (more than 12 hrs from the onset of pain). Recurrent myocardial infarction. Presence of bundle branch block. Development of pericarditis. The following parameters were analyzed among them to know whether they influenced the outcome of thrombolysis. (1) Age (2) Sex (3) Time of SK administration (4) Preinfarction angina (5) Alcohol intake (6) smoking status (7) Systemic hypertension (8) Diabetes mellitus (9) Location of MI (10) Time interval between the onset of pain and the initiation of thrombolytic therapy.

Statistical Method

Univariate analysis was done by the chi-square test and multivariate analysis by logistic regression was done using SPSS windows computer software 18.5.

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RESULTS

TABLE 1: UNIVARIATE ANALYSIS FOR INFLUENCING FACTORS

S.No	Variables	Oddsratio	(X^2) Chi square	P Value	Comments
1	Age <60 years	2.50	4.11	0.04	Significant
2	Gender(female sex)		0.00	0.98	
3	Preinfarction angina	0.46	2.43	0.98	
4	Diabetes	1.11	0.04	0.83	
5	Hypertension		0.04	0.04	
6	Smoking		0.34	0.56	
7	Drinking	2.78	4.55	0.03	Significant
8	Infarct location (anterior)	0.25	8.55	0.004	Significant

Table 2: Clinical Details Of Study Population According To The Outcome Of Thrombolysis

VARIABLE	SUCCESS A GROUP (%)	FAILED B GROUP (%)
Number	44(53%)	39(47%)
Males	36(53%)	32(47%)
Females	8(53%)	7(47%)
Hypertension	11(55%)	9(45%)
Diabetes	11(55%)	9(45%)
Smoking	22(50%)	22(50%)
Drinking	20(69%)	9(31%)
Preinfarction angina	9(39%)	14(61%)
TIMEWINDOW		
0-4 hrs	21(64%)	12(31%)
4 -8 hrs	20(39%)	20(50%)
8-12 hrs	3(30%)	7(70%)
AGE GROUP		
<60 yrs	30(62%)	18(38%)
>60 yrs	14(40%)	21(60%)
Anteriorwall infarct	20(40%)	30(60%)
Inferior wall infarct	24(72%)	9(28%)

Tablev2 A total of 83 patients were studied. Their age ranged from 34 –t o 76years (mean 55.03 yrs).68 of them were males (82%) and 15 females (18%) 20 of them were hypertensives (24%) .44 people were smokers (53%) and 29 (59%) consumed alcohol. 23 patients experienced preinfarction angina (28%). 50 patients had anterior wall infarction (60%) and 33 patients (40%)had inferior infarction.

DISCUSSION

The major finding of this study is that the location of the infarct significantly affects the outcome of thrombolysis. Those with inferior wall myocardial infarction have a 3.18 times chance of undergoing

successful thrombolysis compared to anterior wall myocardial infarction(p=0.02). This is after adjustment for confounding variables like time window, age, smoking status, gender, diabetes, and hypertension. A similar observation was made by Boersma et.al, They found that TIMI grade all flow rates were lower for left coronary and circumflex artery compared to right coronary artery after thrombolytic therapy**.** The reason for this differential response will be evident when we look into the physiology of coronary circulation in the left coronary arteries. Blood flow in the right coronary artery is relatively independent ofthe phases of the cardiac cycle being present in both systole and diastole. Whereas flow in the left coronary artery is almost absent during systole and may even be reversed in conditions of heightened microvascular tone and left ventricular hypertrophy. The relatively thicker wall, the increased wall thickening during systolic contraction, and higher intracavity pressure of the left ventricle may all produce higher intramyocardial pressure than that is observed in the thinner-walled right ventricle which is also subjected to lower filling pressures. Moreover, the extent of necrosis in the anterior wall is more resultingin increased myocardial edema compared to inferior infarctions. This may further decrease the reperfusion rates in anterior infarctions. Yet another mechanism maybe, better drug delivery to the right coronary and prolonged contact of streptokinase with the thrombus, resulting in more efficient fibrinolysis. [8]Alcohol consumption has influenced the outcome of thrombolytic therapy favorably. Univariate analysis revealed a success rate of 9% in the drinkers versus 44% in nondrinkers. (p=0.03, odds ratio=2.78). This advantage of drinkers persisted after logistic regression analysis to remove the confounding factors, even though statistically not significant. (odds ratio=3.16.p=0.06).Alcohol is known to reduce coronary artery disease- related mortality. In a meta-analysis of all experimental studies that assessed the effects of moderate alcohol consumption on the concentrations of LDL cholesterol, apolipoprotein A1, fibrinogen, triglycerides, and other biological markers [9] C Michael Gibson et al concluded that 30mg of alcohol /day would cause an estimated reduction of 24.7% in the risk of coronary artery heart disease. This better success rate observed in patients who consume alcohol may be easily explained by the effect of alcohol on hemostatic factors. In a study conducted on 631 healthy male physicians, the plasma levels of tPA antigen were 10.9, 9.7, 9.1, and 8.1ng/ml respectively in those who consumed alcohol daily, weekly, once a month, and never. [10] Studies have shown alcohol affects platelets also. Alcohol reduces platelet aggregation in response to most agonists like thrombin, ADP, epinephrine, and collagen. By contrast in binge drinkers or alcoholics after alcohol withdrawal response to aggregation especially that induced by thrombin is markedly increased. This rebound phenomenon may be explained by ischemic strokes or sudden death is known to occur after episodes of drunkenness. Ethanol intake is also known to decrease blood fibrinogen levels. Thus those who consume alcohol on a moderate basis are having betterendogenous fibrinolytic responses.[11] Patients older than 60 years are found to have a lesser success rate in univariate analysis. (X2= 4.11,odds ratio = 2.5 ,P = 0.04). after adjustment for other parameters in the logistic regression, a statistically significant reduction in success rate is observed This shows that concerning fibrinolysis elderly people do not behave differently from younger. This is reflected in a reduction in mortality rate among the elderly after thrombolysis. In patients aged more than 75 yrs who were treated with streptokinase in the GISSI-2 trial, there was a reduction of 4.2 fewer deaths per 100 patients than in controls. [12] In ISIS- 2 there were 3.3 fewer deaths per 100 patients in those over 70 yrs of age who were treated. No statistically significant difference was noticed based on gender.[13] Chockalingam et al. performed an angiographic study to find out the patency rate at 90 minutes in men versus women. At 90 minutes TIMI-3 flow rate was 39% in women and 38% in men, which was not statistically significant. But 30-day mortality was 13.1 in women versus 4.8in men(p=0.001). Thus, even though females have a poor outcome after myocardial infarction, they do not behave differently with the thrombolytic therapy.[14] Hypertensives did not show any difference in the success rate in this study. High blood pressure often confers silent cardiovascular risk, and its prevalence is steadily increasing. Most epidemiological studies now recognize the joint contributions of systolic and diastolic blood pressure to the development of cardiovascular risk, an issue that has markedly changed strategies for risk detection. [15] The results of the TROPHY trial support treating pre hypertensive and the feasibility of treatment. However, outcome trials demonstrated that the initiation of pharmacological therapy in pre hypertensives indicated the presence of other major comorbidities such as diabetes, renal dysfunction, or known vascular disease. Patients w h o are superior to initiating treatment at the time of hypertension diagnosis are lacking. [16] By contrast, pharmacological therapy is mandated for those with stage 1 hypertension (systolic blood pressure 140 to 159 mmHg or diastolic blood pressure 90 to 99 mmHg) or stage 2 hypertension (systolic bloodpressure higher than 160 mmHg or diastolic blood pressure higher than 100 mmHg). In this study success rate of thrombolysis in diabetics is not found tobe different from the nondiabetic population[17]. Fiol M et al. found a reduction in reperfusion rates in the thrombolysed diabetic population. Diabetes is a prothrombotic state as reflected by the increased blood levels of fibrinogen, factor Vll, and von Willebrand

