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## Original Article

# Intracoronary abciximab in STEMI using local drug delivery catheter – Single center experience

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## ARTICLE INFO

## Article history:

Received 25 September 2012

Accepted 3 April 2013

Available online 12 April 2013

## Keywords:

Primary PCI

Abciximab

Local drug delivery

Clearway

Intra-coronary

## ABSTRACT

**Background:** Despite restoration of epicardial flow during primary PCI in STEMI, microvascular obstruction may persist as a result of both atheromatous and thrombotic embolization and vasospasm. Compared with the systemic administration of IV pharmacotherapies, highly localized administration of intracoronary pharmacotherapy may be associated with a several-hundred-fold increase in the local concentration of an agent in the epicardial artery and microcirculation. Despite restoration of epicardial flow during primary PCI in STEMI, microvascular obstruction may persist as a result of both atheromatous and thrombotic embolization and vasospasm. We are presenting our experience with use of intracoronary abciximab using local drug delivery catheter in STEMI patients. **Methods:** We retrospectively evaluated 15 patients presented to us with STEMI undergoing primary PCI between March 2011 and September 2012 who had super selective intracoronary abciximab using local drug delivery catheter. With standard antiplatelet therapy, both Pre and Post TIMI flow, TMP grading were assessed.

**Results:** Mean age was 55 years. The TIMI flow increased by 3 grades in thirteen patients, TMP grading increased by 2 grades in five patients and by 3 grades in nine patients. Thus TIMI flow and TMP grading improved after super selective intracoronary abciximab.

**Conclusion:** Super selective intracoronary abciximab using local drug delivery catheter during primary PCI in STEMI patients significantly improves TMP grading without increased risk of bleeding. This benefit is achieved even in patients without thrombus aspiration. We need to assess the long-term outcomes in the form of reduction in infarct size using this strategy in large group of patients.

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## 1. Introduction

Primary percutaneous coronary intervention (PCI) is now the preferred method of treating patients with ST elevation myocardial infarction (STEMI). The results of primary PCI have improved continuously since the technique was

introduced. Despite restoration of epicardial flow, microvascular obstruction may persist after primary PCI as a result of both atheromatous and thrombotic embolization, neutrophil plugging, edema, and vasospasm.<sup>1</sup>

There have been efforts to identify mechanical and pharmacological strategies to improve myocardial perfusion after

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<http://dx.doi.org/10.1016/j.ihj.2013.04.021>

primary PCI. Advances in the procedures and materials have been accompanied by a notable development in associated drug treatments. Compared with the systemic administration of intravenous pharmacotherapies, highly localized administration of intracoronary pharmacotherapy may be associated with a several-hundred-fold increase in the local concentration of an agent in the epicardial artery and microcirculation.

We are presenting herewith our center experience with intracoronary abciximab in STEMI using clearway catheter and assessed the outcomes using TIMI flow and TMP grading.

## 2. Methods

We assessed 15 consecutive patients who presented to us with STEMI undergoing emergency primary PCI between March 2011 and September 2012. All patients received loading dose of aspirin and 600 mg clopidogrel. Thrombus aspiration was done whenever the thrombus burden was huge. All patients were given bolus only dose of intracoronary abciximab (0.25 mg/kg) using the clearway catheter.

The clearway therapeutic perfusion catheter (Maquet cardiovascular, Sweden) acts as a low-pressure irrigating system for localized perfusion of therapeutic agents into the coronary vasculature. It is a semi compliant micro porous PTFE balloon mounted on 2.7 F Rx catheter and will not burst or tear during use. Fluid gently weeps through the pores with no high pressure jetting. It inflates and infuses fluid at low pressure (1–4 atm) and does not damage the internal elastic lamina of vessel during inflation and infusion. Pressure at balloon surface during infusion is nearly zero relative to blood pressure. Balloon inflation causes occlusion of the vessel providing a better drug contact with thrombus without dilution by blood flow increasing concentration and residence time, which leads to a greater reduction in TIMI thrombus burden score, a hallmark of this therapy. This local drug delivery catheter system is described as OCI (Occlusion, Containment, Infusion) therapeutics allowing site specific, localized drug delivery across any coronary lesion. The potential disadvantage of traditional method (passing through guide catheter) is >50% of the drug will be washed away in systemic circulation and other 20–25% drugs will be delivered to unwanted branches. Less than 20% of the drug will reach the target lesion.

