Safety and efficacy of early administration of tirofiban in patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention: a meta-analysis
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CRD summary
The review concluded that early administration of tirofiban was safe in patients undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. There were no differences between early and late tirofiban administration in terms of angiographic and clinical outcomes. The relatively limited evidence means that the recommendations for further research appear appropriate.

Authors' objectives
To compare early versus late administration of tirofiban in patients undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction.

Searching
MEDLINE, EMBASE and Cochrane CENTRAL were searched up to September 2012 with no language restrictions. Search terms were reported. Web of Science and relevant journals were consulted.

Study selection
Randomised controlled trials that compared early (emergency department or ambulance) versus late (catheterization laboratory) administration of tirofiban in patients undergoing primary percutaneous coronary intervention (PPCI) for ST-segment elevation myocardial infarction (STEMI) were eligible. Studies with follow-up data in less than 90% of patients were excluded. The authors did not state how many reviewers selected the studies.

Patient age ranged from 57 to 68 years. Most participants were male. In most studies, patients were preprocedurally treated with aspirin and clopidogrel. Aspirin and thienopyridines were used as postintervention antiplatelet therapy. Where reported, mean door to balloon time ranged from 39 to 168 minutes. The most common tirofiban regimens was a bolus of 10μg/kg followed by an infusion of 0.15μg/kg min⁻¹ for 24 hours.

Assessment of study quality
Study quality was assessed using the Cochrane risk of bias tool. It appeared that quality assessment was performed by two reviewers independently, with disagreements resolved by discussion.

Data extraction
Two reviewers independently extracted data as risk ratios and mean differences on the outcomes: death at 30 days (primary endpoint), re-myocardial infarction at 30 days, post-procedural Thrombolysis In Myocardial Infarction (TIMI) flow grade 3, and corrected TIMI frame count (CTFC) and major and minor bleeding. Definitions of outcomes were provided. Disagreements were resolved by consensus. In case of missing or unclear data, attempts were made to contact study authors.

Methods of synthesis
A meta-analysis was used to pool risk ratios and weighted mean differences along with 95% confidence intervals (CI). Heterogeneity was quantified using $I^2$. Where $I^2$ was above 50% a random-effects model was used and otherwise a fixed-effect model was employed. Publication bias was assessed using a funnel plot.

Results of the review
Eight trials were included (1,577 patients, 58 to 507). Reporting of study designs had multiple gaps. Only four of the eight trials reported adequate randomisation. Two trials reported adequate allocation concealment methods. Five studies were unclear about whether they used blinding. Six out of eight studies had no loss to follow-up.

There were no statistically significant differences in incidence of 30-day mortality (RR 1.69, 95% CI 0.69 to 4.13; five
trials) and re-myocardial infarction (RR 0.71, 95% CI 0.21 to 2.35; five trials) between early and late administration of tirofiban. There were no differences in post-procedural TIMI flow grade 3 (eight trials) and Corrected TIMI Frame Count (three trials) between the two groups. No significant difference was observed in hospital minor bleeding (three trials) and hospital (five trials) and 30-day major bleeding (four trials) between the two groups. There was no evidence of significant heterogeneity except for Corrected TIMI Frame Count (51%).

Authors' conclusions
Early administration of tirofiban was safe in patients undergoing primary percutaneous coronary intervention for STEMI. There were no differences between early and late administration of tirofiban in terms of angiographic and clinical outcomes.

CRD commentary
The review question and selection criteria were clearly reported. Several bibliographic sources were consulted. There were no restrictions on language. Attempts were made to minimise reviewer bias during data extraction and quality assessment but not when selecting the studies. The authors stated that studies with less than 90% follow-up were excluded; it was unclear how many studies were excluded based on this criterion. Reporting of study designs had gaps in most trials (particularly regarding risk of selection bias) and this made assessment of study quality somewhat difficult.

Synthesis methods appeared generally appropriate but a different meta-analytic model would have better accounted for studies with no events. Most results had wide confidence intervals which suggested that the number of participants included in the analyses was insufficient to detect a meaningful effect. Therefore the recommendations for further high-quality trials are likely to be appropriate.

Implications of the review for practice and research
Practice: The authors stated that the dose given in most of the included studies was suboptimal. They stated that a high-dose bolus (25μg/kg·1.3 minute⁻¹ and infusion of 0.15μg/kg·1·minute⁻¹ for 24 to 48 hours) tirofiban is recommended and safe.

Research: The authors stated that more high-quality randomised clinical trials were needed to explore the efficacy of adequate earlier administration of tirofiban in patients undergoing primary percutaneous coronary intervention.

Funding
Not stated.

Bibliographic details

PubMedID
24622446

DOI
10.3760/cma.j.issn.0366-6999.20131795

Original Paper URL

Indexing Status
Subject indexing assigned by NLM

MeSH
Fibrinolytic Agents /adverse effects /therapeutic use; Humans; Myocardial Infarction /drug therapy /surgery; Percutaneous Coronary Intervention /methods; Thrombolytic Therapy; Tyrosine /analsogs & derivatives
AccessionNumber
12014019079

Date bibliographic record published
26/03/2014

Date abstract record published
12/06/2014

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.