
Low-molecular-weight heparins in conjunction with thrombolysis for ST-elevation acute myocardial infarction: a critical review of the literature

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CRD summary

This review concluded that subcutaneous administration of dalteparin, enoxaparin or reviparin in hospital, as an adjunct to various thrombolytics in ST-elevation acute myocardial infarction, appears feasible and at least as effective and safe as intravenous unfractionated heparin. Owing to shortcomings in the review methodology, the conclusions have to be regarded with caution.

Authors' objectives

To evaluate the effectiveness of low molecular weight heparins (LMWH), in association with thrombolysis, in ST-elevation acute myocardial infarction (STEMI).

Searching

MEDLINE was searched from 1995 to December 2005; the search terms were reported. In addition, reference lists and cardiology websites were screened. Only English language publications were eligible.

Study selection

Study designs of evaluations included in the review

Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review

Studies comparing subcutaneous LMWH with placebo or unfractionated heparin (UFH) in association with thrombolysis were eligible for inclusion. The included studies evaluated dalteparin, enoxaparin and reviparin.

Participants included in the review

Patients with STEMI undergoing treatment with thrombolysis were eligible. No further information on the patients in the included studies was provided.

Outcomes assessed in the review

Inclusion criteria for the outcomes were not specified. The included studies reported various clinical outcomes such as arterial embolisms, mortality and adverse events at various follow-up points.

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, but stated that the quality of data was determined by publication in a peer-reviewed journal.

Data extraction

The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis

How were the studies combined?

The studies were grouped by drug and individual study results were presented in a narrative synthesis.

How were differences between studies investigated?

Some differences between the studies were apparent from tables and the text.

Results of the review

Twelve RCTs (n=26,831) were included in the review.

Dalteparin (3 RCTs).

One RCT found that dalteparin was superior to placebo on left ventricular thrombosis and arterial thromboembolism on day 9, with no effects on the reinfarction or mortality rates; however, dalteparin was associated with a higher risk of major and minor bleedings. A second RCT found no significant effect on Thrombolysis in Myocardial Infarction (TIMI) grade 3 flow in the infarct related artery (IRA), but TIMI 0 to 3 flow and its combination with intraluminal thrombus were significantly less frequent in the dalteparin group; the rate of clinical events were also lower in the dalteparin group compared with placebo. Compared with UFH, dalteparin had no significant effect on clinical events and on the IRA late patency, but less thrombus.

Enoxaparin (8 RCTs).

Enoxaparin was statistically superior to placebo regarding medium-term death, reinfarction and angina rate in 2 RCTs. It was also superior to UFH for in-hospital and medium-term occurrence of death, reinfarction and angina in 2 RCTs. Study results varied regarding IRA patency rates. One trial reported a higher incidence of intracranial haemorrhage, twice that obtained with UFH.

Reviparin (1 RCT).

Reviparin significantly reduced early- and medium-term mortality and reinfarction rates without increasing overall stroke rates in comparison to placebo. Life-threatening and major bleeding reported at 7 days were significantly more common in the treatment group.

Cost information

One RCT suggested that the cost of in-hospital treatment is about one half less than that with UFH, despite enoxaparin being more expensive.

Authors' conclusions

Dalteparin, enoxaparin or reviparin, administered in hospital subcutaneously, as an adjunct to various thrombolytics in STEMI, appear feasible and at least as effective and safe as intravenous UFH.

CRD commentary

The review addressed a clear question, but few inclusion criteria were specified. The search was limited, restricted to English language publications, and no attempts were made to locate unpublished material. It is therefore possible that pertinent studies might have been missed and that language and publication bias might have been introduced into the review. The validity of the included studies was not assessed. No attempts to avoid reviewer bias and errors during the various review processes were reported. The decision to present the studies in a narrative was reasonable given the variation in outcome measures, but little attempt was made to further synthesise the findings. Given the limitations in the review methodology and the heterogeneity between studies, the conclusions have to be regarded with caution.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors stated that researchers should address the use of LMWH in elderly patients, in patients with severe renal insufficiency, and in conjunction with glycoprotein IIb/IIIa inhibitors and percutaneous coronary interventions.

Bibliographic details

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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.