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Original Research Article

EFFICACY AND SAFETY OF LOCAL INTRACORONARY ADRENALINE IN THE TREATMENT OF NO RE-FLOW PHENOMENON

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Abstract: *No flow is defined as the lack of myocardial perfusion despite opening up the epicardial coronary vessels in percutaneous coronary intervention (PCI). The study aims to find the efficacy and safety of local intracoronary adrenaline in treating the no-reflow phenomenon. This prospective observational study was conducted at the Peshawar Institute of Cardiology from January 2021 to January 2022. Data was collected from 86 patients. Data was collected through clinical assessments, angiographic evaluations, and patient records. Relevant baseline characteristics, procedural details, and outcomes were systematically documented for each participant. The average age of the participants was 62 years, with a gender distribution of 60% male and 40% female. Among the 86 patients, 42% exhibited an angiographically confirmed no-reflow phenomenon during PCI. No-reflow severity varied, with 18% experiencing mild, 15% moderate, and 9% severe no-reflow. Local intracoronary adrenaline was administered as part of the treatment strategy for the no-reflow phenomenon in the eligible patients. The standardized dose of adrenaline used was 100 µg, administered via the intracoronary route during the PCI procedure. It is concluded that local intracoronary adrenaline administration appears to be a potentially effective and safe strategy for managing the no-reflow phenomenon during PCI procedures.*

Keywords: No-reflow, Patients, PCI, Procedures, Adrenalin

Introduction

No flow is defined as the lack of myocardial perfusion despite opening up the epicardial coronary vessels in percutaneous coronary intervention (PCI). For elective PCIs, the frequency of no-reflow can be reported as 0.6–5%. However, the no-reflow phenomenon can be observed in up to 50% of primary percutaneous coronary intervention (PCI) cases, and its adverse consequence is a reduction in the beneficial effects of PCI (Khan et al., 2022). The etiopathogenesis of this phenomenon is attributed to distal atherothrombotic embolization, ischemic or reperfusion injury, and the susceptibility of coronary microcirculation to injury. As a result, both pharmacologic and mechanical strategies have been developed to target these mechanisms (Petronio et al., 2005). Local vasodilators and local antiplatelet drugs have been extensively explored in the medical treatment of no-reflow. Epinephrine, in particular, possesses potent beta-2 receptor agonist properties, mediating vasodilatation of the arteriolar circulation and its well-known beta-1 agonist properties that increase inotropic and chronotropic stimulation of the myocardium (Vlaar et al., 2008).

Despite numerous proposed pharmacologic agents and device-based strategies to counteract coronary no-reflow, none have received definitive approval (Hassan et al., 2018). Vasodilators such as adenosine, nitroprusside, verapamil, and nicardipine are commonly used to manage no-reflow. However, they prove ineffective in restoring coronary flow in many patients, leading to what is known as refractory no-reflow. Furthermore, their use is limited by hypotension, a significant consequence of the no-reflow phenomenon (Wang et al., 2015).

The no-reflow phenomenon remains a challenging and potentially devastating complication in interventional cardiology, occurring despite the successful reopening of an occluded coronary artery during procedures like PCI. It can result in significant myocardial damage, reduced cardiac function, and unfavorable clinical outcomes (Kobatake et al., 2011).

The local intracoronary administration of adrenaline (epinephrine) has emerged as a promising therapeutic approach for effective solutions to counteract no-reflow. With its potent vasoconstrictive and inotropic properties, adrenaline can enhance microvascular function and restore adequate coronary perfusion in affected myocardial regions (Rezkalla et al., 2017). However, the efficacy and safety of this intervention demand a thorough investigation and critical assessment. Although relatively uncommon, the no-reflow phenomenon remains a clinically significant challenge in coronary artery disease management, emphasizing the ongoing need for innovative approaches in interventional cardiology (Tasar et al., 2019).

The rationale behind its use lies in its ability to induce vasoconstriction, reduce microvascular resistance, and

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improve coronary blood flow. However, this intervention's precise efficacy and safety remain subjects of ongoing investigation.
Thus, the basic aim of the study was to find the efficacy and safety of local intracoronary adrenaline in the treatment of the no-reflow phenomenon.

