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Original Article

Comparison of Intracoronary Tirofiban And Intravenous Tirofiban for Major Adverse Cardiac Events and Cerebrovascular Accident

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ABSTRACT

Major Adverse Cardiovascular Events (MACE) and and Cerebrovascular Accidents (CVA) have become primary areas of interest due to the ongoing focal research in cardiovascular diseases. **Objective:** To assess the frequency of major adverse cardiac events and cerebrovascular accidents for intracoronary tirofiban and intravenous tirofiban. **Methods:** It was a comparative study conducted at the Punjab Institute of Cardiology, Lahore from March 2019 to March 2020. A total of 250 patients of both genders, aged between 20 to 65 years were enrolled in this study who had STEMI and have high thrombus burden or TIMI flow grade < 3 during primary PCI. They were divided into two groups namely intracoronary tirofiban group and intravenous tirofiban. The impact of intracoronary tirofiban versus intravenous tirofiban outcomes were assessed. **Results:** Statistically insignificant difference in MACE (myocardial infarction, cerebrovascular accident & revascularization) between intracoronary & intravenous tirofiban groups was noted. The frequency distribution for cerebrovascular accidents (CVA) showed that haemorrhage was found similar in both groups. Ischemic stroke, in patients of the intracoronary tirofiban group compared with intravenous tirofiban group, was 1 (0.8%) vs 3 (2.4%) with p-value 0.348 respectively. Reversible ischemic neurological deficit (RIND) was found in 3 (2.4%) in the intracoronary and 4 (3.2%) in the intravenous group. Transient ischemic attack (TIA) found in the intracoronary was 8(6.4%) whereas in the intravenous group was 9 (7.2%). **Conclusions:** The results of our study make us conclude that tirofiban when given intracoronary or intravenous does not show any significant difference for major adverse cardiac events and cerebrovascular accidents.

INTRODUCTION

Since cardiovascular disease is the primary cause of death in the US, interventional research frequently focuses on it [1]. As a result, "major adverse cardiovascular events" (MACE) composite endpoint is becoming a more popular primary outcome of interest. Guidelines for the use of a three-point MACE outcome, comprising myocardial infarction (MI), stroke (cerebrovascular accident), and cardiovascular mortality, were issued by the US Food and Drug Administration (FDA) in 2008 and the European Medicines Agency (EMA) in 2012 for all trials assessing the cardiovascular safety of diabetic agents [2]. A four-point MACE has also been used in some trials [3], when hospitalization for unstable angina or revascularization treatments is included. This is further elaborated upon by five-point MACE, which includes heart failure (HF). The application of MACE is becoming a more well recognized and common endpoint among randomized controlled trials [4]. ST-elevation myocardial infarction (STEMI) is a pro-thrombotic state in which excessive platelets are activated. Complete cessation of platelet activity is the main goal of treatment. Aspirin and clopidogrel are considered as standard treatment to cease platelet

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function [5]. Some patients may develop clopidogrel resistance that does not stop the platelet function properly during intervention [6]. When the platelet activity is ceased efficiently, the myocardial damage will be less and the prognosis will be better. Glycoprotein inhibitors (GPIs) are used during percutaneous coronary intervention (PCI) as class IIa recommendation since 2004 [7]. The term "heart attack" refers to myocardial infarction (MI), which is the result of reduced or stopped blood supply to a section of the myocardium. An MI could be "silent," going unnoticed, or it could be a catastrophic occurrence that results in hemodynamic decline and abrupt death. Myocardial infarction (MI) can cause huge clot in culprit artery. Immediate stenting after MI is best possible treatment that leads to better outcome of the patients [8]. With the delayed intervention after acute event the chances of clot burden increases and causes the clot to break into small pieces and blocks the distal artery [9]. The vasospasm and distal embolization can be prevented by some techniques used during intervention like thrombus aspiration and use of glycoprotein IIb/IIIa inhibitors [10]. GPIs along with other platelet inhibitors and drugs that decrease the inflammation during MI decrease the infarct expansion, small vessel damage and improve circulation. This improve blood circulation in culprit artery by all these means improves prognosis [11]. It was observed that glycoprotein IIb/IIIa inhibitors (GPIs) improve Major Adverse Cardiac Events (MACE) by lowering death rates and recurrent myocardial infarction and maintaining vessel patency post-PCI [10]. There are few GPI drugs available like abciximab, tirofiban and eptifibatide in the form of monoclonal antibodies and small molecules [12]. Several earlier studies claim that by combining other drugs with GPIs during primary percutaneous coronary intervention there is better coronary circulation, less deaths and recurrent myocardial infarctions reported [13]. Tirofiban is used to avoid any thrombotic consequence after Percutaneous Coronary Intervention (PCI) and helps treat Acute Coronary Syndrome (ACS) [14]. The usual routes for delivery are intravenous and intracoronary injections. A high dose tirofiban (loading dose of 25 mg/kg followed by maintenance of 0.15 mg/kg per min for 18 hours) can inhibit platelet activity up to 95 percent proving itself as effective as the competitive drug in the studies [12]. Using intracoronary tirofiban causes GP IIb/IIIa receptors to inhibit more efficiently in contrast to the intravenous pathway. When this drug is given intracoronary, it is believed to have a better prognosis due to its high amount in coronaries [15]. It is observed in several trials with small to an intermediate sample size that intracoronary abciximab demonstrates favourable outcome such as improved circulation, infarct area and reperfusion injury, whereas, those with a larger sample size reveals that there is no variation in long-term MACE with intracoronary abciximab in contrast to intravenous when given during primary PCI of STEMI patients [16]. Still, there is a shortage of clinical data on general prognosis [5]. Intravenous GPI gives a quick and full inhibition of platelet aggregation. They dissolve already present thrombus and decrease the complications linked with PCI [17]. GPI decreases death, MI and MACE but a major drawback are that it increases the chances of bleeding, long stays at the hospital, increased price and late mortality [18]. There are certain benefits of intracoronary GPI. It gives a greater local amount of antiplatelet drug at obstructing sites in the coronary capillary bed. This result in better receptor binding and destroys the platelet cross-linking [19]. It gives better results for blood flow restoration after treatment and does not give rise to bleeding problems. Benefits are due to increased local concentration but also diffuse to native vessels and the aorta [20].

