
Adjunctive benefits from low-molecular-weight heparins as compared to unfractionated heparin among patients with ST-segment elevation myocardial infarction treated with thrombolysis: a meta-analysis of the randomized trials

De Luca G, Marino P

CRD summary

This review found that low molecular weight heparins are associated with a reduction in reinfarction and a trend towards reduced mortality, but with a higher risk of major bleeding complications, compared with unfractionated heparin. These conclusions are likely to be reliable, but should be interpreted with some degree of caution given the failure to assess the validity of the included studies.

Authors' objectives

To compare low molecular weight heparins (LMWHs) with unfractionated heparin (UFH) in patients with ST-segment elevation myocardial infarction (STEMI) treated with thrombolysis.

Searching

MEDLINE and the Cochrane CENTRAL Register were searched from 1990 to June 2007; the search terms were reported. Relevant conference proceedings were screened and abstracts and slide presentations were included. No language restrictions were applied.

Study selection

Randomised controlled trials (RCTs) that compared LMWHs with UFH in patients with STEMI treated with thrombolysis were eligible for inclusion. The thrombolytic treatments used were tenecteplase, alteplase, streptokinase, urokinase and anistreplase, or a combination of these. The LMWHs assessed in the included studies were enoxaparin, dalteparin and parnaparin. Treatment duration ranged from 48 hours to 8 days. Inclusion criteria were not defined in terms of the outcomes. The outcomes assessed in the review were mortality and reinfarction at 30-day follow-up, and major bleeding complications.

The authors did not state how the studies 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 data were extracted on an intention-to-treat basis. Data for dichotomous data were extracted as odds ratios (ORs), together with the corresponding 95% confidence intervals (CIs). If the data were incomplete, authors were contacted for further information.

two reviewers independently extracted the data, with any disagreements resolved through consensus.

Methods of synthesis

Pooled ORs were calculated using the Mantel-Haenszel fixed-effect model. Pooled numbers-needed-to-treat (NNT) were also reported. Heterogeneity was assessed using the Breslow-Day test ($p < 0.10$ considered to indicate evidence of heterogeneity). A meta-regression was used to investigate the association between the patient's risk profile and mortality benefits from LMWH.

A funnel plot was used to visually assess publication bias, while a linear regression approach was used to statistically assess funnel plot asymmetry.

Results of the review

Eight RCTs (n=27,758) were included .

There was a trend towards reduced 30-day mortality (OR 0.92, 95% CI: 0.84, 1.01, p=0.08; NNT 167) and a significant reduction in the risk of reinfarction at 30 days (OR 0.65, 95% CI: 0.58, 0.74, p<0.0001; NNT 62) among patients treated with LMWH compared with those treated with UFH. There was a higher risk of major bleeding complications among those treated with LMWH than among those treated with UFH (OR 1.37, 95% CI: 1.16, 1.61, p<0.001). There was no evidence of heterogeneity for any of the analyses.

There was no association between patient risk profile and benefits in mortality (p=0.11).

The results of the assessment of publication bias were not reported.

Authors' conclusions

LMWHs are associated with a reduction in reinfarction and a trend towards reduced mortality, but with a higher risk of major bleeding complications.

CRD commentary

The review addressed a focused question that was supported by clearly defined inclusion criteria in terms of the intervention, participants and study design. The search was adequate and included some attempts to locate unpublished studies. Appropriate steps were taken to minimise bias and errors in the extraction of data, but it is unclear whether such steps were also taken at the study selection stage. A formal validity assessment was not undertaken, so the reliability of the included studies is unclear. Relevant study details were tabulated clearly and the results were plotted on forest plots. The meta-analysis was appropriate. Overall, the authors' conclusions are likely to be reliable, but should be interpreted with some degree of caution given the failure to assess the validity of the included studies.

Implications of the review for practice and research

Practice: The authors stated that, based on the findings of the review and additional practical advantages associated with LMWHs, these should be considered instead of UFH in patients with STEMI treated with thrombolysis.

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

Funding

Not stated.

Bibliographic details

De Luca G, Marino P. Adjunctive benefits from low-molecular-weight heparins as compared to unfractionated heparin among patients with ST-segment elevation myocardial infarction treated with thrombolysis: a meta-analysis of the randomized trials. *American Heart Journal* 2007; 154(6): 1085.e1-1085.e6

PubMedID

18035079

DOI

10.1016/j.ahj.2007.08.029

Indexing Status

Subject indexing assigned by NLM

MeSH

Drug Therapy, Combination; Fibrinolytic Agents /therapeutic use; Heparin /therapeutic use; Heparin, Low-Molecular-Weight /therapeutic use; Humans; Myocardial Infarction /drug therapy /mortality; Thrombolytic Therapy

AccessionNumber

12007004133

Date bibliographic record published

09/08/2008

Date abstract record published

03/11/2008

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.