Abstract  Abciximab (c7E3 Fab) inhibits platelet aggregation and is used to prevent complications of percutaneous coronary intervention. Thrombocytopenia is an often-cited complication of abciximab. Pseudothrombocytopenia is due to ethylenediaminetetraacetate (EDTA)-activated platelet agglutination, resulting in a spuriously low platelet count. We have looked at both “true” and pseudothrombocytopenia after infusion of abciximab. Sixty-six patients receiving their first exposure to abciximab after an unstable coronary event/revascularization were eligible. All the patients received a bolus of c7E3 Fab followed by a continuous infusion. Platelets were monitored in all patients at 2, 4, 12, 24, and 48 h, and more frequently if required. The incidence of thrombocytopenia and acute severe thrombocytopenia (platelet count \( \leq 20,000/\mu l \)) was evaluated. A peripheral blood smear was performed on all patients showing thrombocytopenia to evaluate for pseudothrombocytopenia. Seventeen (25.6%) developed thrombocytopenia and nine (13.6%) developed acute severe thrombocytopenia. However, 18 of these patients had pseudothrombocytopenia. The onset of true thrombocytopenia was at 4 h after the infusion, while pseudothrombocytopenia occurred at anytime during the first 24 h. Only two (3.03%) patients required platelet transfusions. No life-threatening hemorrhagic complications were recognized. Five of six subjects with true thrombocytopenia had positive laboratory findings of disseminated intravascular coagulation; however, none had an adverse outcome. Acute severe thrombocytopenia was noted to be a relatively benign adverse effect of abciximab. There is an increasing incidence of pseudothrombocytopenia in this subgroup of patients. It would be worthwhile examining a peripheral blood smear or collecting blood for platelet counts in a heparin-coated tube in order to exclude this phenomenon and thereby prevent inappropriate discontinuation of this drug.

Keywords  c7E3 Fab (abciximab) · Pseudothrombocytopenia · Thrombocytopenia

Introduction

Abciximab (c7E3 Fab, ReoPro) is a chimeric antibody fragment that acts by inhibiting glycoprotein IIb/IIIa (GPIIb-IIIa) complexes and therefore inhibits platelet aggregation. It acts rapidly, blocking more than 80% of platelet receptors within 2 h of the administration of a 0.25-mg/kg bolus in humans [1]. Saturation of the receptors is maintained during a 10-µg/min infusion for 12–24 h, and recovery of platelet function is gradual after the infusion is stopped [1]. It has been shown to be efficacious in reducing death and/or nonfatal myocardial infarction at 30 days in two different clinical indications – percutaneous coronary vascular intervention and the acute coronary syndromes: unstable angina and non-ST elevation myocardial infarction [2, 3]. A 3-year follow-up of the patients who entered the first trial (EPIC) with an acute coronary syndrome indicates a 60% reduction in mortality; overall the mortality reduction at the latest point of follow-up in the abciximab trials is 35% [2].

Thrombocytopenia is an often-cited complication of the use of GPIIb-IIIa receptor antagonists [1, 2, 3, 4]. In one study, it was recently estimated that profound thrombocytopenia (<20×10^9/l) during abciximab therapy affects 0.5% of patients [4]. Pseudothrombocytopenia is the consequence of ethylenediaminetetraacetate (EDTA)-activated platelet agglutination, resulting in a spuriously low platelet count [5]. It occurs due to presence of anti-platelet antibodies (IgG agglutinins) that are usually temperature dependent [6, 7, 8]. Pseudothrombocytopenia is an important differential diagnosis in acute thrombocyto-
penia in a patient treated with abciximab [9, 10]. The failure to differentiate pseudothrombocytopenia from thrombocytopenia could lead to the interruption of abciximab infusion and to unnecessary platelet transfusions [10].

In this study, we determine the incidence and temporal profile of both true and pseudothrombocytopenia after infusion of abciximab. Also, we evaluate the possible mechanism of each of these findings and try to provide criteria to help differentiate between the two phenomena.

