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Administration of Intra-Coronary Adenosine before Stenting for Prevention of No Reflow/Slow Flow in Patients with Acute ST Elevation MI

Muhammad Ejaz Ayub[1], Kashif Khan[2], Waleed Ahmed Abbasi[1], Muhammad Abdus Salam Azad[1], Asma Shabbir[1], Gul Zaman Khan Niazi[1]

[1]Rawalpindi Institute of Cardiology, Rawalpindi, Pakistan
[2]Department of Interventional Cardiology, Mardan Medical Complex, Mardan, Pakistan

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Correspondence to: Muhammad Ejaz Ayub,
Rawalpindi Institute of Cardiology, Rawalpindi, Pakistan
Email: dr.ejaz.ayub@gmail.com

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ABSTRACT

Background and Aim: The phenomenon of no-reflow/slow-flow during primary percutaneous coronary intervention (PCI) in acute ST-elevation myocardial infarction (STEMI) patients remain a challenging complication causing adverse myocardial perfusion and outcomes. The administration of intra-coronary adenosine, anti- platelet and anti-inflammatory vasodilator has been recommended as latent strategy to prevent and mitigate this complication. The aim of the present study was to assess the efficacy of intra-coronary adenosine administration before stenting in preventing no-reflow/slow-flow in patients presenting with acute STEMI undergoing primary PCI. **Patients and Methods:** A questionnaire-based case-control study investigated 100 patients (50 in the adenosine group and 50 in the control group) at Rawalpindi Institute of Cardiology, Rawalpindi for the duration of three months, from December 21, 2024 to March 20, 2025. STEMI patients with chest pain duration <12 hours and requiring stenting enrolled. Demographic details, comorbidities such as DM, HTN, dyslipidemia, stroke, and obesity, medication use, tobacco usage, medical/surgical/family history, socioeconomic factors, and procedure-related variables including occlusion level, thrombus burden, use of thrombus aspiration, distal drug delivery, TIMI flow grade, and adenosine dose recorded. SPSS v23 used for data analysis. **Results:** 100 patients were randomly assigned to two groups; Group-A (N=50) administrated with adenosine and Group-B (N=50) administrated with standard treatment or control group. Both groups had comparable results in baseline and clinical characteristics with no significant differences ($p > 0.05$). Renal function parameters such as serum creatinine (89.2 ± 18.5 vs. 91.4 ± 20.1 mmol/L) and glomerular filtration rate (76.3 ± 15.2 vs. 73.1 ± 16.8 ml/min/1.73m^2), showed no significant difference between the adenosine and control groups, respectively ($p > 0.05$). Adenosine group had significantly frequent cases (90%) of final TIMI flow grade III compared to control group (70%) ($p=0.01$). However, no significance difference observed in angiographic findings (culprit vessels and thrombus burden). The prevalence of no-reflow phenomenon was 6% in adenosine group compared to control group (24%) ($p=0.02$). Distal drug administration via micro catheter was significantly higher (92%) in adenosine group compared to control group (10%), ($p<0.001$). Stent size, thrombus aspiration, lesion characteristics, and pre- and post-dilation had no significant differences in both groups. **Conclusion:** The pre-stenting administration of intra-coronary adenosine improved the procedural outcomes in acute STEMI patients underwent PCI significantly reduces the prevalence of no-reflow/slow-flow. These observations support the evidence of adenosine clinical utility as a preventive strategy for high-risk STEMI intervention.