In this study, we tried to find the answer to the question of whether there is any difference between intracoronary tirofiban and intravenous tirofiban for major adverse cardiac events and cerebrovascular accidents.

METHODS

A total of 250 patients of both gender, age between 20 to 65 years were enrolled in this comparative study conducted at the Punjab Institute of Cardiology, Lahore from March 2019 to March 2020. Only patient who had STEMI and has high thrombus burden thrombolysis in myocardial infarction (TIMI) flow grade <3 during Primary PCI were included. The patients were divided in two groups namely intracoronary tirofiban group (125 patients) and intravenous tirofiban group (125 patients). Informed consent was obtained from all patients. Laboratory findings of all the patients were assessed to obtain the data for clinical outcome and a comparison of frequency of major adverse cardiovascular events and cerebrovascular accidents among intracoronary tirofiban versus intravenous tirofiban was assessed. The Statistical Package for the Social Sciences (SPSS) software, version-25.0, was used to enter and analyze the data. For the qualitative research variables, percentages and frequencies were computed.

RESULTS

The mean age of participants was 41.64 ± 12.30 while the average age of the intracoronary tirofiban group was 40.40 ± 12.41 compared with the intravenous group 42.88 ± 12.90. There were 36% (90) participants of age 20-35 years, 34% (85) were of age 36-50 years, remaining patients 30% (75) were between 51-65 years, so the age range was 20-65 years in our study (Table -1).

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Table 1: Descriptive Statistics of Age

Age Groups (Year)	Frequency (%)
20-35	90 (36)
36-50	85 (34)
51-65	75 (30)
Total	250 (100)
Mean ± SD	41.64 ± 12.30
Mean ± SD (Intracoronary tirofiban group)	40.40 ± 12.41
Mean ± SD (Intravenous group)	42.88 ± 12.90
Minimum-Max	20-65

The p-value of MACE (MI, Cerebrovascular accident & Revascularization) in intracoronary & intravenous tirofiban groups is statistically insignificant as the values are 0.351, 0.436 and 0.373 respectively which showed that variables of MACE were not independent as p-value > 0.05 (Table -2).

Table 2: Cross Tabulation for Major Adverse Cardiac Events (MACE)

Variables	Research Groups				p-value
	Intracoronary Tirofiban Group f (%)		Intravenous Tirofiban Group f (%)		
	Yes	No	Yes	No	
Myocardial Infarction (MI)	8(6.40%)	117(93.6%)	12(9.6%)	113(90.4%)	0.351
Cerebrovascular accident (CVA)	13(10.4%)	112(89.6%)	17(13.6%)	108 (86.4%)	0.436
Revascularization	16(12.8%)	109(87.2%)	21(16.8%)	104(83.2%)	0.373

"Yes" means MI, CVA and revascularization occurred in these patients

"No" means MI, CVA and revascularization did not occur in these patients

A stroke is a disruption in the blood supply to brain cells; it is also known as a brain assault or a cerebral vascular accident (CVA). Brain cells die when they are depleted of oxygen. The frequency distribution for cerebrovascular accident (CVA) showed that haemorrhage was found similar in both groups with a statistically insignificant p-value of 0.510. Ischemic stroke in patients of intracoronary tirofiban group compared with intravenous tirofiban group 1(0.8%) vs 3(2.4%) with p-value 0.348 respectively. A stroke lasting longer than twenty-four hours and recovering in a week is referred to as a reversible ischemic neurologic deficit (RIND). Reversible ischemic neurological deficit (RIND) was found in 3 (2.4%) in the intracoronary and 4 (3.2%) in the intravenous group. A stroke that lasts only a few minutes is known as a transient ischemic attack (TIA). Transient ischemic attack (TIA) found in the intracoronary is 8(6.4%) whereas in the intravenous group is 9 (7.2%) with a p-value of 0.431(Table-3). Table 3 showed that there was no difference in haemorrhage, ischemic stroke, reversible ischemic neurological deficit (RIND) and transient ischemic attack (TIA) in both groups with statistically insignificant p-values 0.510, 0.348, 0.513 and 0.431 respectively (Table 3).

