ORIGINAL ARTICLE

FREQUENCY OF NO-REFLOW IN PATIENTS UNDERGOING PRIMARY PERCUTANEOUS CORONARY INTERVENTION AND THE IMPACT OF INTRACORONARY ADRENALINE AND TIROFIBAN ON TIMI FLOW

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Background: Coronary interventions, including percutaneous coronary intervention (PCI), have significantly improved management of coronary artery disease by restoration of coronary blood flow to myocardium. However, despite of so many advancements in PCI procedural techniques, there is still a significant and challenging complication known as the "no-reflow" phenomenon exists which worst effect the PPCI outcome. **Methods:** It was Cross sectional study conducted at Department of Cardiology, Lady Reading Hospital Peshawar. Study was conducted from 1/1/2023 to 30/6/2023 for six months**.** All patients who developed no reflow were subjected to intracoronary Tirofiban. Those who do not responded to Tirofiban were given intracoronary adrenalin and effect was noted. Data were analyzed using SPSS Version 23.0. Mean and standard deviation were calculated for quantitative variables like age. Frequencies and percentages were calculated for categorical variables like gender. The *p*-value less than 0.05 was considered significant. **Results:** Among 151 participants, 18% experienced the no-reflow phenomenon. Intracoronary adrenaline and Tirofiban individually showed a significant positive impact on TIMI flow. It was found that 40% patients with no reflow responded to Tirofiban administration. Remaining patients with no reflow were subjected to intracoronary adrenalin therapy and 74% of these patients had improved TIMI flow. It was also found that combine effect of Tirofiban and adrenalin was found in 84% of patients. **Conclusion:** No reflow phenomenon is common finding in Primary PCI and can be effectively managed by Tirofiban and intracoronary adrenalin administration in most cases.

Keywords: STEMI; No reflow; TIMI; PPCI

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INTRODUCTION

Acute myocardial infarction (AMI) is associated with high short and long term morbidity and mortality throughout the world.[1] it has been found that 25% to 40% of patients presenting with myocardial infarction are known to have STEMI.[2] Myocardial infarction related mortality is decreasing owing to more aggressive medical therapy and timely intervention in the form of primary PCI.[2]

Early diagnosis of myocardial infarction and timely reperfusion is the key for improving outcome.[3] Delay in reperfusion is associated with increase mortality and morbidity.[4] Thrombolytic therapy (TT) or primary percutaneous coronary intervention (PCI) is used to restore patency and reflow of blood in the coronary artery occluded by thrombus during STEMI.[5]

Coronary interventions, including percutaneous coronary intervention (PCI), have significantly improved management of coronary artery disease by restoration of coronary blood flow to myocardium.[6] However, despite of so many advancements in PCI procedural techniques, there is still a significant and challenging complication known as the "no-reflow" phenomenon exists which worstly effect the PPCI outcome.[7] The no-reflow phenomenon refers to an impaired myocardial perfusion despite the restoration of epicardial coronary artery patency, often observed during or after PC.[8]

There are various mechanisms attributed to no-reflow phenomenon. These includes, micro vascular spasm, endothelial dysfunction, distal embolization of thrombus or atheromatous debris, and inflammation.[9] These various factors leading to inadequate microcirculatory perfusion, and consequently myocardial ischemia even after successful restoration of epicardial blood flow.[8]

No-reflow phenomenon is of great importance as it is directly related with PPCI outcomes. Impairment of microvascular perfusion is associated with larger infarct sizes, increased risk of heart failure, and increasing mortality rates.[10] So recognition and proper management of no-reflow phenomenon can markedly reduce myocardial

damage, improve ventricular function, and improve overall prognosis.[8]

The aim of this study is to investigate the frequency of the no-reflow phenomenon in patients undergoing coronary interventions at Lady Reading Hospital, Peshawar. Furthermore, the research aims to evaluate the impact of intracoronary administration of adrenaline and Tirofiban on Thrombolysis In Myocardial Infarction (TIMI) flow. By addressing these objectives, the study aims to contribute valuable insights into the prevalence of no-reflow in this particular population and assess the efficacy of specific interventions in ameliorating microvascular dysfunction, thereby optimizing patient outcomes in the context of coronary interventions.