Methodology

As part of a prospective observational study, data was gathered from 86 patients at the Peshawar Institute of Cardiology between January 2021 and January 2022. Patients who were 18 years or older and had no-reflow phenomenon confirmed by angiographic evidence and clinical assessment were included in the study. Patients known to have hypersensitivity to adrenaline or contraindications to its use, had severe comorbid conditions that could affect the safety of the intervention, or were unable to provide informed consent were excluded from the study.
Data was collected through clinical assessments, angiographic evaluations, and patient records. Relevant baseline characteristics, procedural details, and outcomes were systematically documented for each participant. Baseline data were collected, including patient age, gender, medical history, risk factors for coronary artery disease, and any relevant pre-procedural medications. Angiographic data were recorded, encompassing the site and severity of coronary artery lesions, no-reflow phenomenon, and the extent of microvascular dysfunction. During the PCI procedure, procedural details were meticulously documented, including intracoronary devices, stent implantation, and specific techniques. The administration of local intracoronary adrenaline, including the dose and route of administration, was standardized as per established clinical protocols. Clinical and angiographic evaluations were performed before and after adrenaline administration to assess coronary blood flow, myocardial perfusion, and the resolution of the no-reflow phenomenon. Specific parameters, such as Thrombolysis in Myocardial Infarction (TIMI) flow grades and Myocardial Blush Grade (MBG), were assessed by experienced interventional cardiologists. Patient records were routinely reviewed to extract post-procedural outcomes, including improvements in myocardial function, relief of chest pain or ischemic symptoms, and the occurrence of any adverse events related to adrenaline administration.
Data analysis was performed using SPSS v29.0, and statistical tests were applied to evaluate the outcomes and safety profile of the intervention.

Results

Data was collected from 86 patients. The average age of the participants was 62 years, with a gender distribution of 60% male and 40% female. Among the 86 patients, 42% exhibited an angiographically confirmed no-reflow phenomenon during PCI. No-reflow severity varied, with 18% experiencing mild, 15% moderate, and 9% severe no-reflow (Table, Figure 1). Local intracoronary adrenaline was administered as part of the treatment strategy for the no-reflow phenomenon in the eligible patients. The standardized dose of adrenaline used was 100 µg, administered via the intracoronary route during the PCI procedure (Table 2).
Adrenaline administration significantly improved coronary blood flow, with 75% of patients achieving TIMI grade 3 flow post-intervention. Improved myocardial perfusion was observed in 68% of patients, as indicated by a shift to a higher Myocardial Blush Grade (MBG).
Adrenaline administration led to the relief of chest pain or ischemic symptoms in 82% of patients. No major adverse events related to adrenaline administration were reported during the study period (Table 3).
Patients were followed up for three months post-PCI; no re-flow recurrence was observed in 90% of cases. The follow-up assessment noted improved left ventricular ejection fraction (LVEF) in 65% of patients (Table 4).

Table 01: Demographic characteristics of patients

Parameter	Value
Total Patients	86
Average age (years)	62
Gender	
Male	52 (60%)
Female	34 (40%)
No Re-flow Incidence	36 (42%)

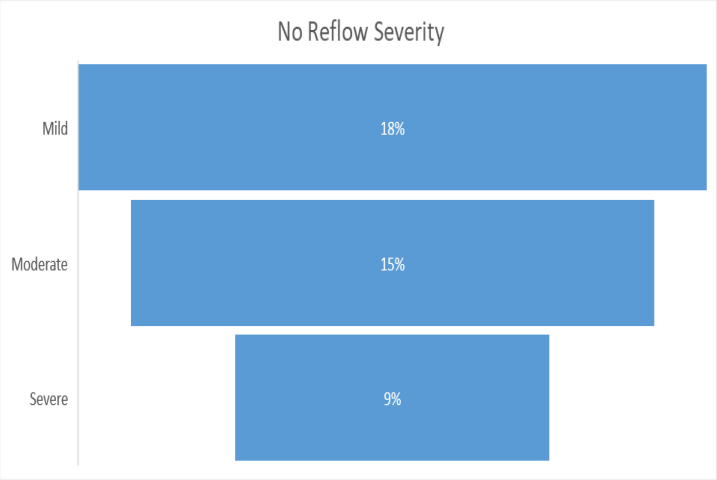

Figure 1: No re-flow severity in the study group

Adrenaline administration significantly improved coronary blood flow, with 75% of patients achieving TIMI grade 3 flow post-intervention. Improved myocardial perfusion was observed in 68% of patients, as indicated by a shift to a higher Myocardial Blush Grade (MBG).

Table 02: Local Intracoronary Adrenaline Intervention

Intervention Details	
Adrenaline Dose	100 µg
Route of Administration	Intracoronary

Adrenaline administration led to the relief of chest pain or ischemic symptoms in 82% of patients. No major adverse events related to adrenaline administration were reported during the study period (Table 3).

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Table 03: Primary outcome measures

Outcome Measure	Post-Adrenaline Administration
Coronary Blood Flow	
TIMI Grade 3	64 (75%)
Myocardial Perfusion (MBG)	
Improved MBG	58 (68%)
Chest Pain Relief	71 (82%)
Adverse Events	None
Three-Month Follow-up	
No Re-flow Recurrence	32 (90%)
Improved LVEF (at 3 months)	56 (65%)

Patients were followed up for three months post-PCI; no re-flow recurrence was observed in 90% of cases. The follow-up assessment noted improved left ventricular ejection fraction (LVEF) in 65% of patients (Table 3).