INTRODUCTION

The preferred treatment for ST-segment elevation myocardial infarction (STEMI) patients during the early hours following symptom onset is Primary percutaneous coronary intervention (PCI) [1]. However, despite its widespread use, primary PCI does not always guarantee complete coronary revision or adequate myocardial reperfusion. A significant range is the occurrence of no-reflow phenomenon, characterized by low coronary blood flow (TIMI flow grade <3 or myocardial blush grade [MBG] <3), which affects about 5% to 50% of STEMI patients passing through PCI [2, 3]. This phenomenon is strongly associated with poor clinical outcomes and increased mortality, underlining the important requirement for

effective preventive strategies [4]. Among the most deadly diseases haunting humankind for ages are those that arise due to obstruction or narrowing of coronary arteries due to multiple known and idiopathic reasons. Literature suggests that almost 50% of deaths worldwide are due to heart diseases particularly due to ischemic heart diseases that lead to myocardial infarction and death as MI still holds the significant weightage as leading cause of heart failure too. Myocyte death can occur within hours of ischemia [5].

The No-Reflow Phenomenon has a complex and multifactorial pathophysiology, with various contributing factors influencing its development [5, 6]. Consequently, numerous strategies have been explored to prevent its occurrence during primary PCI, including administration of a series of medicinal agents [7]. These interventions span from pre-procedural medicines to the use of intracoronary drugs during the procedure. Of these, several clinical studies of adenosine, an endogenous purine nucleoside, have been examined-often for its possible efficacy in reducing the no-perpetual event in combination with other agents [8]. Although the exact mechanism of adenosine not perfectly understood in preventing the no-flow phenomenon, but believed that neutrophils promote its effects and protect the endothelium from damage [9]. Studies using intravenous adenosine have not demonstrated significant clinical benefits, while intracoronary administration has shown results that are more promising [10]. In previous studies, variability in results attributed to the differences of the methods used to assess administration routes, adenosine supplements and the no-flow phenomenon [11].

The phenomenon of no-reflow/slow-flow during primary percutaneous coronary intervention (PCI) in acute ST-elevation myocardial infarction (STEMI) patients remain a challenging complication causing adverse myocardial perfusion despite successful revascularization. Given its multifactorial pathophysiology, numerous pharmacologic interventions have been explored to prevent this phenomenon. Among them, adenosine, an endogenous purine nucleoside, has shown potential due to its anti-inflammatory and endothelial protective properties. However, previous investigations have yielded unreliable outcomes, largely due to variations in the route of administration, dosage, and assessment methods for detecting no-reflow. Intracoronary administration of adenosine has demonstrated more promising outcomes compared to intravenous use. Therefore, this study designed to assess the intracoronary adenosine administration efficacy before stenting in preventing the no-reflow/slow-flow phenomenon among STEMI patients undergoing primary PCI, aiming to clarify its clinical value and optimize myocardial reperfusion strategies.

METHODOLOGY

The study designed as a questionnaire-based case-control study conducted on 100 cases at Rawalpindi Institute of Cardiology (RIC), Rawalpindi, the tertiary care center specializing in cardiovascular interventions, for the duration of three months, from December 21, 2024 to March 20, 2025. STEMI patients requiring stent deployment and having chest pain duration less than 12 hours enrolled and divided equally into two groups: Adenosine Group (n = 50): Patients who received intracoronary adenosine prior to stenting. Control Group (n = 50): Patients who underwent standard percutaneous coronary intervention (PCI) without adenosine administration. Patients failed to give Inform Consent, having less than TIMI 3 flow before stenting, and chest pain more than 12 hours in STEMI patients excluded.

Demographic details, comorbidities such as DM, HTN, dyslipidemia, stroke, and obesity, medication use, tobacco usage, medical/surgical/family history, socioeconomic factors, and procedure-related variables including occlusion level, thrombus burden, use of thrombus aspiration, distal drug delivery, TIMI flow grade, and adenosine dose recorded. SPSS v23 used for data analysis. A p-value <0.05 was considered statistically significant.

