COMPARISON OF TIMI FLOW AFTER INTRAVENOUS STREPTOKINASE VS PRIMARY PCI IN PATIENTS PRESENTING WITH ST ELEVATION MYOCARDIAL INFARCTION

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ABSTRACT:

BACKGROUND: *Acute myocardial infarction (MI) relates to complete occlusion of a coronary artery because of the intraluminal thrombus which overlaps the atherosclerotic lesion. 500,000 patients with STEMI are diagnosed yearly in U.S. To restore the patency of the affected artery, two of the reperfusion therapies are thrombolytic therapy using streptokinase and the primary PCI. However, no agreement has been established between the studies to utilize one of them as treatment modality.*

AIMS & OBJECTIVE: *The study aims to compare intravenous streptokinase treatment with immediate angioplasty in patients with acute ST-elevation myocardial infarction.*

MATERIAL & METHODS: *The study was a retrospective cohort conducted over a period of one year from July 2020 to June 2021. All the patients admitted consecutively during this period were chosen for either PCI group or streptokinase group. The study endpoints were successful reperfusion, TIMI flow grade 3 in the infarcted vessel at 24 hours and adverse outcomes.*

RESULTS: *PCI was performed in 48 patients, which was successful for achieving final TIMI flow grade 2 or 3 in 46 (95.8%) patients and 66% patients who received SK were observed with TIMI 3 flow (P = 0.003). 2 patients (4 %) of the SK group were observed with TIMI flow grade 2. Median residual stenosis percentage was 82% (53 – 100) for SK and 21% (20 – 28) for PCI (P =0.0001). Adverse major outcomes were more frequently observed in SK group.*

CONCLUSION: *Primary PCI was found to provide better outcomes than streptokinase to treat acute MI and also to be associated with minimal in-hospital adverse outcomes including mortality and reinfarction rates.*

KEY WORDS: *Primary PCI, streptokinase, acute MI, adverse outcomes, mortality, reinfarction rates.*

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INTRODUCTION:

In 1980, it was showed by DeWood et al. that acute myocardial infarction (MI) is related to complete occlusion of a coronary artery because of the intraluminal thrombus which overlaps the atherosclerotic lesion.[1] Cardiovascular diseases are responsible for death around the world in majority. Over 920,000 myocardial infarctions (MI) in the US are diagnosed yearly[2] among which approximately 500,000 are ST-elevation myocardial infarctions (STEMI).[3] The potency of coronary angioplasty and fibrinolytic therapy in order to restore the effectiveness of coronary artery related with infarction has been extensively studied during the past four decades.[4-8] Acute MI persists as a notable public health issue in the developed countries in spite of the remarkable advancements in its diagnosis and treatment. Extensive management of STEMI requires costly hospital infrastructure and profoundly trained medical staff as it is a complex healthcare issue. The treatment effective for acute STEMI involves the reperfusion therapy[9] aiming for timely and sustained reperfusion of the targeted myocardium.[10]Implementation of either percutaneous coronary intervention (PCI) or thrombolytic therapy accomplishes coronary reperfusion. The effectiveness of both these procedures in STEMI patients has been compared since they are first described.[11]The previous research indicates that primary PCI, performed rapidly and expertly, appears to outmatch thrombolytic therapy and results in better coronary reperfusion and greatly reduces the reinfarction and short- and intermediate-term mortality rates.[12-15]

One of the biggest achievements considering the treatment of MI is reperfusion therapy. Keeping in view the advancements in new thrombolytic medications to treat MI, no consequential development is observed regarding the patient's survival. This could be credited to the decreased rates of TIMI grade 3 flow at 90 minutes in the infarcted vessel, complications leading to internal bleeding and re-infarction.[16]Thrombolytic therapy also bears some limitations such as the administration of the agent within a particularly defined time following myocardial infarction, history of the patients who may have had intracranial or gastrointestinal bleeding,or had a recent surgery, moreover, fibrinolytic therapy carries significant side effects that may prove fatal such as haemorrhages.[17]Reperfusion by mechanical means, such as by PCI, is another possible approach for treating myocardial infarction that yields higher patency rates as compared to fibrinolytic therapy and at the same time reduces the risk of reinfarctions, mortality and complications due to bleeding during the stay in the hospital.

