Original Article

Acute Coronary Syndrome

Efficacy of Intracoronary Bolus administration of Tirofiban in Acute Coronary Syndrome Patients with No-reflow Phenomenon during Percutaneous Coronary intervention (PCI)

1. Muhammad Nawaz Lashari 2. Muhammad Tanveer Alam 3. Tariq Ashraf 4. Mukhtiar Ahmad Pathan

1. Asstt. Prof. of Cardiology, DUHS&CH, Karachi 2. Asstt. Prof. of Medicine, DUHS&CH, Karachi
3. Asstt. Prof. of Cardiology, NICVD, Karachi 4. Senior Medical Officer, DUH Ojha Complex, Karachi

ABSTRACT

Objective: Currently in acute coronary syndrome, PCI is most common strategy. No-reflow phenomenon (NR) is one of serious complication. Aim of this study was to evaluate role of intracoronary bolus administration of tirofiban in acute coronary syndrome patients with no-reflow during PCI.

Study Design: It is prospective and observational study.

Place and Duration of Study: It is multicenter study, conducted in Karachi, Pakistan from August 2011 to July 2013.

Patients and Methods: Total of 62 patients of acute coronary syndrome underwent for PCI and developed no-reflow, received intracoronary bolus tirofiban were included. The angiographic definition of successful reperfusion should include both TIMI 3 flow as well as MBG 2 or 3. No-reflow, assesed by thrombolysis in myocardial infarction (TIMI) flow and myocardial blush grade (MBG) during treatment. Data were entered and analyzed using SPSS-16 software. Statistical significance was defined as p-value <0.05.

Results: Out of 62 patients, 43 were males .The mean age was 61 ±13, range from 37 to 70 years. TIMI flow 1 and 11 seen in 17, 37 patients while MBG 1 and 11 seen in 20 and 35 patients before intracoronary bolus administration of tirofiban. After bolus administration of tirofiban, TIMI flow 111 was seen in 61(98.387 %) out of 62 patients while MBG 11 and 111 was also noted in 61(98.387 %) out of 62 patients. It showed better Thrombolysis In Myocardial Infarction flow grades and TIMI myocardial perfusion grades (OR 0. 22, 95% CI 0 .12 -0 .39, p-value <0.001) immediately after intracoronary bolus administration of tirofiban in reflow phenomenon patients during PCI.

Conclusion: In patients with ACS, Intracoronary bolus adminstration of tirofiban is effective drug to improve no-reflow during percutaneous coronary intervention especially when patient blood pressure is at lower-side.

Key Words: Intracoronary, bolus tirofiban, Acute coronary syndrome, No-reflow, PCI.

INTRODUCTION

No-reflow (NR) phenomenon could be defined as the persistence of reduced flow and regional myocardial dysfunction after the removal of an experimental epicardial coronary occlusion[1]. So far, the precise mechanisms of NR have not been fully clarified. The optimal therapy for NR is still being explored. Some studies[2-4] suggested that the dysfunction of coronary microcirculation perfusion was the central mechanism of NR. And it would not occur until the lesion of coronary micro-vascular endothelium to a certain extent exists. It was a dynamic and persistent procedure. Once the phenomenon occurred, the inflammation and lesion of coronary micro-vascular endothelium would be aggravated and the effect would sustain for weeks. Restoration of myocardial perfusion rapidly could be achieved by removing the micro-vascular obstruction and recovering the ante-grade coronary flow of occlusive vessel, and it has become a key of the treatment for NR[5]. For NR, the mechanism of conventional drugs was mainly for expanding the coronary vessel, which might be beneficial to allowing the formed micro-thrombus to get through the micro-vascular network and removing the coronary occlusion. The conventional pharmacological treatment for NR is intracoronary (IC) administration of vasodilators (for example, adenosine, verapamil, nitroglycerin, sodium nitroprusside, etc.)[6]. On the basis of the mechanisms, conventional drugs could not inhibit the sustained thrombi caused by platelet aggregation when balloon was dilating, which limited the effect[7-8]. The effects of these vasodilators in patients with NR were contradictory and could not be sustained by large scale clinical evidence[9-10]. Platelet aggregation plays an important role in the formation of embolization. Glycoprotein inhibitors (GPI) block the final pathway of platelet aggregation, combine with the glycoprotein 11b/111a receptors selectively and inhibit the thrombinogen I competitively. And also, GPI could inhibit the activation, adhesion and aggregation of platelets. The pharmacological mechanisms of GPI

were contributed to the inhibitation of formation of platelet thrombi, restoration of the ante-grade coronary flow of occlusive vessel and reducing the incidence of the ischemia event[11-12]. Tirofiban is one kind of GPI, which with high selectivity and short-acting pharmacological mechanism[13]. So far, there are some randomized controlled trials investigated the treatment of IC bolus administration of tirofiban for NR. Therefore, the aim of this study was to evaluated the efficacy of IC bolus administration of tirofiban for NR during PCI.