RESULTS

100 patients were randomly assigned to two groups; Group-A (N=50) administrated with adenosine and Group-B (N=50) administrated with standard treatment or control group. Both groups had comparable results in baseline and clinical characteristics with no significant differences ($p > 0.05$). Renal function parameters such as serum creatinine (89.2 ± 18.5 vs. 91.4 ± 20.1 mmol/L) and glomerular filtration rate (76.3 ± 15.2 vs. 73.1 ± 16.8 ml/min/1.73m^2), showed no significant difference between the adenosine and control groups, respectively ($p > 0.05$). Adenosine group had significantly frequent cases (90%) of final TIMI flow grade III compared to control group (70%) ($p=0.01$). However, no significance difference observed in angiographic findings (culprit vessels and thrombus burden). The prevalence of no-reflow phenomenon was 6% in adenosine group against control group (24%) ($p=0.02$). Distal drug administration via micro catheter was significantly higher (92%) in adenosine group compared to control group (10%), ($p<0.001$). Stent size, thrombus aspiration, lesion characteristics, and pre- and post-dilation had no significant differences in both groups. Demographic and clinical details presented in Table 1. Procedure-Related Characteristics and Outcomes shown in Table 2. Comparison of Angiographic and Angioplastic Characteristics between Study Groups demonstrated in Table 3.

Table 1

Demographic and Clinical Characteristics of Study Participants (N=100)

Variables	Adenosine Group (n=50)	Control Group (n=50)	p-value
Mean Age (years)	57.4 ± 9.2	56.8 ± 8.7	0.68
Gender (Male)	42 (84%)	40 (80%)	0.61
Diabetes Mellitus	18 (36%)	17 (34%)	0.83
Hypertension	30 (60%)	32 (64%)	0.68
Dyslipidemia	22 (44%)	20 (40%)	0.69
History of Stroke	3 (6%)	2 (4%)	0.64
Obesity (BMI >30 kg/m^2)	10 (20%)	11 (22%)	0.81
Smoking History	21 (42%)	24 (48%)	0.54
Positive Family History (IHD)	14 (28%)	12 (24%)	0.65
Low Socioeconomic Status	33 (66%)	36 (72%)	0.49
Serum Creatinine (mmol/L)	89.2 ± 18.5	91.4 ± 20.1	0.53
GFR (ml/min/1.73m^2)	76.3 ± 15.2	73.1 ± 16.8	0.31

Table 2
Procedure-Related Characteristics and Outcomes

Variables	Adenosine Group (n=50)	Control Group (n=50)	p-value
Culprit Artery Occlusion (Proximal LAD)	20 (40%)	22 (44%)	0.69
High Thrombus Burden	28 (56%)	29 (58%)	0.85
Use of Thrombus Aspiration	32 (64%)	31 (62%)	0.84
Distal Drug Delivery Used	46 (92%)	5 (10%)	<0.001
Final TIMI Flow Grade III	45 (90%)	35 (70%)	0.01
No-Reflow Phenomenon	3 (6%)	12 (24%)	0.02
Adenosine Dose (mcg) (mean ± SD)	1200 ± 300	—	—

Table 3
Comparison of Angiographic and Angioplastic Characteristics between Study Groups

Parameter	Adenosine Group (n=50)	Control Group (n=50)	p-value
Culprit Vessel			
LAD (Left Anterior Descending)	22 (44%)	24 (48%)	0.69
RCA (Right Coronary Artery)	18 (36%)	17 (34%)	0.84
LCX (Left Circumflex)	10 (20%)	9 (18%)	0.79
Thrombus Burden (High)	28 (56%)	29 (58%)	0.85
TIMI Flow Grade Before PCI			
0 (No re-flow)	40 (80%)	38 (76%)	0.64
I	6 (12%)	7 (14%)	0.76
II/III	4 (8%)	5 (10%)	0.72
Use of Thrombus Aspiration	32 (64%)	31 (62%)	0.84
Pre-dilatation Performed	38 (76%)	35 (70%)	0.48
Stent Diameter (mm)	3.12 ± 0.45	3.09 ± 0.41	0.67
Stent Length (mm)	23.5 ± 4.8	22.9 ± 5.1	0.53
Final TIMI Flow Grade III	45 (90%)	35 (70%)	0.01*
No-Reflow Phenomenon	3 (6%)	12 (24%)	0.02*
Use of Post-Dilatation	27 (54%)	25 (50%)	0.69
Distal Drug Delivery (Micro catheter)	46 (92%)	5 (10%)	<0.001*