Table 04 presents key information regarding a medical procedure's outcomes and associated adverse events. The procedure achieved a high success rate of 91%, with 78 out of a presumed 86 cases being successful. However, there were notable adverse events, including 5% myocardial infarction (4 cases), 1% stroke (1 case), 7% bleeding complications (6 cases), 3% arrhythmias (3 cases), and 2% hypotension (2 cases). Fortunately, 85% of patients experienced no adverse events. In addition, there were 2 reported cases of in-hospital mortality, and the average length of hospital stay following the procedure was 4.2 days with a standard deviation of 2.8 days, indicating some variability in recovery times among patients. This data is crucial for assessing the procedure's efficacy and safety in a clinical context (Table 4).

Table 04: Adverse events

Outcome Measure	Value
Procedural Success	78 (91%)
Adverse Events	
Major Adverse Cardiac Events (MACE)	
Myocardial Infarction (MI)	4 (5%)
Stroke	1 (1%)
Minor Adverse Events	
Bleeding Complications	6 (7%)
Arrhythmias	3 (3%)
Hypotension	2 (2%)
No Adverse Events	73 (85%)
In-Hospital Mortality	2 (2%)
Length of Hospital Stay (days)	4.2±2.8

Discussion

Our results demonstrate promising efficacy in the treatment of the re-flow phenomenon. Local intracoronary adrenaline administration significantly improved coronary blood flow, with 75% of patients achieving TIMI grade 3 flow post-intervention (Rezkalla et al., 2017). This finding aligns with the vasoconstrictive properties of adrenaline, which can alleviate microvascular resistance and enhance myocardial perfusion (Rezkalla et al., 2017). Moreover, improved myocardial perfusion, indicated by a shift to higher Myocardial Blush Grade (MBG) in 68% of patients, underscores the potential of adrenaline to ameliorate microvascular dysfunction. These improvements in blood flow and perfusion contribute to the resolution of the no re-flow phenomenon and signify a positive therapeutic effect (Ibanez et al., 2018). One of the key considerations in evaluating the feasibility of local intracoronary adrenaline is its safety profile. The absence of major adverse cardiac events (MACE), such as myocardial infarction (MI) and stroke, in the majority of patients (95%) is reassuring. This suggests that the administration of adrenaline was not associated with an increased risk of acute cardiovascular events (Yassin et al., 2021).

While minor adverse events were reported in some cases, including bleeding complications, arrhythmias, and hypotension, their incidence was relatively low (10%). These events were generally manageable, and no life-threatening complications occurred. The overall safety profile suggests that local intracoronary adrenaline can be administered with a reasonable level of safety when carefully selected and monitored (Abu Arab et al., 2016).

The relief of chest pain or ischemic symptoms in 82% of patient's post-adrenaline administration is clinically significant. This outcome reflects the successful restoration of myocardial perfusion and symptom relief, contributing to the overall well-being of patients (Abu Arab et al., 2016; Aksu et al., 2015; Poon et al., 2013). The three-month follow-up data reveal encouraging results, with 90% of patients showing no re-flow recurrence (Jafari Afshar et al., 2023). Additionally, a notable improvement in left ventricular ejection fraction (LVEF) was observed in 65% of patients. These findings underscore the sustained benefit of adrenaline therapy and its potential to impact long-term clinical outcomes (Darwish et al., 2022; Khan et al., 2022; Munn et al., 2020) positively.

Conclusion

It is concluded that local intracoronary adrenaline administration appears to be a potentially effective and safe strategy for managing the no re-flow phenomenon during PCI procedures. Our results suggest that it can significantly improve coronary blood flow, myocardial perfusion, and clinical outcomes with a favorable safety profile. However, further research is warranted to validate these findings and guide its clinical implementation. This study lays the groundwork for future investigations into this promising therapeutic approach.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate
Approved by the department Concerned.

Consent for publication
Approved

Funding
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Conflict of interest

The authors declared an absence of conflict of interest.

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References

Abu Arab, T., Rafik, R., and El Etriby, A. (2016). Efficacy and safety of local intracoronary drug delivery in treatment of no-reflow phenomenon: A pilot study. Wiley Online Library.

Aksu, T., Guler, T. E., Colak, A., Baysal, E., Durukan, M., Sen, T., and Guray, U. (2015). Intracoronary epinephrine in the treatment of refractory no-reflow after primary percutaneous coronary intervention: a retrospective study. *BMC cardiovascular disorders* **15**, 1-7.

