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Original research article

COMPARISON OF INTRAVENOUS TIROBAN AND INTRACORONARY TIRO BAN IN TERMS OF ADVERSE CARDIAC EVENTS AND CEREBROVASCULAR ACCIDENTS

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Abstract: *Patients with acute coronary syndrome (ACS) and a high thrombus burden undergoing percutaneous coronary intervention (PCI) are at risk for major adverse cardiac events (MACE) and cerebrovascular complications. Tirofiban, a glycoprotein IIb/IIIa inhibitor, is used to reduce thrombus burden, with administration routes (intracoronary vs. intravenous) potentially influencing outcomes. Limited data exist comparing the effects of intracoronary and intravenous administration of tirofiban on adverse cardiac and cerebrovascular events in these high-risk patients* ***Objective:*** *To compare intravenous tiroban and intracoronary tiroban in terms of adverse cardiac events and cerebrovascular accidents.* ***Methods:*** *A randomized controlled trial was conducted on eighty patients aged ≥ 40 years with ACS and high thrombus burden scheduled for PCI were randomized, with 40 patients receiving intracoronary tirofiban (Group A) and 40 receiving intravenous tirofiban (Group B). Group A received a bolus of tirofiban (10 µg/kg) directly at the thrombus site during PCI, followed by a 24-hour intravenous infusion (0.15 µg/kg/min). Group B received the same bolus dose intravenously, followed by an identical infusion protocol. MACE and cerebrovascular accidents were compared in both groups.* ***Results:*** *MI occurred in 5 patients (12.5%) in Group A while 6 patients (15.0%) in Group B (p=0.74). Repeat revascularization was required in 8 patients (20.0%) in Group A and 5 patients (12.5%) in Group B (p=0.36). Cerebrovascular events occurred in 4 patients (10.0%) in Group A and 7 patients (17.5%) in Group B (p=0.33).* ***Conclusion:*** *Both intracoronary and intravenous tirofiban administration result in comparable outcomes regarding MACE and cerebrovascular events in patients undergoing PCI with a high thrombus burden.*

Keywords: Tirofiban, intracoronary, intravenous, percutaneous coronary intervention, myocardial infarction, revascularization, cerebrovascular events, randomized controlled trial.

Introduction

One of the main causes of morbidity and death globally is acute coronary syndrome (ACS), which includes a variety of clinical disorders such as unstable angina, non-ST elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI). Antiplatelet therapy is the cornerstone of ACS management since it reduces thrombotic occlusions, especially during procedures like percutaneous coronary interventions (PCI). Given that cardiovascular disease stands as the leading cause of mortality in the US, it is common for interventional studies to concentrate on this area (1, 2). In certain trials, a four-point MACE has been utilised, particularly when hospitalisation for angina that is unstable or revascularisation treatments are factored in. This is further detailed by the five-point MACE, which encompasses heart failure (HF) (3).

The delay in intervention following an acute event leads to an increased clot burden, which can result in the clot breaking into smaller fragments that obstruct the distal artery (4). Techniques such as thrombus aspiration and the application of glycoprotein inhibitors can effectively prevent vasospasm and distal embolisation during interventions (5). Glycoprotein inhibitors, in conjunction with additional platelet inhibitors and medications, reduce infarct expansion, mitigate small vessel damage, and enhance circulation. This enhances blood circulation in the affected artery, thereby improving prognosis (6). Several Glycoprotein inhibitors exist, including tirofiban, and eptifibatide, which are available as monoclonal antibodies as well as small molecules (7). The standard methods for administration include intravenous along with intracoronary injections. A high dose of tirofiban can inhibit platelet activity by as much as 95 percent, demonstrating its effectiveness comparable to the competitive drug within the studies (7).

