

Review: Glycoprotein IIb/IIIa inhibitors reduced death or MI in acute coronary syndromes not routinely scheduled for revascularization

Boersma E, Harrington RA, Moliterno DJ, et al. Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: a meta-analysis of all major randomised clinical trials. *Lancet*. 2002 Jan 19;359:189-98.

QUESTION

In patients with acute coronary syndromes not routinely scheduled for early coronary revascularization, what is the efficacy and safety of glycoprotein (GP) IIb/IIIa inhibitors?

DATA SOURCES

Trials reported from 1990 were identified by searching MEDLINE; reviewing scientific sessions abstracts in 3 cardiology journals; and scanning bibliographies of retrieved articles.

STUDY SELECTION

Studies were selected if they randomly allocated ≥ 1000 patients who had acute coronary syndromes without persistent ST-segment elevation to a GP IIb/IIIa inhibitor or to placebo or control therapy and if early (< 48 h) coronary revascularization during drug infusion was not recommended.

DATA EXTRACTION

Data from individual patients were extracted on baseline characteristics, medication details, death, myocardial infarction (MI), coronary artery bypass grafting (CABG), percutaneous coronary intervention (PCI), stroke, intracranial hemorrhage, major bleeding, and 30-day follow-up. The main efficacy outcome was a composite of death or nonfatal MI.

MAIN RESULTS

6 trials ($n = 31\,402$, mean age 64 y, 65% men) were included in the analysis. Patients

who received GP IIb/IIIa inhibitors had a lower risk for the composite of death or MI than did those who received placebo or control therapy at 5 days and 30 days, but they did not differ for mortality or receipt of either CABG or PCI (Table). Subgroup analysis showed that men who received GP IIb/IIIa inhibitors had a reduced risk for the composite end point, whereas women had an increased risk (Table). GP IIb/IIIa inhibitors increased risk for major bleeding complications (Table).

CONCLUSION

In patients with acute coronary syndromes not routinely scheduled for early coronary revascularization, glycoprotein IIb/IIIa inhibitors reduced the combined end point of death or myocardial infarction but increased major bleeding complications.

Source of funding: Not stated.

For correspondence: Dr. E. Boersma, University Hospital Rotterdam, Rotterdam, The Netherlands. E-mail boersma@thch.azr.nl. ■

Glycoprotein (GP) IIb/IIIa inhibitors vs placebo or control for acute coronary syndromes not routinely scheduled for coronary revascularization*

Outcomes	GP IIb/IIIa inhibitors	Placebo or control	RRR (95% CI)	NNT (CI)
Death or MI at 5 d	5.7%	6.9%	15% (7 to 22)	97 (67 to 223)
Death or MI at 30 d	11%	12%	8% (2 to 14)	106 (63 to 479)
Death at 5 d	1.2%	1.3%	7% (-14 to 24)	Not significant
Death at 30 d	3.4%	3.7%	9% (-3 to 18)	Not significant
CABG or PCI at 5 d	18%	20%	4% (-1 to 8)	Not significant
CABG or PCI at 30 d	38%	39%	1% (-2 to 4)	Not significant
Death or MI at 30 d (men only)	10%	13%	17% (10 to 23)	47 (36 to 82)
			RRI (CI)	NNH (CI)
Death or MI at 30 d (women only)	12%	10%	13% (1 to 26)	73 (37 to 1072)
Major bleeding at 30 d	2.4%	1.4%	61% (35 to 92)	121 (80 to 207)

*CABG = coronary artery bypass grafting; MI = myocardial infarction; PCI = percutaneous coronary intervention. Other abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article.

COMMENTARY

The acute coronary syndromes are unstable angina pectoris (UA) and non-ST-elevation MI (NSTEMI). The meta-analysis by Boersma and colleagues summarizes the treatment results of 4 platelet GP IIb/IIIa inhibitors from 6 randomized trials. The combined end point of death or nonfatal MI was reduced, but the individual end point reductions did not reach statistical significance. Of the drugs evaluated in the 6 trials, eptifibatid and tirofiban, but not lamifiban or abciximab, are currently approved for use in the United States for patients with acute coronary syndromes not routinely scheduled for coronary revascularization.

Two subgroup analyses are noteworthy. First, the treatment benefit was present in patients with positive troponin values (odds ratio [OR] 0.85, 95% CI 0.71 to 1.03) but not in those with negative values (OR 1.17, CI 0.94 to 1.44). One conclusion might be that use of these agents should be limited to patients with NSTEMI. Many patients diagnosed with UA are actually misdiagnosed and do not have acute vascular injury; thus, they would not benefit from antithrombotic therapy. Second, although not scheduled for coronary revascularization, 38% of patients actually had PCI or CABG within 30 days. They ben-

efited from treatment (OR 0.89, CI 0.80 to 0.98), whereas those who did not have revascularization did not appear to benefit (OR 0.95, CI 0.86 to 1.05). The 2002 American College of Cardiology–American Heart Association guidelines (1) conclude that “GP IIb/IIIa inhibitors are of substantial benefit in patients with UA/NSTEMI who undergo PCI; they are of modest benefit in patients who are not routinely scheduled to undergo PCI (but who may do so); and they are of questionable benefit in patients who do not undergo PCI.” The women in this analysis were more likely to have negative troponin values and less likely to have revascularization, which probably explains the reported sex difference in treatment effect. Current trials are evaluating combinations of GP IIb/IIIa antagonists, clopidogrel, and enoxaparin.

Eric R. Bates, MD
University of Michigan
Ann Arbor, Michigan, USA

Reference

- American College of Cardiology/American Heart Association. www.acc.org/clinical/guidelines/unstable/update%5Fexplantext.htm.