A Comparison of Platelet Aggregation Between Diabetics and Non-diabetics Receiving Glycoprotein IIb/IIIa nhibitors During Percutaneous Coronary Intervention

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A. Study Purpose and Rationale

Agents resulting in glycoprotein IIb/IIIa platelet inhibition have been recently introduced in the practice of interventional cardiology [1-8]. Several large randomized trials have studied their use in unstable angina/non-Q-wave myocardial infarction (MI) and in the cardiac catheterization laboratory [9-18]. Results from the GOLD multicenter study demonstrated that decreasing platelet aggregation leads to less major adverse cardiac events (MACE: death, MI, or urgent target vessel revascularization) after percutaneous coronary intervention (PCI) [19]. In the GOLD trial >80% platelet inhibition appeared to correlate with less major adverse cardiac events Previously abciximab has been reported to produce >80% inhibition of platelet aggregation *ex vivo* and *in vitro*, the *in vivo* degree of GPIIb/IIIa inhibition and platelet aggregation during coronary intervention continues to be an area of active research.

Our study will compare the efficacy of IIb/IIIa inhibitors, as measured by platelet inhibition during percutaneous coronary intervention (PCI), in diabetic and non-diabetic patients. It has previously been shown that diabetic patients have worse outcomes following PCI as compared to non-diabetics [20,21 potential explanation is a difference in degree of platelet inhibition between the two groups.

B. Study Design and Statistical Analysis

The study is an observational prospective trial comparing diabetics to non-diabetics receiving abciximab with heparin in patients undergoing an elective PCI with a stent, or with an acute coronary syndrome (unstable angina or non-ST elevation MI) were considered eligible for the study.

Using an unpaired t-test the number of subject needed for enrollment, based on a 80% power (β) for detecting a 10% difference in platelet inhibition between diabetics and non-diabetics with a standard deviation (SD) of 10 is with $\alpha = 0.05$:

$$N=1 + 16\ (SD/effect)^2 = 1 + 16\ (10/10)^2 = 17$$

C. Study Procedure

Percutaneous coronary intervention

Percutaneous coronary intervention with a stent (PCI) is a well established procedure utilized in patients with known coronary artery disease. Briefly, the procedure involves catheter based technology that allow for percutaenous access to the coronary blood vessels of the heart. To access the vasculature an initial arterial puncture is made in a central artery (femoral or axillary). Contrast material is used to define the coronary vasculature and identify areas of blood vessel disease. A stent is deployed by inflating a balloon with an overlying stent in an area of vessel narrowing. Risks of the procedure include bleeding, arterial dissection, contrast reaction, and myocardial infarction. A procedure takes approximately 1 hour.

Determination of Platelet Aggregation

Analysis of platelet aggregation is a study procedure used for research purposes. Blood samples will be obtained at baseline (prior to drug infusion) and at 30 minutes. Using methods previously

described and validated samples are tested with a rapid function platelet assay, which evaluates the fibrinogen-induced platelet aggregation. Briefly, pharmacological blockade of GP IIb/IIIa receptors prevents the interaction between platelet GP IIb/IIIa receptors and fibrinogen-coated beads thereby diminishing agglutination in proportion to the degree of receptor blockade achieved. The light absorbance of the sample is measured as a function of time, and the rate of agglutination is quantified as platelet activation units (PAUs). In this study specimens are reported as a percentage of the baseline value.

D. Study Drugs

Abciximab is an FDA approved medication for patients undergoing elective PCI with a stent, or with an acute coronary syndrome (unstable angina or non-ST elevation MI). The drug is administered for a total of 12 hours. All heparin therapy is administered for the duration of the invasive procedure and terminated at the time that the patient is discharged from the catheterization lab. Abciximab is dosed as 0.25mg/kg bolus given at least 15 minutes before the intervention, followed by 0.125μg/kg/min for 12 hours. PCI commences following administration of the IIb/IIIa antagonist.

Known adverse drug effects include bleeding often separated into major and minor bleeding events with major events defined as CNS bleeds, bleeding requiring red blood cell transfusion, or hemodynamically significant bleeding.

E. Study Subjects

Patients undergoing an elective PCI with a stent, or with an acute coronary syndrome (unstable angina or non-ST elevation MI) were considered eligible for the study.

Patients were excluded from the study if they had a non-stentable primary lesion, prior history of thrombolytic therapy within 3 days, therapy with abciximab within the previous 15 days, serum creatinine > 2.0mg/dl, or any absolute or relative contraindication to anticoagulation.

F. recruitment of Subjects and Confidentiality

Patients being referred to the Columbia Presbyterian Medical Center catheterization laboratory will be approached for study enrollment. All patients will be followed by a predetermined number 1 through 100 and data will only be accessible to the study investigators.

G. Conflict of Interest

The investigator enrolling and analyzing the study data will be separate from the physicians performing the procedure. The investigators have no proprietary interest in the study drug and do not stand to benefit financially from the results of the trial.

H. Potential Harm

Known adverse drug effects include bleeding often separated into major and minor bleeding events with major events defined as CNS bleeds, bleeding requiring red blood cell transfusion, or hemodynamically significant bleeding. Based on the results of the TARGET Trial major bleeding events can be expected in 0.7% of patients receiving abciximab and minor bleeding events in up to 5% of patients.

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