Efficacy and safety of abciximab on acute myocardial infarction treated with percutaneous coronary interventions: a meta-analysis of randomized, controlled trials

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CRD summary
The use of abciximab as an adjuvant treatment to percutaneous coronary interventions for acute myocardial infarction reduced mortality, major cardiac events and revascularisation. This occurred with stenting, but not with balloon angioplasty. A 70 U/kg heparin bolus must be used to prevent major bleeding. The methodological quality of the included studies was not reported, so the results should be interpreted with caution.

Authors' objectives
To determine the efficacy and safety of abciximab for acute myocardial infarction (MI) in patients treated with percutaneous coronary interventions (PCIs).

Searching
MEDLINE and the Cochrane Controlled Trials Register were searched from 1996 to July 2003. In addition, the scientific session abstracts of the American Heart Association, the American College of Cardiology, the European Society of Cardiology, and the Transcatheter Therapeutics Meetings were searched from 1998 to 2003. The reference lists of identified studies checked for further relevant trials. The authors did not report the search terms or state whether any language restrictions were applied to the search.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials with patient follow-up of at least 30 days were eligible for inclusion. The length of follow-up in the included studies was 1 month in one study and 6 months in all others.

Specific interventions included in the review
Studies evaluating the use of abciximab in addition to PCIs were eligible for inclusion. All included studies used abciximab in addition to the following PCIs: stenting, balloon angioplasty, and directional arterectomy. One study administered an initial heparin bolus of 100 U/kg, while all others used the current standard schedule of heparin (initial heparin bolus 70 U/kg).

Participants included in the review
Patients with clinical and electrocardiographic diagnoses of ST elevation acute MI who received revascularisation with a PCI within 48 hours of the onset of pain were eligible for inclusion.

Outcomes assessed in the review
The authors did not state any inclusion criteria in relation to outcomes. Mortality, reinfarction, target vessel revascularisation (TVR), major cardiac events (MACE) and major bleeding were included in the review. Reinfarction was defined as 'the presence of typical chest pain, new ST-segment changes, and an increase in creatine kinase of at least 50% over the previous level'. TVR was described as 'urgent or elective coronary artery bypass surgery or repeat percutaneous transluminal angioplasty involving the target vessel'. MACE included death from any cause, reinfarction, and any repeated intervention or revascularisation of the target vessel as a result of ischaemia. Major bleeding was defined as 'important or life-threatening blood loss with substantial haemodynamic compromise requiring transfusion'.

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
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. For each trial, the data from the longest follow-up were extracted; the data were extracted on an intention-to-treat basis. An odds ratio (OR) with 95% confidence interval (CI) was calculated for each trial.

Methods of synthesis
How were the studies combined?
The ORs for each trial were pooled using a fixed-effect model (Mantel-Haenszel method). Where there was a high level of statistical heterogeneity between the studies, a random-effects model was used.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared test. Trials that encouraged stenting as the primary approach and those that used balloon angioplasty preferentially were analysed separately. Trials that used higher dosages of heparin (initial bolus 100 U/kg) and those that used lower dosages (initial bolus 70 U/kg) were also analysed separately in order to determine the effects of heparin dosage on major bleeding.

Results of the review
Six randomised controlled trials with a total of 3,755 participants were included in the review.

Overall, there were significantly fewer deaths among patients receiving abciximab (3.4%) than patients in the control group (4.9%); the OR was 0.70 (95% CI: 0.50, 0.97, P=0.03). TVR occurred in significantly fewer patients receiving abciximab than in those not receiving abciximab (11.8% versus 14.4%); the OR was 0.79 (95% CI: 0.65, 0.96, P=0.02). The number of patients that experienced MACE was significantly smaller in the abciximab group (17%) than in the control group (21.1%); the OR was 0.76 (95% CI: 0.65, 0.90, P=0.02). There was no statistically significant difference between patients receiving abciximab and the control group for reinfarction. No statistically significant heterogeneity was detected across the studies.

In studies where stenting was used preferentially (4 studies and one arm of another trial), significantly fewer patients receiving abciximab had TVR (8.5%) than patients in the control group (11.6%); the OR was 0.71 (95% CI: 0.53, 0.94, P=0.02). The number of patients experiencing MACE was also smaller in the abciximab group (13.7% versus 19.1%); the OR was 0.66, (95% CI: 0.53, 0.84, P=0.0005). However, abciximab had no statistically significant effect on mortality or reinfarction in comparison with the control group.

In one study and one arm of another study, angioplasty and directional arterectomy were used and the use of stenting was discouraged. These studies found no significant differences between patients receiving abciximab and patients in the control group in terms of mortality, reinfarction, TVR or MACE.

Overall, patients receiving abciximab were more likely to experience major bleeding than patients in the control group (5.9% versus 4.3%); the OR was 1.39 (95% CI: 1.03, 1.87, P=0.03). When an initial heparin bolus dosage of 100 U/kg was used, major bleeding was also significantly more frequent in patients receiving abciximab (16.6% versus 9.5% in the control group); the OR was 1.89 (1 study; 95% CI: 1.10, 3.28, P=0.02). However, when an initial heparin bolus dosage of 70 U/kg was used, abciximab had no significant effect on major bleeding relative to the control (5 studies).

Authors' conclusions
The use of abciximab in patients treated with PCIs for acute MI can reduce mortality, TVR and MACE. These benefits were generally seen in patients treated with stenting, but not in those receiving balloon angioplasty. Abciximab can increase the risk of major bleeding, but the current schedule for this drug infusion (which included an initial heparin bolus of 70 U/kg) did not increase major haemorrhagic complications.
CRD commentary
The authors set out a clear objective at the beginning of the review and the inclusion criteria were clearly defined. Two databases were searched, and an attempt was made to obtain further trials from other sources. However, the authors did not state if they imposed any language restrictions on the search. The authors did not assess the validity of the included studies, nor did they give any details of how the papers were selected or the data extracted. If these procedures were carried out by one reviewer alone, there is an increased risk of introducing bias.

Sufficient details of the individual studies were provided. Despite some differences in the patients included in each of the primary studies, no statistical heterogeneity was detected. The pooling of studies seemed appropriate, especially given that sensitivity analyses were used to investigate the effects of intervention differences on the results. The authors' conclusions are an accurate reflection of the results they presented. However, given that some details of the review methodology were not reported, and the quality of the primary studies was unknown, the results should be interpreted with caution.

Implications of the review for practice and research
Practice: The authors stated that abciximab should be considered as an adjunctive therapy for patients being treated for acute MI with mechanical recanalisation. They suggested that a 70 U/kg heparin bolus must be used to prevent major bleeding. However, the authors pointed out that the majority of trials were carried out in centres which had expertise in coronary interventions for acute MI, so the generalisation of the results to clinical practice should be done with caution.

Research: The authors did not state any implications for further research.

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