Role of Parenteral Agents in Percutaneous Coronary Intervention for Stable Patients

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KEYWORDS

• Anticoagulation • Heparin • Glycoprotein IIb/IIIa receptor inhibition • Abciximab • Eptifibatide • Antithrombin • Bivalirudin

KEY POINTS

- Despite significant improvements, it remains important to carefully select anticoagulant agents in the percutaneous treatment of coronary disease with the dual goal of decreasing ischemic events and minimizing bleeding complications.
- In the "elective" population, glycoprotein IIb/IIIa receptor inhibitors tend to be reserved for higher-risk patients, for those not adequately pretreated with thienopyridines, or for those with a suboptimal procedural outcome.
- Unfractionated heparin continues to be a mainstay in the elective PCI population because of its ease of use, simple monitoring, and reversibility.
- Enoxaparin has been shown to have reduced bleeding outcomes, with ischemic events comparable with those in unfractionated heparin in patients undergoing PCI.
- Bivalirudin has become a popular agent across the spectrum of coronary disease, having demonstrated consistent reductions in bleeding and comparable ischemic events when compared with a heparin plus glycoprotein IIb/IIIa receptor inhibitor strategy.

INTRODUCTION

Optimal anticoagulation has proved to be a key component in the management of patients undergoing percutaneous coronary intervention (PCI). There has been a considerable evolution in pharmacotherapy for PCI since the early days of balloon angioplasty. Medications with variable modes of action are used to reduce complications by inhibiting thrombin formation, platelet activation, and platelet aggregation. These medications have targeted different portions of the coagulation cascade, and newer synthetic agents have been developed to specifically target factor Xa or thrombin in an attempt to minimize ischemic and bleeding complications, goals that are often at odds with one another.

The principal aims of pharmacotherapy during PCI are to avoid the adverse consequences related to iatrogenic plaque rupture from balloon inflation or stent deployment after PCI, and to reduce the risk of thrombus formation on intravascular PCI equipment during the procedure. Growing evidence supports use of a variety of agents in the setting of stable ischemic heart disease, unstable angina, non–ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI).

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Most data involving newer antithrombotic drugs focus on their use in acute coronary syndromes (ACS). However, the main aims of this article are to summarize the agents available for anticoagulation during elective PCI, to outline their mode of action, and to review the evidence supporting their use.

ANTIPLATELET THERAPY USING GLYCOPROTEIN IIB/IIIA INHIBITION

Platelet ability to adhere to abnormal surfaces and aggregate is mediated by surface membrane glycoprotein receptors that are expressed in increasing numbers with platelet activation and are potential targets for antiplatelet therapies. The platelet glycoprotein IIb/IIIa receptor plays a central role in platelet aggregation and thus forms an attractive target for therapy.

Abciximab, tirofiban, and eptifibatide are currently available for clinical use. Abciximab is a monoclonal antibody directed against the glycoprotein receptor, whereas tirofiban and eptifibatide are high-affinity non–antibody receptor inhibitors. The use of intravenous glycoprotein IIb/IIIa receptor inhibition (GPI) has been studied in patients with ACS and those undergoing intracoronary stent implantation, and has been associated with improved outcomes (**Fig. 1**).

The use of GPI in patients who are undergoing PCI depends on the clinical setting of PCI and the patient's risk for ischemic complications. Among patients undergoing elective PCI, considered low to intermediate risk for ischemic complications, the ISAR-REACT trial found no benefit for GPI at 30 days or in subsequent follow-up at 1 year in patients who had received clopidogrel (600 mg) at least 2 hours before the procedure.[1,2] The same lack of benefit was apparent for GPI in a subgroup analysis of lower-risk patients from the ESPRIT (Enhanced Suppression of the Platelet IIb/IIIa Receptor with Integrilin Therapy) trial.[3]

These trials were completed before the routine use of stents in patients undergoing PCI, before the use of clopidogrel prior to and/or at high dose before PCI, and before development of more potent oral antiplatelet agents. However, there is evidence that GPI did provide benefit among patients with ACS and some patients undergoing elective procedures (**Table 1**).

Based on available data, many operators limit the use of GPI in elective PCI to those patients considered higher risk, those who have not already received appropriate pretreatment with

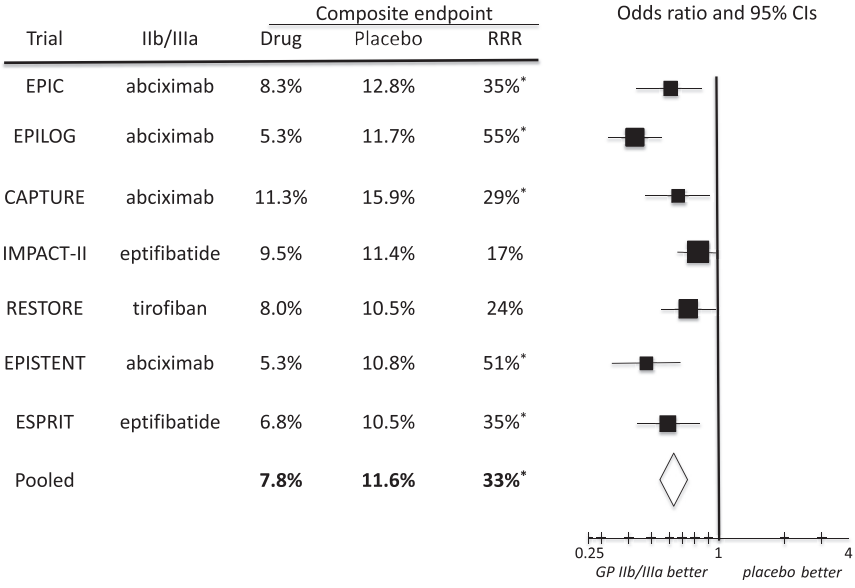

Fig. 1. Glycoprotein IIb/IIIa inhibitors in percutaneous coronary interventions. The composite end point is the risk of death, nonfatal myocardial infarction, or urgent revascularization at 30 days. *Statistical significance at $P<.05$. In EPIC, the abciximab bolus plus infusion group was compared with the placebo group. In EPILOG, the abciximab plus low-dose heparin and the abciximab plus standard-dose heparin groups were combined. In IMPACT-II, the low-dose and high-dose eptifibatide groups were combined. In EPISTENT, the stent plus abciximab group was compared with the stent plus placebo group. CIs, confidence intervals; GP, glycoprotein; RRR, relative risk reduction. (*From* Sabatine MS, Jang IK. The use of glycoprotein IIb/IIIa inhibitors in patients with coronary artery disease. Am J Med 2000;109(3):227; with permission.)

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