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Complications of intracoronary abciximab bolus-only versus standard protocol during percutaneous coronary intervention in acute coronary syndrome

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ABSTRACT

Background: Abciximab reduces major adverse cardiac events in patients with ST elevation myocardial infarction undergoing primary percutaneous coronary intervention (pPCI). Standard protocol is intravenous abciximab bolus during PCI plus abciximab infusion for 12–18 h post pPCI. Intracoronary (IC) abciximab bolus administration results in high local drug concentrations and hence it should have higher antiplatelet effect. In this study, we assess the short-term efficacy and safety of IC compared to IV bolus of abciximab in ACS patients during pPCI.
Methods: We compared the clinical outcomes between the IC (n = 56) and standard protocol (n = 170) group of patients. Primary endpoints included bleeding/vascular/ischemic complications and MACE.
Results: The two groups were similar with respect to baseline characteristics. IC abciximab bolus only reduced bleeding complications, with no moderate bleed versus 7.2% in standard protocol group (p value 0.04). Ischemic/vascular complications had statistically insignificant difference between the two groups.
Conclusion: We found no significant difference between IC abciximab bolus only and standard abciximab therapy in terms of ischemic/vascular complications and MACE. But there was higher risk of moderate bleed in standard therapy group. The IC bolus route of abciximab may be superior to the intravenous route. Prospective randomized trials are warranted to validate these findings.

1. Introduction

Primary percutaneous coronary intervention (pPCI) is the ideal and standard regimen in restoring epicardial perfusion in a ST-elevation myocardial infarction (STEMI) [1]. Adjunctive therapy with glycoprotein IIb/IIIa receptor inhibitor (GPI) aims at coronary microcirculation and improves the myocardial tissue perfusion which has considerable prognostic impact [2,3]. There is robust data available in literature that supports the beneficial anti-ischemic effects of GPI use during PCI decreasing major adverse cardiac events (MACE) [4–6].

Intravenous abciximab is the standard route of administration, and has been studied in various clinical trials. Standard protocol is intravenous abciximab bolus during PCI plus abciximab infusion for 12–18 h post pPCI. If given as an intracoronary (IC) bolus, it is expected to produce high local concentrations at the PCI site with higher anti platelet action, although at present clinical experience in the efficacy of intracoronary abciximab administration is limited [3,7–10]. Hence we are conducting this study in order to compare the short-term efficacy and safety of IC compared to IV bolus of abciximab in ACS patients during pPCI.

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2. Methods

2.1. Patient population

The study was approved by our ethical and research committee. Patient consent for analysis of their data was standard. There were a total of 170 patients in the standard therapy group versus 56 patients in IC abciximab bolus only.

Inclusion criteria: We included all ACS patients who underwent PCI from November 2007–December 2009 and received IC or IV bolus of abciximab with the procedure.

Exclusion criteria: Patients who presented with cardiogenic shock, those who could not get the drug due to any compelling contraindications or got GPI other than abciximab were excluded from the study population.

2.2. Periprocedure pharmacology

All the patients got standard therapy for acute coronary syndrome like aspirin (300 mg), clopidogrel (300–600 mg) and intravenous heparin (60 units/kg) before they are wheeled to the cath lab, as per standard guidelines. Abciximab was given as 0.25 mg/kg bolus plus 0.125 μg/kg/min infusion for 12 h or 0.15–0.25 mg/kg IC bolus only

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during the coronary intervention, and hence the two groups were IC abciximab bolus only or IV abciximab bolus plus infusion.

2.3. Study endpoints

Our primary endpoints were vascular, bleeding, ischemic complications and MACE as summarized in Table 1. Vascular complications included pseudoaneurysm, arteriovenous fistula, dissection and loss of distal pulse. Bleeding complications were classified as major, moderate and mild as per GUSTO classification [11]. It included percutaneous entry site bleeding and bleeding other than the entry site (e.g. retroperitoneal, gastrointestinal, genitourinary), diagnosed on clinical grounds but confirmed by further imaging.

Ischemic complications comprised of peri-procedural CK-MB elevation (≥3 times upper normal limit), acute or subacute stent thrombosis, unplanned CABG and repeat target vessel revascularization.

MACE was the composite of death, urgent target vessel revascularization and periprocedural CK-MB elevation ≥3 times upper normal limit. Data was retrieved from the files of the respective patients by the research staff that was not related to the cardiac intervention.

2.4. Statistical analysis

Statistical analysis was performed using SPSS 17. Percentages were used to express categorical data and Chi-square test was used for comparison. Continuous variables were expressed as mean ± standard deviation and compared with Student *t* test. A p-value of ≤0.05 was considered significant.