MATERIAL AND METHODS

It was Cross sectional study conducted at Department of Cardiology, Lady Reading Hospital Peshawar. Study was conducted from 1/1/2023 to 30/6/2023 for six months. Sample size was calculated using WHO formula for sample size determination in health studies based on, Confidence level of 95%, and margin of error 5 %. Sampling technique was Consecutive non-probability sampling.

All patients age above 18 years presented with NSTEMI and going for coronary angiography were included in the study. Patients having previous history of Stroke, Myocardial infarction, CABG, renal impairment and previous PCI were excluded from study. The study was conducted after getting approval from hospital ethical and research committee. The patients meeting the inclusion criteria were recruited in the study after taking written informed consent. The purpose of the study and the benefits and risks were explained to all the recruited patients.

All patients were managed according to the standard ACS protocol. All patients undergone a detailed history and clinical examination. Biochemical workup was carried out for each patient including complete blood count, serum electrolytes, RFTs, Lipid profile, RBS, HBA1C, LFTs, ECG and echocardiography. Angiography was performed by interventional fellow with supervision of consultant interventional cardiologist. All PCIs were performed by consultant interventional cardiologists.

Intracoronary administration of adrenaline and Tirofiban were conducted in accordance with established clinical protocols. Tirofiban was given at a loading dose of 25Ug/kg including 250Ug intracoronary dose and remaining dose was given intravenous. Adrenalin is given intracoronary at the dose of 0.01mg.

Any patient in whom PPCI was done, were assessed for coronary blood flow and categorized on standard TIMI blood flow criteria (0–3). Any patient who develops TIMI flow less than 2 were given Tirofiban and TIME flow was recorded on next intracoronary injection taken 3-5 minutes after Tirofiban administration. If blood flow observed TIMI flow less than 2 after Tirofiban administration then intracoronary adrenalin were given and TIMI flow recorded on next injection.

Data were analyzed using SPSS Version 23.0. Mean and standard deviation were calculated for quantitative variables like age. Frequencies and percentages were calculated for categorical variables like gender. Chi square test was used for comparing categorical variables whereas student T test was used for quantitative variables. P value less than 0.05 was considered significant. All the results were presented in the form of tables.

RESULTS

Total of 250 participants were included in the study, with 175 (70 %) identified as male and 75 (30%) as female. Mean age of the study population was 58.4±10. Regarding base line characteristics, 98 participants (39.2%) had a history of DM, 155 participants (62%) were hypertensive, 57 (22%) were smoker, 24 (9.6%) were having positive family history of CAD.

Regarding type of myocardial infarction, 57% experienced Anterior Wall MI (AWMI), 40% had Inferior Wall MI (IWMI), 0.7% high lateral MI, O.5% posterior MI and 1.8% had lateral MI.

No-reflow phenomenon was found in 45 (18%) of the total study population, following coronary interventions. Following the administration of administration of Tirofiban, a substantial improvement in TIMI flow grades was observed. Among the 45 patients in this subset, 18 patients (40%) achieved the optimal Grade 2 or 3, denoting good perfusion, indicating a robust response to Tirofiban intervention. It was found that out of 45 patients with no reflow, 27 patients (60%) did not respond to Tirofiban intracoronary dose. These patients were given intracoronary adrenalin and response was checked after 3–5 minutes. It was found that 20 patients (74%) responded to adrenalin with improved TIMI flow from 0 and 1 to TIMI 2 and 3, while 7 patients (26%) failed to respond to adrenalin.

These results highlight the effectiveness of adrenaline and Tirofiban in ameliorating microvascular dysfunction and optimizing coronary blood flow, as reflected in the improved post-PCI TIMI flow grades. The significant proportion of patients achieving Grade 1 and Grade 2 suggests a substantial positive impact on microvascular perfusion, reinforcing the clinical relevance of these interventions in the context of percutaneous coronary interventions. This collective evidence supports the

notion that targeted administration of adrenaline and Tirofiban contributes to enhanced post-PCI microvascular function, providing valuable insights for refining treatment strategies and improving patient outcomes.

Table-1: Base line characteristics of study population.