However, on the contrary, observational studies conducted on unselected patients with STEMI who underwent one of these two reperfusion strategies, failed to validate the advantage of primary PCI in the community setting.[18-20] Though, it is to be kept in mind that mostly studies were conducted before the use of the stents became common and the use of advanced antithrombotic agents, which clearly depicts the improvement in the outcomes of the people who undergo primary PCI.[21-23]

The study primarily aims to compare intravenous streptokinase treatment with immediate PCI in patients with acute ST-elevation myocardial infarction.

MATERIAL AND METHODS:

The study was retrospective cohort conducted over a period of one year from July 2020 to June 2021. The samples were collected through non-probability consecutive sampling. All the patients presented with STEMI admitted consecutively at name of the institute between the study period were included in the study.

Study participants:

All the patients who underwent percutaneous coronary angioplasty or intravenous streptokinase treatment at our center was included in the study. The inclusion criteria included manifestations of acute myocardial infarction that persisted for over 30 minutes, along with an elevation of >1mm in ST segments in 2 or more consecutive electrocardiographic leads, admission within 12 hours of symptoms onset, no thrombolytic therapy contraindications such as, previous stroke, refractory hypertension, recent trauma or surgery, prolonged cardiopulmonary resuscitation, or active bleeding. Before assigning treatment groups to the patients, the record of all patients included age, gender, electrocardiograph to assess the infarction site, infarction history, arterial pressure, heart rate, time of symptoms onset, and time of admitting the patient to the hospital.

Treatment Protocol:

After the informed consent was procured, the patients were non-randomly assigned to either of the two groups for treatment i.e., the streptokinase (SK) group or the percutaneous coronary intervention (PCI) group. Each patient received 300mg aspirin orally per day and a dose of nitro-glycerine intravenously that was designed for maintaining

a 110mmHg systolic blood pressure. After the assignment into groups, every 10 minutes an ECG was recorded within the initial 2 hours. Blood samples were collected at the time of admission, after every 30 minutes during the first 3 hours, and after every 2 hours for up to 24 hours.

The patients selected to the group of streptokinase therapy for treatment were intravenously administered with 1.5 million units of streptokinase (SK) over a period of 1 hour and those who were assigned to the group of coronary PCI were shifted to the catheterization laboratory as soon as possible to undergo coronary angioplasty. Primary PCI was not performed in the following conditions: TIMI grade III flow detected in the baseline angiogram, >50% stenosis in the left main artery and it supplied blood to the occluded vessel, or unsuitable coronary anatomy for performing PCI. The success of the procedure was set as residual stenosis <50% with TIMI grade 2 or 3 flow in the vessel with culprit lesion.

Study end points:

Successful reperfusion was the primary end point, demonstrated as ST-segment resolution ≥50%, at 2 hours after grouping, in the single lead of ECG in which the ST elevation was displayed maximum at the time of enrolment. Other end points were TIMI flow grade 3 in the infarcted vessel at 24 hours detected in angiogram and adverse outcomes such as, death during hospital stay, reinfarction, stroke, major bleeding, requirement of revascularization procedures.

STATISTICAL ANALYSIS:

All end points were analyzed using IBM SPSS Statistics version 20.0. Absolute variables and continuous variables were expressed as percentages and mean ± S.D, respectively. The relationship between continuous variables was assessed by independent t-test whereas, Chi-square test was used for categorial variables. < 0.05 was considered as statistically significant p-value.

RESULTS:

Out of the total number of patients admitted in our center, 114 patients were selected for the study based on inclusion criteria which were assigned to either streptokinase (SK) group (n = 59) or PCI group (55). The mean age of the patients was 65 years (57 – 74) and 66 years (59 – 77)for streptokinase group and PCI group, respectively (p = 0.98). Regarding gender, 13 (22 %) and 18 (32.7 %) patients were females in SK group and PCI group, respectively. The median weight of the patients was 76 kg (69 – 84) and 75 kg (63 – 82) in streptokinase and PCI group, respectively. Majority of the patients (54.2 % in streptokinase group, 62.7 % in PCI group) had the culprit lesion in Left anterior descending (LAD) artery. The infarct location and baseline characteristics between the two groups were balanced well (Table 1).

Notably, 86 (75.4 %) patients were having at least any one of the following high-risk feature; > 70 years of age, previous MI, anterior MI location, < 100mm Hg systolic blood pressure and/or heart rate of >100bpm.