DISCUSSION

The study investigated the role of intracoronary adenosine administration in patients introduced with acute ST-Elevation Myocardial Dominance (STEMI), especially focused on its efficacy in improving coronary perfusion results and preventing no-re-Flo/Slow-Flow Phenomenon. The key findings of the study reveal that while baseline clinical and demographic characteristics were comparable across both groups, the use of adenosine was associated with significantly improved post-procedural coronary perfusion outcomes.

The most clinically critical result was the high frequency of the final TIMI flow grade III in the adenosine group (90%), which indicates a strong relationship between adenosine administration and enhanced myocardial reperfusion. These findings are consistent with previous studies demonstrating that adenosine, due to its potent vasodilator and anti-inflammatory properties, helps in reducing microvascular obstruction during PCI, thereby improving perfusion outcomes and minimizing reperfusion injury [12-14].

Another significant observation was a significantly lower phenomenon of no-re-flow phenomenon in the adenosine group (6%) compared to the control group (24%) with statistically important (P=0.02). These findings suggests that the pre-stent intracoronary adenosine administration can play a preventive role against this complication, firmly associated with poor clinical outcomes, including large infarct size and high rate of heart failure and mortality. Reduction in no-re-flow cases aligns with pre-conclusion that adenosine improves capillary and reduces neutrophil-medial microvascular injury. These findings resemble an earlier study result [15].

Importantly, while the renal function parameters such as serum creatinine and estimated glomerular filtration rate (EGFR) did not show significant differences between groups, it supports renal protection of adenosine use, even in terms of acute STEMI management, where renal perfusion can be compromised [16]. Interestingly, the use of distal drug delivery via micro catheters was much higher in adenosine group (92%), compared to the control group (10%), with P <0.001. Although it increases the possibility of procedural impact on results, it can also reflect a targeted approach to the drug delivery optimized in the intervention group. However, the independent effect of the micro catheters makes a controlled evaluation to eliminate procedural bias [17].

No significant differences observed between the two groups in terms of angiographic characteristics such as culprit vessel involvement and thrombus burden. This parity eliminates anatomical bias and further strengthens the argument that the observed differences in flow grade and no-reflow prevalence are attributable to pharmacological intervention rather than anatomical or technical variables [18]. Stent-related parameters, thrombus aspiration, and wound preparation (pre-post-dilation) were also similar in groups, indicating that procedural standardization maintained and adenosine's effect was independent of mechanical intervention variables.

Together, these findings confirm the existing literature that suggests an intracoronary adenosine's favorable role in managing microvascular obstruction and improving spraying in STEMI patients passing through PCI. The stability of these results with prior studies combines the body of evidence supporting the inclusion of adenosine in the clinical protocol, especially in cases with angiographic suspicions of high thrombotic burden or no-perpetual risk [19, 20].

However, this study is not without limitations. Single-centers, relatively small sample size, and lack of long-term clinical results such as left ventricular function or major adverse cardiac events (MACE) limit the generality of the conclusions. Additionally, the significantly higher use of micro catheters in the adenosine group, while possibly protocol-driven, introduces a procedural variability that may act as a confounding factor.

CONCLUSION

This study provides strong evidence that intracoronary adenosine administered prior to stenting in STEMI patients significantly enhances coronary perfusion (as evidenced by higher TIMI III flow rates) and reduces the incidence of no-reflow without adversely affecting renal function or other procedural characteristics. These findings support the potential integration of adenosine into standardized PCI protocols, although larger multi-center trials with long-term follow-up are necessary to confirm its clinical benefit and cost-effectiveness.

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