factor. These changes are even more increased if diabetic people are happened to be smokers. Platelet function is also impaired in diabetics, they aggregate more readily to stimuli like ADP and collagen. Glycolisation of membrane proteins due to chronic exposure to high blood sugar levels change in the fluidity of platelet membrane brought out by high concentration of cholesterol and triglycerides are the proposed mechanisms for these abnormalities. On the other hand, patients with type ll diabetes have profound suppression of fibrinolysis. Plasminogen activator inhibitor –l levels are high in type II diabetic people which is responsible for this effect. Nevertheless, thrombolytic therapy should be administered to diabetics with acute myocardial infarction, because for 100 diabetic patients treated withthrombolytic therapy four lives are saved.[18] Karha J et al demonstrated by the angiographic method that those Acute myocardial patients who experienced peri infarction angina within seven days preceding the acute event had more rapid thrombolysis. Patency rates were higher at 35 minutes but at 90 minutes both were the same. In this study success rate was the same at 90 minutes in both groups. This is because ECG monitoring was not continuous in this study. Continuous ST-segment monitoring may be needed to demonstrate the early achievement of patency in pre-infarction angina patients. The outcome of thrombolysis is not affected by smoking. In this study, there is a statistically insignificant trend towards a bad outcome.[19**]** Murphy SA et al reported similar patency rates in smokers and nonsmokers at 90 minutes (73% versus 74%). Smokers tended to have reduced in-hospital mortality compared to nonsmokers. but this was due to the favorable baseline clinical and angiographic variables in smokers. Smokers tended to be younger and thrombosis of less critical atherosclerotic plaque was the culprit lesion in them. Smoking increases blood hematocrit, fibrinogen levels, and platelet levels contributing to the hypercoagulable state and promoting coronary thrombosis. Smokers are also found to have lesser fibrinolytic activity than nonsmokers. This is the most powerful predictor of success rate. In this study also it is evident. The success rate was 64% in those patients who thrombolysis within 4 hours from the onset of symptoms. The success rate decreased to 55% when they were thrombolysis after 4 hours but within 8 hours of the onset of chestpain. The success rate came down to 33% when streptokinase was administered after 8 hours but within 12 hours.[20]

CONCLUSION

In this study, the overall success rate of thrombolysis was 54%. Inferior wall myocardial infarctions had a better success rate than anterior wall myocardial infarctions and it was statistically significant. Smokers had a lesser success rate than nonsmokers, but it did not reach statistical significance. Alcohol intake was associated with a better success rate even though statistically not significant. Hypertensives didn't show any difference in the success rate. Diabetics do not differ from nondiabetics concerning the success rate of thrombolysis. There was a trend towards a worse outcome in those aged more than 60 years. But it was not statistically significant. Gender was not found to influence the success rate of thrombolysis. Pre infarction angina did not affect the success rate of thrombolysis.

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