Intravenous glycoprotein IIb/IIIa receptor antagonists reduce mortality after percutaneous coronary interventions

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CRD summary
This review evaluated the impact of intravenous platelet glycoprotein IIb/IIIa receptor antagonists on mortality in patients undergoing percutaneous coronary intervention. Glycoprotein IIb/IIIa receptor antagonists were found to confer a significant and sustained decrease in the risk of death. Although full details of the methods of the review were not given, the conclusions are supported by the evidence presented.

Authors’ objectives
To evaluate the impact of intravenous platelet glycoprotein (GP) IIb/IIIa receptor antagonists on mortality in patients undergoing percutaneous coronary intervention (PCI).

Searching
MEDLINE, EMBASE and the Cochrane Controlled Trials Register were searched to April 2002. The search terms were ‘abciximab’, ‘eptifibatide’, ‘tirofiban’ and ‘lamifiban’, together with terms to identify controlled trials. The bibliographies of relevant articles and reviews were also checked.

Study selection

Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were included.

Specific interventions included in the review
The inclusion criteria stated comparisons of intravenous GP IIb/IIIa receptor antagonists (e.g. abciximab, eptifibatide, tirofiban, lamifiban) with placebo or no treatment. Studies that used different doses of concomitant heparin were acceptable. In the included trials, abciximab, eptifibatide and tirofiban were evaluated. In some studies heparin was used post-PCI. The doses of the drugs used were not stated in the review.

Participants included in the review
The inclusion criteria specified participants undergoing any PCI, elective or urgent/emergent: percutaneous transluminal coronary angioplasty, stent placement, or directional, rotational or excimer laser atherectomy. Studies were only included if both study arms were targeted for the same PCI. Studies where only selected participants eventually underwent PCI were excluded. In the included studies, the initial procedures were stent placement, percutaneous transluminal coronary angioplasty or atherectomy. Some of the targeted participants were people with acute myocardial infarction (MI); some also had a history of diabetes, hypertension, MI, PCI or coronary artery bypass graft. Both males and females were included, although the included studies had predominantly male participants (65% to 87% male). The mean ages ranged from 59 to 64 years.

Outcomes assessed in the review
The primary outcome of interest was death at 30 days and 6 months. Data on longer follow-up (1 to 3 years) were also looked at. The secondary outcomes included MI and a composite of major adverse cardiac events (MACE; i.e. death, MI or revascularisation) at 30 days and 6 months. The safety outcomes included major bleeding (assessed by the Thrombolysis in Myocardial Infarction criteria), severe/moderate bleeding (assessed by the Global Utilization of Streptokinase and TPA for Occluded Arteries criteria) and intracranial haemorrhage.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.
Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Two of the authors extracted the data independently. Any discrepancies were discussed and consensus was reached with the help of a third author. Data were extracted on study design, trial quality, participant characteristics and outcomes. In trials with more than two arms, arms using different dosing schedules were merged. The data were extracted on an intention-to-treat basis.

Methods of synthesis
How were the studies combined?
Risk ratios (RRs) and 95% confidence intervals (CIs) were calculated using fixed-effect and random-effects models. Fixed-effect results were reported unless the random-effects results differed, in which case random-effects results were reported. Subgroup analyses were performed for mortality according to patient population: acute MI versus non-acute MI, intended PCI, type of GP IIb/IIIa receptor antagonist, and heparin use post-PCI.

How were differences between studies investigated?
Heterogeneity was assessed using the chi-squared-based Q statistic (significant for P<0.10). Bias was evaluated by analysing subgroups of studies (based on large versus small and early versus late studies).

Results of the review
Nineteen placebo-controlled RCTs (20,137 participants) were included. Thirteen studies (11,607 participants) evaluated abciximab, 4 studies (6,297 participants) evaluated eptifibatide and 2 studies (2,234 participants) evaluated tirofiban. One study evaluating abciximab had four arms, so contributed two pertinent comparisons.

GP IIb/IIIa receptor antagonists significantly reduced mortality at 30 days (RR 0.69, 95% CI: 0.53, 0.90), at 6 months (RR 0.79, 95% CI: 0.64, 0.97) and for longer follow-up (RR 0.79, 95% CI: 0.66, 0.94). There was no significant between-study heterogeneity.

The results were similar for participants with or without acute MI, where heparin was used post-PCI, and in studies using stents versus those using other PCI procedures. GP IIb/IIIa receptor antagonists significantly reduced MI and MACE at 30 days and 6 months (P<0.001 for all).

Major bleeding was significantly increased in studies where heparin was continued post-PCI (RR 1.70, 95% CI: 1.36, 2.14). There was no excessive bleeding when heparin was discontinued (RR 1.02, 95% CI: 0.85, 1.24).

GP IIb/IIIa receptor antagonists did not increase the risk of haemorrhagic stroke (RR 0.89, 95% CI: 0.46, 1.72).

Authors' conclusions
In people undergoing PCI, the use of GP IIb/IIIa receptor antagonists provided a significant and sustained decrease in the risk of death. These data should not be generalised to people who are not likely to undergo PCI.

CRD commentary
This was a clearly written review with well-stated aims and inclusion criteria. The search was somewhat limited and it is possible that studies may have been missed. Full details of the methods of the review (e.g. study selection, validity assessment) were not given and the information about the included participants was limited. However, the authors only included RCTs, they clearly described the statistical methods used, and the meta-analysis was appropriate. The authors looked for heterogeneity and analysed the data to take into account differing clinical aspects of the studies. The results supported the authors' conclusions.
Implications of the review for practice and research
The authors did not state any implications for practice or further research.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.