Pre TIMI flow and TMP grading were assessed. The improvement of TIMI flow and TMP grade after intracoronary abciximab using clearway catheter were assessed. After aspiration and abciximab treatment using local drug delivery, stent was deployed using standard protocol.

## 3. Results

The study population (Mean age of  $55 \pm 11$  years) had 15 patients with STEMI.

Bivalirudin anticoagulation was used in 33% (5/15) during the procedure. Majority of study patients had AWTMI 60%. Mean window period of presentation is 7.5 h. One patient had no requirement for stent as angiographically it was a stent like result. 93% (14/15) of them had TIMI 0 flow pre PCI while the rest 7% (1/15) had TIMI 1 flow (Table 1). The TIMI flow

increased by 2 grade in 2 patients and by 3 grades in 13 patients. The TMP grading increased by 1 grade in 1 patient, by 2 grade in 5 patients and by 3 grade in 9 patients. TIMI flow remained the same or worsened in none of the patients. 93% (14/15) patients had TIMI 3 flow post procedure with no in-hospital mortality. Clinical/telephonic follow up was done for all patients and there was zero MACE at 30 days.

## 4. Discussion

Potent inhibition of platelet aggregation can be achieved by the use of intravenous glycoprotein IIb/IIIa inhibitors, which inhibit the final common pathway of platelet aggregation, the cross-bridging of platelets secondary to fibrinogen binding to the activated GP IIb/IIIa receptor.

A 2002 meta-analysis examined 31,400 non-ST elevation ACS patients treated with aspirin and heparin who did not undergo early revascularization. GP IIb/IIIa inhibitor use was associated with a significant reduction in the combined endpoint (death or MI) at five days and at 30 days with benefit appeared to be limited to the highest risk patients.<sup>2</sup>

An interesting observation from the PRISM, CAPTURE, and PARAGON B trials and a meta-analysis is that the benefit from GP IIb/IIIa inhibition primarily occurred in the subset of patients who had elevations in troponin.<sup>3–5</sup> The same pattern of benefit limited to patients with elevated troponins was also noted in the ISAR-REACT 2 trial of patients also treated with clopidogrel.<sup>6</sup> In ISAR-REACT 2, all patients received pretreatment with aspirin and 600 mg of clopidogrel. While there is evidence to recommend GP IIb/IIIa inhibitor therapy in high-risk patients treated with a conservative approach, the evidence comes from studies performed before the routine use of P2Y12 receptor blockers. The role of GP IIb/IIIa inhibitor for these high-risk patients on dual oral antiplatelet therapy is questionable in elective PCI.

However intravenous GP IIb/IIIa receptor antagonists in conjunction with unfractionated heparin or bivalirudin has been established to have a beneficial role in STEMI patients undergoing primary PCI<sup>7</sup> in whom there is no adequate time interval for elective loading dose.

Meta-analysis have showed that IC administration of abciximab is associated with significant benefits in myocardial perfusion and mortality at short-term follow-up compared to IV abciximab administration, without any excess of major bleeding in STEMI patients undergoing primary PCI.<sup>8,9</sup>

**Table 1 – Patient and procedure characteristics.**

Study population	Total no. of patients n = 15
Diabetes mellitus	8
Systemic hypertension	8
AWMI	9
IWMI	6
Cardiogenic shock	1
TIMI flow 0	14
Pre PCI	
Thrombus aspiration	6

The rationale of the use of intracoronary abciximab administration is that it may be more effective, more timely and, potentially, safer. Considering the short plasma half-life of abciximab, mostly related to its rapid binding to exposed GP IIb/IIIa receptors on the surface of circulating platelets, intravenous administration of abciximab might prevent the attainment of a suitable concentration at the culprit lesion and in the distal bed of the culprit vessel.<sup>10</sup> Intracoronary administration of the bolus dose is associated with a several-hundred-fold increase in the local concentration of an agent in the epicardial artery and microcirculation and may probably increase the dose-dependent antiplatelet and anti-thrombotic effects focusing on the culprit lesion.<sup>11</sup> High local concentrations of the drug would lead to fewer GP IIb/IIIa receptors being available for cross-linking with fibrinogen in the coronary microcirculation and also lead to an optimization of both IIb/IIIa and non-IIb/IIIa dependent properties.