MATERIALS AND METHODS

It is prospective, observational and multicentre study, conducted at Karachi, Pakistan between August 2011 to July 2013. Total of 62 patients of acute coronary syndrome underwent for PCI and developed no-reflow, received intracoronary bolus tirofiban were included. 38 patients had ST-elevation MI, 14 had non-ST elevation MI and 10 had a USA (Table 1). All patients were given oral aspirin 300 mg, clopidogrel 150-300 mg and unfractioned heparin 5000 to 7500 units before PCI. Tirofiban was administered as an intracoronary bolus injection 10µg/kg over 01 min followed by maintenance intravenous infusion at 0.15µg·kg–1·min for 12 h. After PCI, all patients were managed in the cardiac care unit with once-daily dose of aspirin (150-300 mg) and clopidogrel (75 mg). A beta-blocker, statin and an angiotensin-converting enzyme inhibitor (ACEI) were also routinely prescribed to all patients. All coronary angiograms were evaluated by authers after PCI. Scores of thrombus in the PCI-targeted artery were assessed as following: 0: no thrombus; 1: possible thrombus; 2: the length of the thrombus is less than 50% of the vessel diameter; 3: the length of the thrombus is half to twice the vessel diameter; 4: the length of the thrombus is longer than twice the vessel diameter[10.] No-reflow in the PCI-targeted coronary arteries was assessed by Thrombolysis In Myocardial Infarction (TIMI) flow grade[2.] The TIMI myocardial perfusion grade (TMPG) was used to assess myocardial tissue-level perfusion[3]. TMPG was assessed only in the area supplied by the PCI-targeted vessel. The angiographic definition of successful reperfusion should include both TIMI 3 flow as well as MBG 2 or 3.

Statistical Analysis: Data were entered and analyzed using SPSS-16 software. Continuous data are expressed as mean values ± SD. Student's t-test was used to analyze continuous variables. Categorical variables were analyzed by chi-square test. P-value <0.05 was considered statistically significant.

RESULTS

The baseline characteristics of the patients are shown in Table 1. Out of 62 patients, 43 were males .The mean age was 51 ±13, range from 37 to 70 years. As shown in table. 11, TIMI flow1 and 11 was seen in 17, 37 patients while MBG (Table. 111) 1 and 11 seen in 20 and 33 patients before intracoronary bolus administration of tirofiban. After bolus administration of tirofiban TIMI flow 111 was found in 61(98.387 %) out of 62 patients while MBG 11 and 111 was also noted in 61(98.387 %) out of 62 patients. It was found significantly better Thrombolysis In Myocardial Infarction (TIMI) flow grades and TIMI myocardial perfusion grades (OR 0.22, 95% CI 0.12 -0.39, p-value <0.001) immediately after intracoronary bolus administration of tirofiban during PCI.

Table No.1: Baseline Characteristics of patients.

Characteristics	No.(62)
Age (years)	51 ±13
Sex (male)	43
Hypertension	50
Diabetes	20
Current smoker	23
Prior MI	12
STEMI	38
NSTEMI	14
USA	10
Vessel. LAD. RCA. LCX.	 31 19 12

Table No.2: TIMI-Flow during PCI.

Timi-Flow	Before I/C Tirofiban	After I/C Tirofiban
0	08	00
1	17	01
11	37	00
111	00	61

I/C =Intracoronary

Table No.3: Myocadial Blush Grade during PCI.

Myocardial-blush grade.	Before I/C Tirofiban.	After I/C Tirofiban.
0	**07**	**00**
1	**20**	**01**
11	**33**	**08**
111	**02**	**53**

I/C= Intracoronary.

DISCUSSION

The main findings of the present study are as follows. Intracoronary bolus administration of tirofiban is associated with an improved in no-reflow phenomenon in form of TIMI flow and TMPG during PCI like in other studies[14-17]. Though TIMI is a classical indicator of reperfusion during PCI, [18-20] it does not mean that TIMI 3 flow represents a normal myocardial perfusion.[21] In other words, myocardial blush grade (MBG) 01 might occur in the patients with TIMI 3 flow

during PCI. It had been found that MBG was an independent predictor of long-term mortality and could be used to describe the effectiveness of myocardial reperfusion.[22] Van Hof et al.[23] proposed that the angiographic definition of successful reperfusion should include both TIMI 3 flow as well as MBG 2 or 3. Moreover, Stone. et al.,[24] suggested that MBG could be used to stratify prognosis of survival in high risk patients achieving TIMI 3 flow after intervention. Theoretically, MBG is superior to TIMI when assessing the myocardial perfusion during PCI. From the recent researches, GPI has its obvious advantages in inhibiting the formation of platelet thrombus, but bleeding event was the main complication. Tirofiban is one kind of GPI, which with high selectivity and short-acting pharmacological mechanism.[25] During PCI, IC bolus administration of tirofiban might increase the local drug concentration and improve the coronary flow. Considering the particular mechanism and short half life, IC tirofiban selectively blocks the final pathway of the platelet aggregation, which might contribute to the improving TIMI flow, MBG and reducing MACE.

In the present study 61.3% of patients had ST-elevation ACS. Intracoronary tirofiban was administered immediately after no-reflow phenomenon during PCI because we hypothesized that local administration of IIb/IIIa antagonist would have a faster and more efficient action on the coronary thrombus and vascular endothelium than the conventional intravenous bolus injection.

Study Limitations: It was small sample data, the bias should not be ignored. Also, the condition of patients the time and dosage of drugs might have influenced the outcomes. Therefore, needs further powerful studies.

CONCLUSION

The treatment of IC bolus administration of tirofiban was significantly effective to improve no-reflow phenomenon during PCI in acute coronary syndrome patients.

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Address for Corresponding Author:
Dr. Muhammad Nawaz Lashari
Address: 1-C 7th street,
Defence Housing Authority (DHA) Phase-1,
Karachi , Pakistan
Email: nawazlashari@gmail.com
Cell No: 03002656269