Variables		Values
Age (mean)		58.4±10
Gender	Male	175 (70%)
	Female	75 (30%)
Hypertension	Yes	155 (62%)
	No	95 (38%)
Diabetes	Yes	98 (39.2%)
	No	152 (60.8%)
Family history	yes	24 (9.6%)
	No	226 (90.4 %)
Smoker	Yes	57 (22%)
	No	193 (78%)
Type of MI	anterior	57%
	inferior	40%
	Lateral	1.8%
	Posterior	0.5%
	High lateral	0.8%

Table-2: No reflow phenomenon and effect of tirofiban and adrenalin

Variables	Parameters	Number	Percentage	*p*-value
Total population N=250	Normal flow	205	82%	
	No reflow	45	18%	
Effect of Tirofiban N=45	Flow improved	18	60 %	.04
	Flow not improved	27	40%	
Effect of adrenalin N=27	Flow improved	20	74%	.003
	Flow not improved	7	26%	
Effect of both Tirofiban and adrenalin N=45	Flow improved	38	84.44%	.001
	Flow not improved	7	15.66%	

DISCUSSION

The comprehensive analysis of our research findings at Lady Reading Hospital, Peshawar, augments the existing body of knowledge on the no-reflow phenomenon and intracoronary interventions during percutaneous coronary intervention (PCI). Our study, which revealed a no-reflow frequency of approximately 18%, aligns with the multifactorial nature of this phenomenon reported in previous research[11]. This frequency underscores the persistent challenge in achieving optimal microvascular perfusion despite advancements in PCI techniques. According to several reports, the incidence of no reflow is vary, ranging from 2–44% of all patients undergoing both primary and elective PCI.[12–14] This much and diverse findings may be due to different ethnicity, PCI techniques, types of myocardial infarction, patient door to balloon or ischemia to balloon time .Similarly other studies also shows different findings and frequency of no reflow. Rao PS *et al*[15] described 23% frequency of no reflow in their study whereas, yang L *et al*[16] found 28 % frequency of no reflow in primary PCI cases. These studies shows that our findings of 18% no reflow PPCI is not surprising but actually this high frequency exist worldwide.

However, the variation in the frequency of no-reflow, the efficacy of interventions, and patient outcomes across different studies underscores the heterogeneity of patient populations, procedural techniques, and healthcare settings. Our study, conducted at Lady Reading Hospital, contributes unique insights into a specific population, emphasizing the importance of tailored interventions. Comparative analyses highlight the need for localized approaches in managing no-reflow, considering the diverse clinical contexts in which PCI is performed.

Comparing our results to existing literature, the observed improvement in post-PCI Thrombolysis in Myocardial Infarction (TIMI) flow grades following adrenaline and Tirofiban administration is consistent with previous findings.[17] Adrenaline and Tirofiban demonstrated a substantial positive impact on microvascular perfusion, leading to Grades 3 and 4 TIMI flow in the majority of patients. This aligns with the proposed mechanisms of adrenaline mitigating microvascular spasm and Tirofiban preventing microvascular obstruction, emphasizing the clinical relevance of these interventions.

Previous studies also demonstrate significant effect of Tirofiban and adrenalin in coronary no reflow. A study performed by Akpek M *et al*[18]demonstrated significant improvement in coronary flow after Tirofiban administration in patients who developed no reflow after Primary PCI. They found that 32% of patient TIMI flow improved from TIMI 1 and 2 to TIMI 3 and 4. This finding is very close to our findings of 40% in current study. Another study performed by Aksu T *et al*[19] studied the effect of intracoronary adrenalin in no reflow. They found that intracoronary adrenalin is effective in 75% of cases. This finding is exactly same to our findings of 74% efficacy of intracoronary adrenalin.

While our results provide valuable insights, the inclusion of data from other research papers strengthens the generalizability of findings. Future research should explore these variations in-depth, considering factors such as geographical, demographic, and procedural differences. This comparative approach will refine our understanding of the no-reflow phenomenon, guide interventions, and

contribute to the development of standardized protocols for enhanced PCI outcomes.

AUTHORS' CONTRIBUTION

Ikramullah: Concept, Statistics. FA: Final proof, data collection. Hamidullah, SK, HAB: Literature search, data collection. SR: Data collection

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