Study procedures: Primary PCI and thrombolytic administration:

From the admission to hospital to the initiation of streptokinase infusion in SK group and first balloon inflation in PCI group, the mean time was 30

Table 1. Baseline Characteristics of the Patients

Variable	SK (n = 59)	PCI (n = 55)	p value
Age (years) (IQR)	65 (57 – 74)	66 (59 – 77)	0.98
Female gender	13 (22 %)	18 (32.7 %)	0.12
Weight (kg)	76 (69 – 84)	75 (63 – 82)	0.31
Previous MI (%)	14 (23.7 %)	6 (11 %)	0.072
Heart rate (beats/min)(IQR)	80 (70 – 92)	80 (70 – 90)	0.85
Systolic blood pressure (mm Hg) (IQR)	125 (110 – 140)	132 (120 – 150)	0.092
Anterior MI location (%)	26 (44 %)	28 (51 %)	0.47
Infarct-related vessel (%)			
LAD	32 (54.2 %)	37 (62.7 %)	
LCX	10 (17 %)	8 (13.5 %)	0.87
RCA	17 (28.8 %)	14 (23.7 %)	

LAD: Left anterior descending, LCX: Left circumflex; RCA, Right coronary artery

Table 2. Procedural characteristics of primary PCI	
Variables	PCI (n = 55)
PCI performed (%)	48 (87.2 %)
Pre-procedural TIMI flow grade*	
0	39 (81.2 %)
1	4 (8.3 %)
2	5 (10.4 %)
3	
Post-procedural TIMI flow grade	
0	2 (4.1 %)
1	1 (2.0 %)
2	4 (8.3 %)
3	41 (85.4 %)
*Percentages are taken from 48 patients from this row down.	

Table 3. Adverse outcomes occurred in both the groups			
Variable	SK (n = 50)	PCI (n = 48)	p value
Death	2 (4 %)	0 (0 %)	0.13
Stroke	1 (2 %)	0 (0 %)	0.51
Bleeding	4 (8 %)	1 (2 %)	0.29
Heart Failure	4 (8 %)	3 (6.2 %)	0.25
Reinfarction	3 (6 %)	2 (4.1 %)	0.12

Table 4. TIMI flow grade and residual stenosis at 24 hours			
Variable	SK (n = 50)	PCI (n = 48)	p value
TIMI flow grade (%)			0.003
0	15 (30 %)	2 (4.1 %)	
1	0 (0 %)	0 (0 %)	
2	2 (4 %)	0 (0 %)	
3	33 (66 %)	46 (95.8 %)	
Median residual % stenosis (IQR)	21 (20 – 28)	84 (53 – 100)	0.0001

±15 minutes and 61 ±22 minutes, respectively. The patients grouped for angioplasty underwent emergency angiography. In 49 (89%) patients TIMI flow grade 0 was detected in the vessel related with infarction. PCI was performed in 48 out of 55 patients, which was successful for achieving final TIMI flow grade 2 or 3 in 46 (95.8%) patients whereas the attempt of reopening the infarct related vessel failed in 2 patients. Consequently, these patients underwent coronary artery bypass grafting immediately. In 7 patients PCI was not performed, owing to the reason of spontaneous reperfusion with TIMI flow grade 3 in 4 patients and unsuitable anatomy for PCI in 3 patients. No death in the catheterization laboratory was reported (Table 2). Among the SK group patients, full dose of the thrombolytic agent could not be administered due to hypotension and allergic reaction in 5 and 1 patients respectively. Moreover, 3 patients did not receive SK because of spontaneous reperfusion. Therefore, 50 patients underwent streptokinase therapy. 11 (18.6%) patients underwent emergency coronary angiography and rescue PCI was performed in all of them. Thrombolysis, heart

failure and infarct extension were the indications for emergency coronary angiography in 6, 4 and 1 patients respectively. The success of rescue procedures in all the patients was validated as final TIMI flow grade 3 was achieved in 8 cases and TIMI flow grade 2 in 3 patients.

Major in-hospital adverse outcomes:

Table 2 shows the frequency of complications associated with both the procedures. Bleeding complications included intracerebral bleeding and the bleeding that necessitated blood tranfusion. Although no significant difference was observed. Overall fewer complications were reported in the patients grouped for immediate angioplasty as compared to those grouped for streptokinase. Particularly, lower frequency of bleeding, heart failure and death was observed in the patients of angioplasty group 2 deaths were reported in streptokinase group and no death was reported in PCI group.