Multiple previous studies suggest that the combination of other medications with Glycoprotein inhibitors during primary percutaneous coronary intervention leads to improved coronary circulation, reduced mortality, and fewer instances of recurrent myocardial infarctions reported (8). Tirofiban is utilised to prevent thrombotic events following PCI and aids in the management of ACS (9). Administering intracoronary tirofiban enhances the inhibition of GP IIb/IIIa receptors more effectively compared to the intravenous route. Administering this drug intracoronary is thought to improve prognosis because of its elevated concentration in the coronary arteries (10).

This comparison is crucial for evaluating the effectiveness of the two administration routes in preventing stent

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thrombosis, reinfarction, and other thrombotic complications. It also allows for an assessment of the safety trade-offs concerning adverse cardiac events and cerebrovascular accidents, aiming to refine treatment strategies tailored to individual patient factors like thrombus burden, coronary anatomy, and bleeding risk.

Methodology

This study was conducted as a randomized controlled trial in the cardiology department of RMI, Peshawar from August 2023 to August 2024 after taking ethical approval from the hospital.

Participants were recruited based on predefined inclusion and exclusion criteria. Eligible patients included adults aged ≥ 40 years diagnosed with ACS and scheduled for PCI due to high thrombus burden confirmed by angiographic assessment. Patients were excluded if they presented with hemodynamic instability or cardiogenic shock, had known contraindications to tirofiban, experienced a recent stroke or transient ischemic attack (within the last six months), had a history of major bleeding disorders or active bleeding, suffered from severe renal or hepatic dysfunction, or received tirofiban within the previous 30 days.

Once eligibility was confirmed, patients were randomized in a 1:1 ratio to receive either intracoronary or intravenous tirofiban. Randomization was implemented using a blocked randomization. Patients in the intracoronary group received an initial bolus of tirofiban (10 µg/kg) administered directly into the coronary artery at the site of the thrombus during PCI. This was followed by an intravenous infusion of tirofiban at a maintenance dose (0.15 µg/kg/min) for 24 hours post-procedure. Patients in the intravenous group received the same initial bolus dose (10 µg/kg) administered intravenously, followed by an intravenous infusion at the same maintenance dose (0.15 µg/kg/min) for 24 hours. Patients were followed for a period of 30 days post-PCI for major adverse cardiac events (MACE) and cerebrovascular accidents.

Statistical analysis was conducted on an intention-to-treat basis, including all randomized patients in the analysis. Categorical variables, such as the incidence of MACE and cerebrovascular events, were compared between groups using the chi-square test or Fisher's exact test, as appropriate keeping the value of P significant at < 0.05.

Results

Our results show that the mean age in Group A (Intracoronary) was 44.5 ± 2.9 years, while in Group B (Intravenous), it was 46.35 ± 4.47 years. Gender distribution was comparable, with males representing 24 (60.0%) in Group A and 26 (65.0%) in Group B, with a p-value of 0.64. Among comorbid conditions, diabetes was observed in 19 (47.5%) of Group A and 13 (32.5%) of Group B patients, yielding a p-value of 0.17. Hypertension was present in 15 (37.5%) of Group A and 10 (25.0%) of Group B, with a p-value of 0.22. Previous myocardial infarction (MI) was reported in 12 (30.0%) of Group A and 8 (20.0%) of Group B, with a p-value of 0.30.

For CVA stroke, there was one incident (2.5%) in Group A and three incidents (7.5%) in Group B, with a p-value of 0.30. TIA occurred in two patients (5.0%) in Group A and three patients (7.5%) in Group B, with a p-value of 0.64. RIND was observed in one patient (2.5%) in Group A and two patients (5.0%) in Group B, with a p-value of 0.55. Hemorrhagic events were rare, with no cases (0.0%) in Group A and one case (2.5%) in Group B, yielding a p-value of 0.31.

In terms of major adverse cardiac events (MACE), revascularization was performed in eight patients (20.0%) in Group A and five patients (12.5%) in Group B, with a p-value of 0.36. MI occurred in five patients (12.5%) in Group A and six patients (15.0%) in Group B, with a p-value of 0.74. Total cerebrovascular events, including CVA stroke, TIA, and RIND, were observed in four patients (10.0%) in Group A and seven patients (17.5%) in Group B, with a p-value of 0.33.