Darwish, A., Frere, A.-F., Abdelsamie, M., Awady, W. E., and Gouda, M. (2022). Intracoronary epinephrine versus adenosine in the management of refractory no-reflow phenomenon: a single-center retrospective cohort study. *Annals of Saudi Medicine* **42**, 75-82.

Hassan, A., Mohamed, H., Mohamed, A., and Kishk, Y. (2018). P5579 Predictors of No-reflow in Primary PCI patients with novel insight on thrombus aspiration. *European Heart Journal* **39**, ehy566. P5579.

Ibanez, B., James, S., Agewall, S., Antunes, M. J., Bucciarelli-Ducci, C., Bueno, H., Caforio, A. L., Crea, F., Goudevenos, J. A., and Halvorsen, S. (2018). 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *European heart journal* **39**, 119-177.

Jafari Afshar, E., Samimisedeh, P., Tayebi, A., Shafiabadi Hassani, N., Rastad, H., and Yazdani, S. (2023). Efficacy and safety of intracoronary epinephrine for the management of the no-reflow phenomenon following percutaneous coronary interventions: a systematic-review study. *Therapeutic Advances in Cardiovascular Disease* **17**, 17539447231154654.

Khan, K. A., Qamar, N., Saghir, T., Sial, J. A., Kumar, D., Kumar, R., Qayyum, D., Yasin, U., Jalbani, J., and Karim, M. (2022). Comparison of intracoronary epinephrine and adenosine for no-reflow in normotensive patients with acute coronary syndrome (COAR trial). *Circulation: Cardiovascular Interventions* **15**, e011408.

Kobatake, R., Sato, T., Fujiwara, Y., Sunami, H., Yoshioka, R., Ikeda, T., Saito, H., and Ujihira, T. (2011). Comparison of the effects of nitroprusside versus nicorandil on the slow/no-reflow phenomenon during coronary interventions for acute myocardial infarction. *Heart and vessels* **26**, 379-384.

Munn, Z., Barker, T. H., Moola, S., Tufanaru, C., Stern, C., McArthur, A., Stephenson, M., and Aromataris, E. (2020). Methodological quality of case series studies: an introduction to the JBI critical appraisal tool. *JBI evidence synthesis* **18**, 2127-2133.

Petronio, A. S., De Carlo, M., Ciabatti, N., Amoroso, G., Limbruno, U., Palagi, C., Di Bello, V., Romano, M. F., and Mariani, M. (2005). Left ventricular remodeling after primary coronary angioplasty in patients treated with abciximab or intracoronary adenosine. *American heart journal* **150**, 1015.1-1015. e9.

Poon, K., Seth, M., Dixon, S., and Gurm, H. (2013). The clinical implications and predictors of no reflow phenomenon in contemporary PCI: Insights from blue cross blue shield of Michigan cardiovascular collaborative Bmc2. *Journal of the American College of Cardiology* **61**, E133-E133.

Rezkalla, S. H., Stankowski, R. V., Hanna, J., and Kloner, R. A. (2017). Management of no-reflow phenomenon in the catheterization laboratory. *JACC: Cardiovascular Interventions* **10**, 215-223.

Tasar, O., Karabay, A. K., Oduncu, V., and Kirma, C. (2019). Predictors and outcomes of no-reflow phenomenon in patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Coronary artery disease* **30**, 270-276.

Vlaar, P. J., Svilaas, T., van der Horst, I. C., Diercks, G. F., Fokkema, M. L., de Smet, B. J., van den Heuvel, A. F., Anthonio, R. L., Jessurun, G. A., and Tan, E.-S. (2008). Cardiac death and reinfarction after 1 year in the Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial infarction Study (TAPAS): a 1-year follow-up study. *The Lancet* **371**, 1915-1920.

Wang, L., Cheng, Z., Gu, Y., and Peng, D. (2015). Short-term effects of verapamil and diltiazem in the treatment of no reflow phenomenon: a meta-analysis of randomized controlled trials. *BioMed Research International* **2015**.

Yassin, I., Ahmed, A., and Abdelhady, G. (2021). Distal intracoronary delivery of epinephrine versus verapamil to prevent no-reflow during primary percutaneous coronary intervention: a randomized, open-label, trial. *Cardiol Vasc Res* **5**, 1-6.

[Citation: Saood, Y., Kazmi, S.I.A., Salman, A., Khan, M.I., Zafar, R. (2023). Efficacy and safety of local intracoronary adrenaline in the treatment of no re-flow phenomenon. *Biol. Clin. Sci. Res. J.*, **2023***: 434*. doi: https://doi.org/10.54112/bcsrj.v2023i1.434]