**Patients and methods**

Sixty-six patients (46 men and 20 women) receiving their first exposure to the drug after an unstable coronary event/revascularization were eligible for our study. The age range of the patients was 36–74 years (mean age: 62 years). All the patients received an initial weight-based bolus of c7E3 Fab followed by a continuous infusion ranging from 12 to 17 h.

Platelets were monitored in all patients at the 2-h, 4-h, 12-h, 24-h, and 48-h intervals per protocol and more frequently if deemed necessary by the treating physician. The incidence of thrombocytopenia (defined as \( \leq 150,000/\mu l \) or a fall of \( \geq 40\% \) from baseline) and acute severe thrombocytopenia (defined as a platelet count \( \leq 20,000/\mu l \)) was evaluated. A peripheral blood smear was performed on all patients showing thrombocytopenia to determine the presence of pseudothrombocytopenia.

Patients who had received heparin or other drugs known to cause thrombocytopenia prior to receiving c7E3 therapy were excluded from the study.

**Results**

In our study, of the 66 patients evaluated, 26 patients (39.39%) developed thrombocytopenia, 17 (25.6%) developed non-severe thrombocytopenia, and 9 (13.6%) developed acute severe thrombocytopenia (platelet count \( \leq 20,000/\mu l \)) detected by automated Coulter technique. However, of these 26 patients, 18 (69.23%) were found to have pseudothrombocytopenia. Seven of the nine patients (77.7%) with acute severe thrombocytopenia and 11 of 17 patients (64.7%) with any degree of thrombocytopenia were found to have pseudothrombocytopenia (platelet clumping on a peripheral smear that resolved when repeat blood samples were tested in heparin-coated tubes).

Of the 11 patients who were diagnosed to have non-severe thrombocytopenia, and later shown to have pseudothrombocytopenia, only 4 samples revealed platelet clumping on their initial peripheral smears (the 2- and 4-h postinfusion samples). The remaining samples tested positive on subsequent blood draws, up to 24 h postinfusion. The relationship between c7E3 Fab therapy and true/pseudothrombocytopenia is depicted in Table 1.

The onset of any degree of true thrombocytopenia was consistently seen at 4 h after the infusion of c7E3 Fab was given. Platelet counts reduced further over the next 12 h.

The severity and the incidence of true and pseudothrombocytopenia were independent of the cumulative dose/infusion time of abciximab. Only two (3.03%) patients required platelet transfusions for bleeding episode (epistaxis) and/or decreasing hemoglobin associated with severe thrombocytopenia. The decrease in hemoglobin in the entire study group ranged from 0.1 to 1.3 g/dl.

No life-threatening hemorrhagic complications were recognized. Among the untreated true thrombocytopenic patients, platelet counts remained depressed for 48–72 h but returned to baseline in about 2 weeks. Interestingly, five of six subjects with true non-severe thrombocytopenia evaluated for possible disseminated intravascular coagulation (DIC) had positive laboratory findings (elevated D-dimer and decreased fibrinogen); however, none had an adverse outcome. The above DIC parameters returned to normal values within 2 weeks postinfusion of abciximab.

**Discussion**

In our study, 26 out of 66 patients (39.39%) developed thrombocytopenia. However, of these 26 patients, 18 (69.23%) were found to have pseudothrombocytopenia.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Relationship between c7E3 Fab therapy and true/pseudothrombocytopenia. (DIC=disseminated intravascular coagulation)</th>
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<tbody>
<tr>
<td></td>
<td>True thrombocytopenia (n=8)</td>
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<tr>
<td>Age range (years)</td>
<td>36–71 (mean: 61)</td>
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<tr>
<td>c7E3 Fab</td>
<td>0.25 mg/kg loading and 9 mg continuous</td>
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<td>Infusion time (h)</td>
<td>12–16 (mean: 15)</td>
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<td>Thrombocytopenia Onset</td>
<td>4 h (postinfusion)</td>
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<tr>
<td>Range</td>
<td>2,000–146,000/\mu l (mean: 51,000/\mu l)</td>
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<tr>
<td>DIC parameters Fibrinogen</td>
<td>Decreased</td>
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<tr>
<td>D-dimer</td>
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