A comparison of intracoronary with intravenous glycoprotein IIb/IIIa inhibitors during percutaneous coronary intervention in patients with acute coronary syndrome: a meta-analysis of randomized controlled trials

CRD summary
This review concluded that compared to intravenous administration, intra-coronary glycoprotein IIb/IIIa inhibitors did not significantly improve clinical outcomes in people undergoing percutaneous coronary intervention for acute coronary syndromes. However, there was an increase in target coronary flow and myocardial perfusion. The review appears generally well conducted and conclusions appear reasonable given the evidence presented.

Authors' objectives
To compare the effects of intra-coronary glycoprotein IIb/IIIa inhibitors to intravenous glycoprotein IIb/IIIa inhibitors, in people with acute coronary syndromes undergoing percutaneous coronary intervention.

Searching
PubMed, EMBASE and The Cochrane Library and were searched from January 1990 to November 2011; search terms were reported. Google Scholar (January 1990 to November 2011) and seven relevant websites were checked (January 2002 to November 2011). No language restrictions were applied.

Study selection
Randomised controlled trials (RCTs) were eligible if they compared intra-coronary to intravenous administration of glycoprotein IIb/IIIa inhibitors in patients who had acute coronary syndrome and were undergoing percutaneous coronary intervention. The primary outcomes of interest were short-term (one to three months) and mid/long-term (six or 12 months) mortality, reinfarction or target vessel revascularisation. Secondary outcomes were thrombolysis in myocardial infarction grade 3 flow, and thrombolysis in myocardial infarction myocardial perfusion grade 2 to 3 flow after intervention, left ventricular ejection fraction (after intervention within two weeks) and minor and major bleeding during hospital stay.

Most participants had ST-segment elevation myocardial infarction; some studies also included those with unstable angina or non ST-segment elevation myocardial infarction. Mean ages ranged from 59 to 75 years. In most studies the glycoprotein IIb/IIIa inhibitor was abciximab, in some tirofiban or eptifibatide. After bolus, dose abciximab was continuously intravenously infused for 12 hours, tirofiban for 36 hours and eptifibatide for 18 hours. Some studies used aspiration thrombectomy. Some drugs were delivered before angioplasty and some after thrombus aspiration. All participants were pre-treated with aspirin, and most with clopidogrel, but some with prasugrel. All were discharged with aspirin 75 to 100mg/day and clopidogrel 75mg/day or ticlopidine 250mg twice/day for one to 12 months. A single dose of unfractionated heparin was also administered, and this was supplemented if activated clotting time was less that 250 to 300 seconds during intervention. Percutaneous intervention was initiated within 12 hours of onset of chest pain.

Two authors independently assessed studies for inclusion.

Assessment of study quality
Quality was assessed on methods of randomisation, blinding, reporting of withdrawals, generation of random number and concealment of allocation. A point was awarded for each criterion met with a maximum score of five.

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Data were extracted in order to calculate odds ratios and 95% confidence intervals for dichotomous data, and mean differences and 95% confidence intervals for continuous data.

Two reviewers independently extracted data. Where necessary, authors were contacted for missing information.
Methods of synthesis
A random-effects model was used to calculate pooled odds ratios (ORs) and 95% confidence intervals (CIs), and weighted mean differences (WMD) and 95% confidence intervals. Heterogeneity was assessed using Cochran’s Q test and the I² statistic. Subgroup analysis investigated type of glycoprotein IIb/IIIa inhibitors (abiximab versus small molecule glycoprotein IIb/IIIa inhibitors). Sensitivity analyses only included studies containing patients with ST-segment elevation myocardial infarction. Publication bias was investigated using funnel plots and Egger’s test.

Results of the review
Eleven RCTs (3,655 participants) were included. One study included 2,065 participants, others ranged from 41 to 534 participants. Follow-up ranged from one to 17 months. Two studies scored 5 for quality, five scored 3 and four scored 2. Four did not report method of randomisation, and only two were double blinded. Tests showed no evidence of publication bias.

Compared to intravenous glycoprotein IIb/IIIa inhibitors, intra-coronary glycoprotein IIb/IIIa inhibitors had no statistically significant effect on short-term mortality (I²=14%; six trials), reinfarction (I²=0%; six trials) or target vessel revascularisation (I²=0%; five trials). Results were similar at six months (three trials) and 12 months (two trials).

Subgroup analyses and sensitivity analyses of short term outcomes showed similar results to the main analyses.

Compared to intravenous glycoprotein IIb/IIIa inhibitors, intra-coronary glycoprotein IIb/IIIa inhibitors were associated with a significant increase in thrombolysis in myocardial infarction grade 3 flow rate (OR 1.48, 95% CI 1.06 to 2.06; I²=35%; 10 trials) and thrombolysis in myocardial infarction myocardial tissue level perfusion grade 2 to 3 (OR 2.63, 95% CI 1.53 to 4.51; I²=49%; six trials). There was no statistically significant difference in left ventricular ejection fraction (I²=60%; six trials). Six trials reported on bleeding: there was no statistically significant difference in minor bleeding (I²=0%) or major bleeding (I²=11%).

Authors’ conclusions
Compared to intravenous administration, intra-coronary glycoprotein IIb/IIIa inhibitors did not significantly improve clinical outcomes in people undergoing percutaneous coronary intervention for acute coronary syndromes. However, there was an increase in target coronary flow and myocardial perfusion, without an increased risk of bleeding.

CRD commentary
Review aims were clearly stated in terms of inclusion criteria. The search was not restricted by language or publication status, which reduced the possibility of language or publication bias. The methods of study selection and data extraction were those aimed at reducing possible reviewer error or bias, those for quality assessment weren’t clear. Quality was assessed using a scoring system, although helpfully details for individual items were also presented. The methods of synthesis appeared appropriate and heterogeneity was assessed and explored.

The review appears well conducted and conclusions appear reasonable given the evidence presented.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.
Research: The authors stated that adequately powered RCTs with longer follow-up that look at clinical outcomes were needed to assess intracoronary glycoprotein IIb/IIIa inhibitors in people undergoing percutaneous coronary intervention for acute coronary syndromes.

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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.