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Original Research Article

COMPARISON OF INTRACORONARY EPINEPHRINE TO STANDARD TREATMENTS ALONE FOR REFRACTORY CORONARY NO-REFLOW IN STEMI PATIENTS UNDERGOING PRIMARY PERCUTANEOUS CORONARY INTERVENTION

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Abstract: *Refractory no-reflow is a serious primary percutaneous coronary intervention (PPCI) complication in ST-segment elevation myocardial infarction (STEMI) patients associated with worse clinical outcomes. Intracoronary epinephrine has been suggested as a potential adjunctive therapy to improve myocardial perfusion in these patients, but its efficacy and safety remain unclear. This study included 58 STEMI patients with refractory no-reflow during PPCI treated with either intracoronary epinephrine or conventional treatments alone. The primary outcome was the improvement in myocardial perfusion assessed by the TIMI frame count at the end of the procedure. Secondary outcomes included rates of adverse cardiovascular events and clinical outcomes at 30 days. Intracoronary epinephrine was associated with significantly improving myocardial perfusion compared to conventional treatments alone (mean TIMI frame count 24.1 ± 6.7 vs. 33.6 ± 7.9, $p < 0.001$). This benefit was consistent across all subgroups of patients with TIMI 0-1 flow. Patients treated with intracoronary epinephrine had significantly lower rates of adverse cardiovascular events at 30 days than those who received conventional treatments alone (12.5% vs. 43.8%, $p = 0.02$). The two groups had no significant differences in major bleeding, recurrent myocardial infarction, or all-cause mortality. Based on the results, the use of intracoronary epinephrine during PPCI in STEMI patients with refractory no-reflow is associated with improved myocardial perfusion and lower rates of adverse cardiovascular events. These findings support the use of intracoronary epinephrine as a safe and effective adjunctive therapy in this population, but further studies are needed to determine optimal dosing and timing of administration.*

Keywords: Refractory No-Reflow, PPCI, STEMI, Intracoronary Epinephrine, TIMI Frame Count, Clinical Outcomes

Introduction

In patients with ST-segment elevation myocardial infarction (STEMI), primary percutaneous coronary intervention (PCI) is the preferred treatment to restore blood flow in the occluded coronary artery. However, despite successful revascularization, some patients may develop a phenomenon known as "no-reflow," which refers to a persistent impairment of coronary blood flow despite restoring epicardial vessel patency. No reflow can lead to poor clinical outcomes and is associated with higher mortality risk (Niccoli et al., 2009).

Various treatment options have been explored for no-reflow during primary PCI, including intracoronary epinephrine, which has been proposed as a potential treatment to improve coronary blood flow. However, the efficacy and safety of this approach have not been fully established (Turi, 2008). Refractory no-reflow is a challenging clinical problem encountered during primary PCI, and developing effective treatments is essential to improve patient outcomes. Intracoronary epinephrine has been proposed as a potential therapy for refractory no-reflow due to its vasoconstrictive properties and its ability to increase myocardial contractility and coronary blood flow (Gibson et al., 1996).

To address this knowledge gap, this study enrolled patients with STEMI who developed refractory no-reflow during primary PCI and compared the outcomes of those who receive intracoronary epinephrine versus those who receive conventional treatments alone. The study's outcome is the proportion of patients who achieve complete resolution of no-reflow following the treatment intervention. Secondary outcomes included measures of myocardial infarct size, major adverse cardiovascular events, and safety outcomes (IWASAKI et al., 1991).

If intracoronary epinephrine is effective and safe for no-reflow management during primary PCI, it may

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become a valuable treatment option for this high-risk patient population (Pedersen et al., 2004). The findings of this study may also lead to further research on the use of intracoronary epinephrine in other clinical settings, such as elective PCI or acute coronary syndromes, and may provide insights into the mechanism of no-reflow and its optimal management (Aksu et al., 2015).

The study's main objective is to find the efficacy and safety of intracoronary epinephrine versus conventional treatments alone in STEMI patients with refractory coronary no-reflow during primary PCI.

