Benefits of pharmacological facilitation with glycoprotein IIb-IIIa inhibitors in diabetic patients undergoing primary angioplasty for STEMI: a subanalysis of the EGYPT cooperation


CRD summary
This individual patient data meta-analysis concluded that early administration of glycoprotein IIb-IIIa inhibitors in diabetic patients with ST-segment elevation myocardial infarction undergoing primary angioplasty was associated with significant benefits in angiographic endpoints, without significant benefits in mortality rates. However, poor reporting of review methodology means that some caution is required in interpreting these conclusions.

Authors' objectives
To assess the benefit of primary angioplasty facilitated by the use of early glycoprotein IIb-IIIa inhibitors in patients with diabetes.

Searching
MEDLINE and EMBASE were searched without language restrictions from January 1990 to October 2007. Search terms were reported. Scientific session abstracts of four relevant journals were also searched.

Study selection
Randomised controlled trials (RCTs) of early glycoprotein IIb-IIIa inhibitor facilitation of primary angioplasty in patients with diabetes with ST-segment elevation myocardial infarction were eligible for inclusion. The comparator was late administration of glycoprotein IIb-IIIa inhibitors. Early administration of glycoprotein IIb-IIIa inhibitors was defined as administration begun in the ambulance, in a community hospital before or during transportation to percutaneous coronary intervention centres, or in an emergency room or intensive care unit of percutaneous coronary intervention hospitals.

The outcomes assessed were: angiographic (including pre- and post-procedural TIMI 3 flow and distal embolisation); myocardial perfusion (including myocardial blush); ST-segment resolution; enzymatic infarct size and abortion of myocardial infarction; and mortality and safety (including major bleeding complications).

In the included trials, the molecules assessed were abciximab, tirofiban and eptifibatide. Patients in the included studies had a median age of 62 years (range 56 to 70 years) in the early administration groups, and 67 years in the late administration groups (range 58 to 75); a majority (70.7% and 68.9%) were male. Approximately 40% of the patients were smokers.

The authors did not state how the papers were selected for the review.

Assessment of study quality
The data sets were checked for completeness and consistency, and compared with any publications. Queries were resolved by correspondence with the study investigators.

The authors did not state how many reviewers performed the data verification.

Data extraction
Individual patient data (IPD) were obtained from the trial investigators and managed on an intention-to-treat basis. Angiogram and electrocardiogram (ECG) data were provided by the principal investigators.

Methods of synthesis
The data were combined in modified Mantel-Haenszel random-effects meta-analyses. Peto odds ratios (OR) with 95%
confidence intervals (CI) were calculated for dichotomous variables; weighted mean differences (WMDs) with 95% confidence intervals were calculated for continuous outcomes. Survival analyses were calculated using stratified Cox-regression analysis and non-stratified Kaplan-Meier curves were presented. Heterogeneity between trials was assessed using the I² statistic.

**Results of the review**

Individual patient data (IPD) were obtained from 11 of the 14 trials (1,662 patients) that met the inclusion criteria; 281 of the patients were diabetic. Of these 281 patients, 133 were randomised to early administration of glycoprotein IIb-IIIa inhibitors and 148 to late administration.

**Clinical outcomes**: Early use of glycoprotein IIb-IIIa inhibitors was not associated with significant benefits in mortality rate (hazard ratio 0.85, 95% CI 0.38 to 1.87) or in major bleeding complications (Peto OR 2.39, 95% CI 0.23 to 24.52; seven RCTs).

**Angiographic endpoints**: Early use of glycoprotein IIb-IIIa inhibitors was associated with significant improvements in both pre-procedural (Peto OR 2.33, 95% CI 1.27 to 4.26; 10 RCTs) and post-procedural (Peto OR 2.76, 95% CI 1.37 to 5.54; 10 RCTs) TIMI three flow. Early use was also associated with statistically significant benefits in distal embolisation (Peto OR 0.45, 95% CI 0.21 to 0.99; seven RCTs) and myocardial blush (Peto OR 1.81, 95% CI 1.02 to 3.21; nine RCTs). There was no statistically significant benefit in ST-segment resolution (10 RCTs) or enzymatic infarct size (nine RCTs).

**Authors’ conclusions**

Early administration of glycoprotein IIb-IIIa inhibitors in diabetic patients with ST-segment elevation myocardial infarction undergoing primary angioplasty was associated with significant benefits in terms of pre-procedural and post-procedural TIMI flow, and improved myocardial perfusion, without significant benefits in the mortality rate. However, caution should be exercised in extrapolating the results to the majority of patients in this group.

**CRD commentary**

The review question and the inclusion criteria were clear. Two relevant databases and some additional sources were searched without language restrictions, making the omission of relevant studies or the introduction of language bias less likely. The authors did not report using methods designed to reduce reviewer bias and error at any stage of the review process.

Appropriate steps were taken to verify the individual patient data. The statistical synthesis was appropriate. The authors’ cautious conclusions reflected the results of the review, but poor reporting of aspects of the review process means that some caution may be required in assessing their reliability.

Several authors disclosed financial links with pharmaceutical companies that manufactured glycoprotein IIb-IIIa inhibitors.

**Implications of the review for practice and research**

**Practice**: The authors stated that, while caution should be exercised in extrapolating the results of this meta-analysis to the great majority of ST-segment elevation myocardial infarction patients with diabetes undergoing primary angioplasty, facilitation with glycoprotein IIb-IIIa inhibitors may be considered for this population.

**Research**: The authors stated that the results of additional large RCTs are required for a more definitive answer as to the benefits of early glycoprotein IIb-IIIa inhibitors in ST-segment elevation myocardial infarction patients with diabetes.

**Funding**

None.

**Bibliographic details**

PubMedID
19030969

DOI
10.1007/s11239-008-0296-9

Original Paper URL
http://www.springerlink.com/content/6032335453784219/

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Angioplasty; Diabetes Mellitus /drug therapy; Diabetic Angiopathies /prevention & control /surgery; Humans; Myocardial Infarction /surgery; Platelet Aggregation Inhibitors /therapeutic use; Platelet Glycoprotein GPIIb-IIIa Complex /antagonists & inhibitors; Randomized Controlled Trials as Topic /statistics & numerical data; Treatment Outcome

AccessionNumber
12009110003

Date bibliographic record published
14/04/2010

Date abstract record published
10/11/2010

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.