

Review: Glycoprotein IIb/IIIa inhibitors reduce combined end points in acute coronary syndromes

Bhatt DL, Topol EJ. Current role of platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes. *JAMA*. 2000 Sep 27;284:1549-58.

QUESTION

In patients with acute coronary syndromes (ACSs), are platelet glycoprotein IIb/IIIa (GP) inhibitors effective for reducing coronary events, including death?

DATA SOURCES

Studies were identified by searching MEDLINE (1966 to June 2000) and reviewing conference abstracts and presentations from the 1998 and 1999 annual meetings of the American Heart Association (AHA), American College of Cardiology (ACC), and European Society of Cardiology.

STUDY SELECTION

English-language, randomized, controlled, double-blind trials were selected if ≥ 500 patients were studied and GP inhibitors (abciximab, eptifibatide, tirofiban, or lamifiban) with or without heparin were compared with placebo.

DATA EXTRACTION

Data were extracted on mortality, myocardial infarction (MI), ischemic events, and major bleeding.

MAIN RESULTS

15 studies were evaluated, and 10 met the inclusion criteria. 33 081 patients (82% with ACS) were studied. GP inhibitors were given as a blockade during percutaneous coronary intervention (PCI) (6 studies) or for treatment of ACSs (4 studies). Composite end points were death and MI in all 10 studies, with the addition of refractory ischemia in 2 studies, urgent revascularization (UR) in 3 studies, UR and unplanned stenting in 2 studies, and UR and stent or balloon-pump placement in 1 study.

In the PCI studies, abciximab was compared with placebo in 4 studies (1 studied abciximab plus stents vs stents alone), and eptifibatide and tirofiban were compared with placebo in 1 study each. All 6 studies showed a decrease in composite end points, and 1 study showed a decrease in mortality. 3 studies had subgroup analyses: 1 showed a greater reduction in the rate of 30-day death, MI, and UR for patients with unstable angina ($P = 0.008$); in another study, only patients with elevated serum troponin-T levels showed a decreased risk for death or MI at 6 months ($P = 0.002$).

In the ACS treatment studies, tirofiban was evaluated in 2 studies (1 study used 2 doses), and eptifibatide and lamifiban (2 doses) were evaluated in 1 study each. All 4 studies showed a decrease in composite end points for at least 1 intervention group (the tirofiban-only study group in 1 study was stopped early because of an increase in mortality).

CONCLUSION

Glycoprotein IIb/IIIa inhibitors reduce composite end points in patients with acute coronary syndromes who are treated medically or with a percutaneous coronary intervention.

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COMMENTARY

The review by Bhatt and Topol shows benefit from GP inhibitors in patients who are having PCI or who have high-risk unstable angina. The ACC/AHA Unstable Angina Guidelines (1) for 2000 recommend that all patients with ACS who are having PCI (or who are at high risk) should receive GP inhibition. "Upstream" GP inhibition has been shown to reduce the size of an evolving non-ST-elevation MI, to reduce coronary thrombus, and to improve flow while also reducing major cardiac events. These benefits were part of the reason that the Treat Angina with Aggrastat and Determine Cost of Therapy with Invasive or Conservative Strategy-Thrombolysis in Myocardial Infarction (TACTICS-TIMI) 18 trial (2), which used upstream tirofiban, showed an advantage in early invasive strategy over that of the TIMI-IIIIB trial (3).

The authors discuss the Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) IV trial for ACSs (4), noting that the lack of benefit from abciximab in conservatively managed patients with unstable angina may be caused by patient selection or by the variable level of platelet inhibition achieved. In PCI, however, the as-yet-unpublished Do Tirofiban and ReoPro Give Similar Efficacy Outcomes Trial (TARGET) (5) found a lower rate of death, MI, or urgent revascularization with abciximab than with a different dose of tirofiban that was not approved by the U.S. Food and Drug

Administration. Data from another recent study show that the dose of tirofiban for PCI may not have been high enough at the early time points after the bolus (6). The potential need for a second bolus with "small molecule" agents has also been raised as an issue (7). Finally, although these agents cost more than heparin, they have a favorable cost-effectiveness ratio of approximately U.S. \$6000 per year of life saved in patients with PCI (8) and \$16 000 in patients with high-risk ACSs (9).

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