Comparison of low molecular weight heparin with unfractionated heparin during percutaneous coronary interventions: a meta-analysis

CRD summary
This review found that efficacy and bleeding risk of low-weight molecular heparin in patients who underwent percutaneous coronary interventions were similar to those observed with unfractionated heparin. Methodological flaws and the unknown quality of the included studies mean that the authors' conclusions should be interpreted with caution.

Authors' objectives
To evaluate the efficacy and safety of low-molecular weight heparin (LMWH) compared to unfractionated heparin in patients undergoing percutaneous coronary interventions (PCI) for acute coronary syndromes.

Searching
PubMed, EMBASE and The Cochrane Library databases and Google Scholar were searched for relevant studies; search terms were reported. References from reviews, posters and oral presentations at international meetings of the American Heart Association, American College of Cardiology and European Society of Cardiology were checked. It was not clear where there were any language and date restrictions.

Study selection
Randomised controlled trials (RCTs) that compared intravenous or subcutaneous LWMH with unfractionated heparin with or without glycoprotein IIb/IIa inhibitors in patients who underwent elective or urgent PCI were eligible for inclusion. Studies with concurrent administration of thrombolytics were excluded. The primary efficacy endpoint was defined as a composite of non-fatal myocardial infarction and death with or without target vessel revascularisation. The safety endpoint was a composite of thrombolysis in myocardial infarction (TIMI) major or minor bleeding (as defined in the review).

The principal indications for PCI of the patients in the included trials were stable angina, unstable angina and non-ST elevation myocardial infarction. The LMWH treatments were enoxaparin, most commonly administered intravenously at a dose of 0.75mg/kg body weight. Other LMWH treatments were deltapan and reviparin. The dose of unfractionated heparin was titrated to keep activated clotting time above 300 seconds. Antiplatelet treatments given were aspirin, thienopyridin, clopidogrel, plavix, and ticlopidine. Glycoprotein IIb/IIa inhibitors were given concurrently in most trials. The efficacy endpoints varied across the trials. Follow-up ranged from 24 hours to one year.

The authors did not state how many reviewers performed study selection.

Assessment of study quality
The authors did not state they evaluated methodological quality.

Data extraction
Data were extracted on an intention-to-treat basis to calculate relative risks (RR) and 95% confidence intervals (CI) for the outcomes.

The authors did not state how many reviewers performed data extraction.

Methods of synthesis
Pooled relative risks and 95% CIs were calculated using a fixed-effect model. Statistical heterogeneity of the results was assessed using Cochran's Q. Where statistical heterogeneity was present, the results were pooled using a random-effects model. Subgroup analyses were undertaken on the basis of LMWH administration (intravenously and intravascular) and elective PCI compared to urgent PCI.

Results of the review
Thirteen RCTs (12,254 participants) were included in the review. Sample sizes ranged from 60 to 4,687 patients. Fifty-three per cent of the 6,322 patients who received LMWH and were eligible for the safety endpoints received LMWH intravenously or intra-arterially. Elective PCI was undergone by 38% of the patients. The authors stated that the baseline characteristics of the groups in the trials were similar.

There were no statistically significant differences between the LMWH and unfractionated heparin groups in the number of patients who achieved efficacy endpoints or for the safety endpoint of bleeding events, although trends towards benefit with LMWH were observed for both outcomes. Some heterogeneity ($X^2=15.97$, $I^2=49\%$) was observed across the trials for bleeding.

Patients who had LMWH intravenously or intra-arterially showed statistically significant fewer bleeding episodes compared to those with unfractionated heparin (RR 0.63, 95% CI 0.48 to 0.82, $I^2=0\%$). There was a trend towards fewer deaths and myocardial infarction events in patients treated with LMWH, but this was not statistically significant. There were no significant differences between groups treated with LMWH and groups treated with unfractionated heparin in subgroup analyses of studies of patients who underwent elective or urgent PCI for the efficacy composite outcome and the safety endpoint of bleeding episodes; there was a discrepancy between the text and tables for bleed events in patients who underwent elective PCI.

Authors’ conclusions
The efficacy and bleeding risk of LMWH in patients who underwent percutaneous coronary interventions were similar to those observed with unfractionated heparin. Subgroup analyses showed that intravenous administration of LMWH was safer than unfractionated heparin and had comparable efficacy results.

CRD commentary
The review addressed a clear question. Some criteria were defined for inclusion of studies in the review. Appropriate databases were searched for relevant studies. It was unclear whether any language restrictions were imposed on the search. No search dates were given. Some attempts were made to identify unpublished studies from conference proceedings. No steps were taken to minimise errors and bias at any stage of the review process and there was no assessment of methodological quality of the included studies; this made the reliability of the results in the studies unknown.

The authors combined the results of the review in a meta-analysis and used subgroup analyses to explore sources of heterogeneity. It may not have been appropriate to combine the results of the studies where there was substantial statistical heterogeneity. Two studies had large sample sizes and contributed most of the data and there was a discrepancy in the reporting between text and tables for one result. There appeared to be an additional study included in some meta-analyses that was not listed as a study that met inclusion criteria. It was unclear how this may have affected the results. Only a small number of studies reported safety data.

The authors’ conclusions reflected the evidence presented, but methodological flaws in the conduct of the review and the unknown quality of the included studies means that the authors’ conclusions should be interpreted with caution.

Implications of the review for practice and research
Practice: The authors stated that a single dose of intravenous fixed-weight dose of LMWH significantly reduced bleeding with comparable efficacy and should be the preferred option for patients undergoing elective PCI.

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

Funding
Not stated.

Bibliographic details
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.