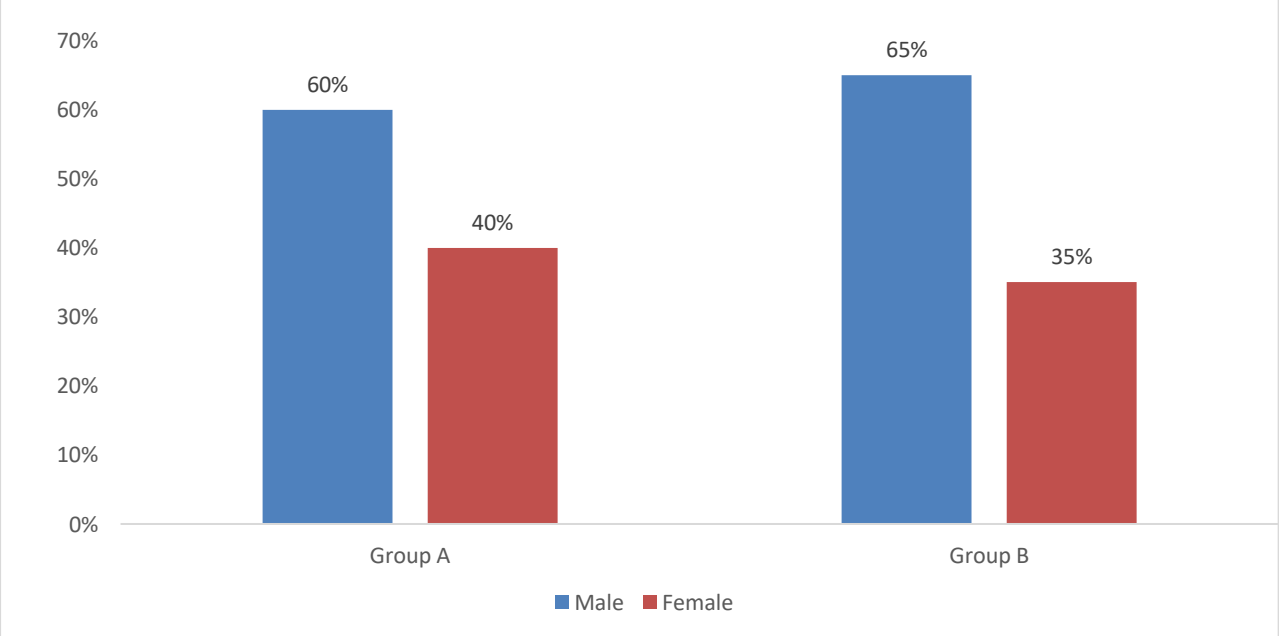

Figure 1 Gender distribution

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Table 1 Baseline characteristics

Baseline characteristics		Groups				P value
		Group A (Intracoronary)		Group B (Intravenous)		
		N	%	N	%	
Gender	Male	24	60.0%	26	65.0%	0.64
	Female	16	40.0%	14	35.0%	
Diabetes	Yes	19	47.5%	13	32.5%	0.17
	No	21	52.5%	27	67.5%	
Hypertension	Yes	15	37.5%	10	25.0%	0.22
	No	25	62.5%	30	75.0%	
Previous MI	Yes	12	30.0%	8	20.0%	0.30
	No	28	70.0%	32	80.0%	

Table 2 Cerebrovascular accident

Cerebrovascular Accident		Groups				P value
		Group A (Intracoronary)		Group B (Intravenous)		
		N	%	N	%	
Cerebrovascular Accident stroke	Yes	1	2.5%	3	7.5%	0.30
	No	39	97.5%	37	92.5%	
TIA	Yes	2	5.0%	3	7.5%	0.64
	No	38	95.0%	37	92.5%	
RIND	Yes	1	2.5%	2	5.0%	0.55
	No	39	97.5%	38	95.0%	
Hemorrhage	Yes	0	0.0%	1	2.5%	0.31
	No	40	100.0%	39	97.5%	