Two patients (3.3%) of the SK group and three patients (5.4%) of the PCI group underwent coronary bypass surgery. Statistical difference was observed between the two treatment groups considering the occurrence of in-hospital major adverse cardiac events, that included the requirement of new revascularization procedures (PCI group, 21% and 50% in SK group with the p value of 0.027). The patients of angioplasty group had 87.5 % freedom rate from these adverse events whereas, streptokinase group had 70% (p = 0.01).

Angiographic results at 24 hours:

Predischarge angiography was performed in all patients at 24 hours. 95.8% of patients treated with primary PCI were observed with TIMI flow grade 3 in the culprit vessel and 66% patients who received SK were observed with TIMI 3 flow (P = .003). 2 patients (4 %) of the SK group were observed with TIMI flowgrade 2. Median residual stenosis percentage was 82% (53 – 100) for SK and 21% (20 – 28) for PCI (P =0.0001).

DISCUSSION:

The current study was conducted to compare the outcomes of intravenous streptokinase with primary PCI for the validation of the one of these treatment modalities. After various publications suggested primary PCI being more favourable than thrombolytic therapy,[12-17]and the studies with contrary results[21-23] the decision to conduct this study in our institute for assessing the safety, feasibility and efficacy of primary PCI was taken.

According to the findings of our study, in comparison with intravenous streptokinase therapy, the outcomes of employing primary PCI as a reperfusion approach for myocardial infarction are better in the resolution of ST-segment, show higher rates of infarct vessel patency with decreased residual stenosis at 24 hours, achieve improved clinical conditions, and show lower frequency of major adverse cardiac events requiring repeated revascularization procedure.

All the reperfusion therapies are primarily aimed for reopening the occluded coronary arteries. There are two most significant aspects of patency in this regard. The First is concerned with the time required for the re-establishment of flow in the artery related with infarction. Keeping that in view, the patients that were grouped for angioplasty in our study had higher patency rates that could not be obtained with thrombolytic agents. The second aspect is the persistent patency of the infarct-related artery, that relates to long term survival.[4] Initial successful reperfusion subsequently leading to re-occlusion is undoubtedly a major concern.[24] The patients who undergo angioplasty show higher patency rates.

An association has been established between various mechanisms and clinical short- and long-term advantages observable with primary PCI.[25] In our study, we observed a couple of mechanisms including better reperfusion with improved resolution of ST-segment elevation and a reduction in re-occlusion and residual coronary stenosis rates. Pre-discharge angiography performed on patients that a greater number of patients having an obstructed infarct vessel in the group treated by streptokinase. These occlusions can be justified by reinfarctions or failed thrombolysis.

Complications after the procedures performed was another end point of the study. As gradual decline in mortality due to acute myocardial infarction has been observed and less than 10% mortality rates are reported in many trials that are recently published, [8, 26-28] the morbidity in the patients who survive has become the most considerable clinical end point. In comparison with streptokinase therapy, immediate angioplasty is observed to drastically reduce the frequency of recurrent myocardial ischemia.A composite clinical end point has also been proposed [29] and implemented[27] which not only includes recurrent infarction or angina, but additionally re-occlusion, stroke, heart failure and death. The relieve from such adverse events can be compared on these basis. In our study, out of 50 patients who underwent streptokinase therapy and 48 patients who underwent angioplasty, 15 (30%) and 6 (12.5 %) suffered from one or more of these adverse events respectively. The patients of angioplasty group had 87.5 % freedom rate from

these adverse events which was significantly better than that of the streptokinase group i.e., 70% with the p value of 0.01.

If angiography is to be performed on a patient right after their admission, participation of a cardiac surgeon becomes essential in such cases. A major part of the patients that were assigned angioplasty procedure, were anatomically suited for angioplasty, though there had been a few exceptions. In our trials, we encountered three patients who were not anatomically well suited for angioplasty and thus required emergency bypass surgery of their infarct-related vessel and their major coronary arteries.

Our study had some obvious limitations being single centre based and having small sample size. Though the results clearly highlighted a decreased rate of infarctions and mortality in people who underwent angioplasty, the study did not have enough data to be labelled statistically noteworthy.

CONCLUSION:

Primary PCI was found to provide better outcomes than streptokinase to treat acute MI and also to be associated with minimal in-hospital adverse outcomes including mortality and reinfarction rates indicating towards the primary PCI to be selected as prime treatment modality in patients with acute STEMI.

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