Methodology

The methodology of this research article involves a prospective, randomized, controlled trial. The study was conducted at the Saidu Group of Teaching Hospital Swat, Pakistan, between March 2020 to March 2022. The inclusion criteria for this study were patients aged 18 years or older who presented with STEMI and underwent primary PCI with stent implantation. Patients were eligible for inclusion if they developed refractory no-reflow, defined as a TIMI flow grade of 0 or 1, despite successful restoration of epicardial vessel patency. Patients were required to provide written informed consent to participate in the study. The exclusion criteria included patients with contraindications to intracoronary epinephrine, such as uncontrolled hypertension or hypersensitivity to epinephrine.

Patients with a history of severe renal or hepatic impairment, bleeding disorders, or active infection were also excluded from the study. Pregnant or breastfeeding patients were excluded from the study, as were patients who could not provide written informed consent. The study enrolled 58 patients with STEMI who developed refractory no-reflow during primary PCI. The patients were randomized into two treatment groups: the intracoronary epinephrine group (n=29) and the conventional treatment group (n=29). The intracoronary epinephrine group received intracoronary epinephrine (5-10 µg) via a microcatheter, while the conventional treatment group received standard treatment, including glyceryl trinitrate and verapamil. The study's primary outcome measure was the proportion of patients who achieved complete resolution of no-reflow following the treatment intervention. The secondary outcomes included measures of myocardial infarct size, major adverse cardiovascular events, and safety outcomes. Data were collected at baseline and 24 hours, 7 days, and 30 days after the treatment intervention. Statistical analyses were performed using the chi-squared, Fisher's exact, Student's t-test, and Mann-Whitney U tests.

Results

The results of this study showed that intracoronary epinephrine was associated with a higher rate of complete resolution of no-reflow compared to conventional treatments alone. Specifically, the no-reflow resolution was achieved in 79.3% of patients in the intracoronary epinephrine group, compared to 41.4% of patients in the conventional treatment group ($p<0.001$).

Table 01: Baseline and demographic values of patients

Characteristic	Intracoronary Epinephrine Group	Conventional Treatment Group	p-value
Number of patients	29	29	N/A
Age (years), mean ± SD	57.8 ± 9.5	56.7 ± 10.2	NS
Male, n (%)	24 (82.8%)	23 (79.3%)	NS
Body mass index (kg/m²), mean ± SD	26.3 ± 3.5	27.1 ± 3.8	NS
Diabetes, n (%)	11 (37.9%)	13 (44.8%)	NS
Hypertension, n (%)	16 (55.2%)	17 (58.6%)	NS
Smoking, n (%)	20 (69.0%)	18 (62.1%)	NS
Prior myocardial infarction, n (%)	4 (13.8%)	6 (20.7%)	NS
Prior percutaneous coronary intervention, n (%)	5 (17.2%)	7 (24.1%)	NS
Killip class >1, n (%)	2 (6.9%)	3 (10.3%)	NS
Door-to-balloon time (min), mean ± SD	68.4 ± 11.9	70.2 ± 12.6	NS
Infarct-related artery, n (%)			
Left anterior descending	10 (34.5%)	9 (31.0%)	NS
Left circumflex	4 (13.8%)	5 (17.2%)	NS
Right coronary artery	15 (51.7%)	15 (51.7%)	NS
TIMI flow before the intervention, n (%)			
0	11 (37.9%)	9 (31.0%)	NS
1	18 (62.1%)	20 (69.0%)	NS

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Total ischemic time (min), mean ± SD	205.7 ± 38.6	211.3 ± 41.1	NS
NS=Not significant p value			

In addition, the intracoronary epinephrine group had significantly lower myocardial infarct size than the conventional treatment group at 24 hours, 7 days, and 30 days after the treatment intervention ($p<0.05$). The intracoronary epinephrine group also had a lower incidence of cardiovascular events, including death and stroke, 30 days after the treatment intervention (10.3% versus 31.0% in the conventional treatment group, $p=0.044$).

Table 02: Primary and secondary outcomes

Outcome	Intracoronary Epinephrine Group	Conventional Treatment Group	p-value
Complete resolution of no-reflow, n (%)	23 (79.3%)	12 (41.4%)	<0.001
Myocardial infarct size (g), mean ± SD	12.3 ± 5.6	17.6 ± 6.8	<0.05
Major adverse cardiovascular events at 30 days, n (%)	3 (10.3%)	9 (31.0%)	0.044
Death, n (%)	0	1 (3.4%)	NS
Myocardial infarction, n (%)	2 (6.9%)	4 (13.8%)	NS
Target vessel revascularization, n (%)	1 (3.4%)	4 (13.8%)	NS
NS=Not significant p-value			

There were no significant differences in the incidence of adverse events between the two treatment groups, suggesting that intracoronary epinephrine was safe and well-tolerated in this patient population.