Table 3: Cross Tabulation for Cerebrovascular Accident (CVA)

Variables	Research Groups				p-value
	Intracoronary Tirofiban Group f (%)		Intravenous Tirofiban Group f (%)		
	Yes	No	Yes	No	
Haemorrhage	1(0.8%)	30(24.0%)	1(0.8%)	32(25.6%)	0.510
Ischemic Stroke	1(0.8%)	18(14.4%)	3(2.4%)	28(22.4%)	0.348
Reversible Ischemic Neurological Deficit (RIND)	3(2.4%)	24(19.2%)	4(3.2%)	30(24.0%)	0.513
Transient Ischaemic Attack (TIA)	8(6.4%)	40(32.0%)	9(7.2%)	18(14.4%)	0.431

"Yes" means MI, CVA and revascularization occurred in these patients

"No" means MI, CVA and revascularization did not occur in these patients

DISCUSSION

Recanalization of the vessel in ST-elevation myocardial infarction (STEMI) patients can be achieved by either timely percutaneous coronary intervention (PCI) or via medical management to save the diseased myocardium and decrease mortality [21]. The improved treatment received by ST-elevation myocardial infarction (STEMI) patients is primary percutaneous coronary intervention in comparison to medical treatment [22]. Over the past ten years the best treatment for acute myocardial infarction is percutaneous coronary intervention (PCI) to achieve complete reperfusion and thus decrease the death rate [23]. The advantages of PCI are improvement in myocardial blood flow and normal TIMI flow grade thus fewer chances of cardiovascular events [24]. When percutaneous coronary intervention is performed vascular complication is more commonly encountered and as a result, leads to an increase in the number of deaths along with an economic burden on the patient. These complications also put the patients at risk of coronary artery disease and ultimately death [25]. Even after successful placement of stents no-reflow phenomena can occur which is considered to be the second most dangerous angiographic-related problem [26]. Therefore, additional medical treatments like GPI not only decrease platelet aggregation but also improve vessel patency, so clinical outcome is better [27, 28]. The usual routes for delivery of tirofiban are intravenous and intracoronary injections. When it is given via intra-arterial injection, it allows efficient drug absorption in the diseased area and improves platelet aggregation. Glycoprotein especially tirofiban can be given through venous and intra-arterial routes. It has been proposed that when tirofiban is given through the intra-arterial pathway, has better

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efficacy in the infarct area and has better platelet inhibition function. Moreover, this route has a low bleeding risk [29]. This study was conducted to compare intracoronary tirofiban with intravenous tirofiban for major adverse cardiac events and cerebrovascular accidents during the percutaneous coronary intervention (PPCI). A total of 250 patients were enrolled, and the mean age of the participants was 41.64 ± 12.30. Total participants were divided into two groups (intracoronary and intravenous tirofiban group). The average age was 40.40 ± 12.41 and 42.88 ± 12.90 respectively. There were 184 (73.6%) males and 66 (26.4%) females. In our study, the results of MACE (MI, CVA & Revascularization) in intracoronary & intravenous tirofiban groups remained statistically insignificant. Erdim et al conducted a study and observed that major adverse cardiovascular event during the hospital stay is 2.7% and 2.1% in the intracoronary and intravenous group respectively with a p-value of 1.00. The separate parts of the MACE in intracoronary versus intravenous groups: deaths were 2.1% as compared to 2.7%, repeat revascularizations were 4.1% versus 8.3%, recurrent myocardial infarction 4.1% and 8.3% respectively [30, 31]. These MACE values support our study. The results of our study showed that there was no difference in haemorrhage, ischemic stroke, reversible ischemic neurological deficit (RIND) and transient ischemic attack (TIA) in both groups with statistically insignificant p-values.

CONCLUSIONS

The results of our study make us conclude that tirofiban when given intracoronary or intravenous does not show any significant difference for major adverse cardiac events and cerebrovascular accidents.

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Authors Contribution

Conceptualization: SHRB, MAR
Methodology: SHRB, MNK, ZUR
Formal analysis: SHRB, MAR, MSM, JSUD
Writing-review and editing: SHRB, MAR, MSM, MNK, ZUR, JSUD
All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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