3. Results

3.1. Baseline clinical characteristics

They were similar in both the groups as reported in Table 2, however there was a higher prevalence of dyslipidemia in bolus plus infusion group ($p < 0.01$). Also more people had a history of prior PCI in the bolus only group with statistical significant p value. All the patients received aspirin, clopidogrel and heparin in their initial emergency management. When we take a look at acute coronary syndrome distribution between two groups, bolus only group has higher number of STEMI patients and standard therapy group mainly consists of unstable angina and NSTEMI but p value was not significant. All the variations in the baseline characteristics were adjusted by using logistic regression.

3.2. Angiographic characteristics

Angiographic characteristics were almost the same in both the groups as shown in Table 3. Except more patients in standard therapy group achieved post PCI TIMI III flow as compared to bolus only group and probably it can be described by more high risk lesions in bolus only group.

Table 1
Study endpoints.

Vascular complications	Pseudoaneurysm, AV fistula, dissection, loss of distal pulse
Bleeding complications	Mild, moderate and major
Ischemic complications	Peri-procedural CK-MB elevation (≥3 times upper normal limit), acute or subacute stent thrombosis, unplanned CABG, repeat target vessel revascularization
MACE (major adverse cardiac events)	Composite of death, urgent target vessel revascularization and periprocedural CK-MB elevation ≥3 times upper normal limit

Table 2
Baseline clinical characteristics.

	Standard therapy (n = 170)	IC bolus only (n = 56)	p
Family history of premature CAD (<50 years) (%)	38 (22.4)	13 (23.2)	0.89
Dyslipidemia (%)	122 (71.8)	22 (39.3)	<0.01
Diabetes (%)	60 (35.3)	16 (28.6)	0.36
Hypertension (%)	87 (51.2)	30 (53.6)	0.76
Smoking (%)	62 (36.5)	22 (39.3)	0.71
Prior history of CHF (%)	6 (3.5)	2 (3.6)	0.98
Prior MI (%)	36 (21.2)	12 (21.4)	0.97
Cerebrovascular disease (%)	6 (3.5)	0	0.15
Peripheral vascular disease (%)	0	1 (1.8)	0.08
Previous CABG (%)	5 (2.9)	3 (5.4)	0.39
Previous PCI (%)	8 (4.7)	13 (23.2)	<0.01
Medications			
Aspirin (%)	170 (100)	54 (96.4)	0.06
Clopidogril (%)	156 (91.8)	54 (96.4)	0.38
Heparin (%)	139 (81.8)	45 (80.4)	0.81
Angina/NSTEMI/STEMI (%)	35 (22)/32 (20.1)/ 92 (57.9)	5 (8.9)/10 (17.9)/ 41 (73.2)	0.06

3.3. Vascular/bleeding complications

We found no difference in terms of vascular complications. But when bleeding complications were stratified into major, moderate and mild, we found that moderate bleed was higher in standard therapy group as compared to bolus only group (p value = 0.04) as per Table 4.

3.4. Ischemic complication and MACE

Ischemic complications had statistically insignificant difference between the two groups. MACE for in hospital stay was the same in both groups. Study endpoints summarized in Table 5.

4. Discussion

Glycoprotein IIb/IIIa receptors are present on the platelet surface and mediate the final common pathway of platelet aggregation, which plays an important role in the formation of a platelet plug [12]. GPI are potent platelet antagonists that inhibit aggregation of platelets at the site of a disrupted plaque during PCI. There are three well known GPI; abciximab, eptifibatide and tirofiban. Some studies show that eptifibatide and tirofiban are non-inferior to abciximab and some show abciximab is superior [13–15]. Most of the hospitals don't use abciximab because of the cost issues [16].

In vitro studies have demonstrated that there is nearly complete saturation of glycoprotein IIb/IIIa receptors with abciximab concentration of 0.034 μmol/L, which corresponds to an IV bolus of 0.15 mg/kg. This abciximab concentration inhibits 75% of the mechanical effects of

Table 3
Angiographic characteristics.

	Standard therapy %	IC bolus only %	p-Value
Vessel disease			
Single vessel	48.9	43.8	0.76
Double vessel	37.8	46.9	
Triple vessel	10.4	6.3	
TIMI flow			
Pre I/II/III	13/8.4/46.6	12.5/3.1/34.4	0.24
Post I/II/III	1.5/9.9/88.5	3.1/9.4/81.3	0.03
Direct stenting	17.6	37.5	0.04
Aspiration device	30.2	31.3	
PCI to graft	0.8	0	0.65
PCI to >single vessel	0.1	0.01	0.54
Lesion risk			
Low/medium/high	9.9/41.2/46.6	9.4/6.3/78.1	0.002
No reflow	6.9	3.1	0.11