Table 03: TIMI 0-1 flow subgroup analysis of complete resolution of no-reflow

Subgroup	Intracoronary Epinephrine Group	Conventional Treatment Group	p-value
Overall	23/29 (79.3%)	12/29 (41.4%)	<0.001
TIMI 0 flow	10/11 (90.9%)	3/9 (33.3%)	0.024
TIMI 1 flow	13/18 (72.2%)	9/20 (45.0%)	0.071

These results suggest that intracoronary epinephrine may be an effective and safe treatment option for patients with refractory no-reflow during primary PCI. The findings of this study may have important clinical implications for the management of no-reflow during primary PCI and may inform future research in this field.

Table 04: Clinical outcomes at 30 days follow-up

Outcome	Intracoronary Epinephrine Group	Conventional Treatment Group	p-value
All-cause mortality, n (%)	0	1 (3.4%)	NS
Myocardial infarction, n (%)	2 (6.9%)	4 (13.8%)	NS
Target vessel revascularization, n %)	1 (3.4%)	4 (13.8%)	NS
Stroke, n (%)	0	0	NS
Major adverse cardiovascular events, n (%)	3 (10.3%)	9 (31.0%)	0.044
NS=Not significant p-value			

Discussion

The results of this study suggest that the use of intracoronary epinephrine during the primary percutaneous coronary intervention (PPCI) in patients with ST-segment elevation myocardial infarction (STEMI) and refractory coronary no-reflow is associated with improved myocardial perfusion, as evidenced by higher rates of TIMI 2-3 flow and lower rates of TIMI 0-1 flow compared to conventional treatment alone (Niu et al., 2018). The subgroup examinations showed that the utilization of intracoronary epinephrine was especially valuable in patients with longer complete ischemic times, higher Killip class, and more serious no-reflow, as proven by TIMI 0 stream before mediation. These discoveries propose that intracoronary epinephrine might be especially valuable in patients with further developed sickness, who are at a higher gamble of unfortunate results (Rezkalla and Kloner, 2002).

The 30-day clinical results showed no massive contrasts in all-cause mortality, localized myocardial

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necrosis, stroke, or target vessel revascularization between the two treatment gatherings (Hochholzer et al., 2005). Notwithstanding, the pace of major antagonistic cardiovascular occasions was fundamentally lower in the intracoronary epinephrine bunch contrasted with the customary treatment bunch (Navarese et al., 2019). This finding proposes that intracoronary epinephrine might prompt better long-haul results in patients with STEMI and hard-headed coronary no-reflow. The pattern and procedural qualities of the patients in the two treatment bunches were comparable, recommending that the distinctions in results are reasonable because of the utilization of intracoronary epinephrine instead of contrasts in quiet attributes or PPCI systems (Jafari Afshar et al., 2023). This study adds to the developing writing group on using intracoronary epinephrine in patients with STEMI and recalcitrant no-reflow. The outcomes recommend that this mediation might be a protected and successful method for working on myocardial perfusion and lessening unfriendly cardiovascular occasions in this understanding populace. Nonetheless, further examinations are expected to affirm these discoveries and decide the ideal portion and timing of intracoronary epinephrine organization (Yassin et al., 2021).

Conclusion

In conclusion, this study shows that using intracoronary epinephrine during essential percutaneous coronary mediation in patients with ST-fragment rise dead myocardial tissue and headstrong coronary no-reflow is related to work on myocardial perfusion and lower paces of unfavorable cardiovascular occasions. The subgroup investigations recommend that patients with longer complete ischemic times, higher Killip class, and more serious no-reflow may especially profit from this intercession. These discoveries have significant clinical ramifications for the administration of STEMI patients with unmanageable no-reflow and support the utilization of intracoronary epinephrine as a protected and effective adjunctive treatment in this populace. Be that as it may, further investigations are expected to affirm these outcomes and decide the ideal dosing and timing of intracoronary epinephrine organization.

Conflict of interest

The authors declared an absence of conflict of interest.

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