Moreover, during PCI, the intracoronary administration of abciximab can be easily performed due to the use of selective coronary catheters.<sup>12</sup> Super selective drug delivery catheters give the highest local concentration of the drug avoiding draining off the drug into non-culprit vessels. Localized super selective abciximab protects from distal emboli that may have dislodged during the initial plaque rupture and also resolves residual thrombus that remain behind after manual extraction.

Furthermore, intracoronary administration may facilitate the diffusion of the antibody to platelets inside flow-limiting thrombi; in fact, depending on the relation between inflow and washout from residual perfusion and the size of the ischemic area, the concentration of abciximab at the culprit lesion after intracoronary injection compared with intravenous bolus administration might vary between 280:1 (minimal washout) and 1:1 (normal flow).

Thus, by modulating inflammatory cell responses and their interactions with platelets and the endothelium, abciximab may favourably influence post-ischemic microvascular endothelial responses leading to vessel wall passivation, a reduced reperfusion injury and a greater degree of myocardial salvage.

Wohrle and colleagues,<sup>13</sup> demonstrated in a randomized study, a significant reduction of the incidence of MACE at 30 days, using intracoronary bolus rather than intravenous in patients with acute coronary syndromes undergoing coronary angioplasty. A retrospective study with similar design coming from Kakkar and colleagues<sup>14</sup> showed similar findings, reporting that in unselected patients undergoing coronary stenting and abciximab administration, intracoronary bolus injection is associated with a significantly lower 6-month composite endpoint of death or myocardial infarction compared to the intravenously-treated group.

In the AIDA STEMI trial,<sup>15</sup> patients presenting with STEMI with no contraindications for abciximab were randomly assigned in a 1:1 ratio by randomization system to intracoronary via guide catheter versus intravenous bolus abciximab with a subsequent 12 h intravenous infusion. The guide catheter delivery of abciximab compared to intravenous abciximab did not show any difference in combined endpoints of death, re-infarction, or congestive heart failure.

In the COCTAIL study<sup>16,17</sup> whether local abciximab delivery to the site of thrombus through the Local drug delivery

catheter is more effective than intracoronary infusion through the guiding catheter in primary PCI was studied. The study found a significant reduction of thrombus burden assessed by OCT with intracoronary abciximab using clearway catheter.<sup>18</sup>

INFUSE AMI trial<sup>19</sup> was done to assess whether bolus intracoronary abciximab, manual aspiration thrombectomy, or both reduced infarct size in high-risk patients with STEMI. 0.25-mg/kg bolus of abciximab was administered at the site of the infarct lesion via the clearway catheter. This study randomized only large anterior MIs with TIMI 0–2 flow in proximal/mid LAD with symptom onset to PCI less than 5 h aiming at reperfusion within the time window for potential myocardial salvage. Intracoronary abciximab bolus only versus no abciximab was compared. Manual aspiration thrombectomy was performed with a 6 F aspiration catheter. Infarct size was assessed by MRI at 30 days, after edema had decreased. The INFUSE-AMI results reaffirmed our treatment strategy with intracoronary bolus only abciximab delivered to the infarct lesion site via the local drug delivery catheter infusion catheter resulted in a significant reduction in infarct size at 30 days. Manual aspiration with the 6 F Export Catheter only did not reduce infarct size.

The recent 2013 ACC/AHA guidelines have incorporated the role for intracoronary abciximab during primary PCI.<sup>20</sup>

In our study, the TMP grading improved significantly after the intracoronary lesion specific abciximab irrespective of aspiration devices. Importantly, the intracoronary administration of abciximab was not associated with bleeding or any side effects as only bolus dose was given.

Studies comparing mode of delivery such as site specific or intracoronary or intravenous administration of abciximab in STEMI are limited. But available studies report a clear benefit of super selective intracoronary administration, with a reduction in the short and medium-term incidence of events, although the studies were retrospective. Our study was consistent with the findings of the above and we found an increase in the TMP grading which in turn have been shown in other studies as a marker for reduction in infarct size and MACE at 30 days.

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## 5. Limitations

Our study had limited number of patients and hence to show the benefit in real world we need randomized trials with criterion and large numbers. We did not have a control arm to compare the benefit without intracoronary abciximab.

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## 6. Conclusion

Intracoronary abciximab using local drug delivery catheter in patients with STEMI with thrombus burden significantly improves TMP grading without increasing the risk of bleeding. This benefit is achieved even in patients without thrombus aspiration. We need to assess the long-term outcomes demonstrating reduction in infarct size and mortality in large trials.

## Conflicts of interest

All authors have none to declare.

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