Table 3 Major Adverse Cardiac Events (MACE)

MACE		Groups				P value
		Group A (Intracoronary)		Group B (Intravenous)		
		N	%	N	%	
Revascularization	Yes	8	20.0%	5	12.5%	0.36
	No	32	80.0%	35	87.5%	
MI	Yes	5	12.5%	6	15.0%	0.74
	No	35	87.5%	34	85.0%	
Cerebrovascular Events	Yes	4	10.0%	7	17.5%	0.33
	No	36	90.0%	33	82.5%	

Discussion

Patient demographics and baseline characteristics in our study, such as age, gender distribution, and prevalence of comorbid conditions (diabetes, hypertension, and previous myocardial infarction [MI]), were similar between the two groups. This balance minimizes confounding factors and enhances the reliability of outcome comparisons. In the study by Bukhari SHR et al., the groups were similarly well-matched, with no significant baseline differences observed between the intracoronary and intravenous groups, which strengthens the comparability of results. (11) This congruence with our results supports a well-controlled comparison of outcomes between the two routes.

Regarding MACE, both our study and the studies by Bukhari SHR et al. and Tang X et al. indicated similar frequencies of MI and revascularization events across the two groups. (11, 12) Bukhari et al. found no significant differences in MI or revascularization rates between the intracoronary and intravenous tirofiban groups, with p-values above 0.05, supporting a lack of statistically significant differences between the groups. Our study reflected these findings, with both groups experiencing equivalent rates of revascularization and MI events, suggesting that the administration route may not markedly influence these particular outcomes. This observation aligns with previous research, indicating that while glycoprotein IIb/IIIa inhibitors like tirofiban reduce thrombotic events effectively, the specific route of administration may not drastically alter this effect in PCI patients.

Cerebrovascular events, including ischemic stroke, transient ischemic attack (TIA), and reversible ischemic neurological deficit (RIND), were also observed at similar rates across both groups in our study and the studies by Bukhari SHR et al. and Tang X et al. (11, 12) Our study indicated a slight increase in cerebrovascular incidents in the intravenous group compared to the intracoronary group, though this difference was not statistically significant ($p > 0.05$). This was corroborated by Bukhari SHR et al., who similarly reported no significant differences in cerebrovascular events across groups, underscoring the comparable safety

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profiles of both administration methods. (11) Although minor variations were noted, such as a marginally higher rate of TIA in the intravenous group, these were not substantial enough to suggest a clinical difference. This reinforces the notion that either administration route can be used without concern for increased cerebrovascular risks.
The overall MACE totals, encompassing revascularization, MI, and cerebrovascular events, further emphasize the similarity between intracoronary and intravenous tirofiban administration in high-risk PCI patients. In both our study and the studies by Bukhari SHR et al. and Tang X et al., the MACE totals were nearly identical, with p-values indicating no statistically significant differences between groups. (11, 12) This finding supports the conclusion that intracoronary tirofiban does not offer substantial clinical advantages over intravenous tirofiban for reducing cumulative MACE incidents. However, it's worth noting that studies such as Tang X et al. suggest that intracoronary administration may yield improvements in TIMI flow and myocardial perfusion, implying potential benefits for certain patient subpopulations or situations where targeted drug delivery to the coronary arteries is beneficial. (12)

Conclusion

We conclude that intracoronary and intravenous tirofiban administration results in comparable outcomes regarding MACE and cerebrovascular events in patients undergoing PCI with a high thrombus burden. Either route may be suitable, with selection based on clinical discretion.

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. (IRBEC-TCK-02/23)
Consent for publication
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Conflict of interest

The authors declared an absence of conflict of interest.

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Concept & Design of Study

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