Low-molecular-weight heparin vs. unfractionated heparin in percutaneous coronary intervention: a combined analysis

CRD summary
This review compared the use of low molecular weight heparin with unfractionated heparin in people undergoing percutaneous coronary intervention. It concluded that the effects on clinical events (death, myocardial infarction or revascularisation) and on bleeding outcomes were similar with both treatments. There was little detail about the methods of the review, but the conclusions appear suitably cautious.

Authors' objectives
To assess the effects of intravenous low molecular weight heparin (LMWH), compared with unfractionated heparin (UFH), in people undergoing percutaneous coronary intervention (PCI).

Searching
MEDLINE was searched from January 1998 to March 2003; the search terms were given. The bibliographies of relevant papers and international meeting abstracts were checked. Experts and trial investigators were contacted for further studies.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) and non-randomised studies were eligible for inclusion.

Specific interventions included in the review
Studies that compared the use of a single bolus of intravenous LMWH with UFH during PCI, where patients had received no prior treatment with anticoagulant, were eligible for inclusion. The LMWHs used in the included studies were reviparin, enoxaparin and dalteparin. Enoxaparin was used in the majority of studies (6 of the 8 studies included in the meta-analysis). The dosing regimens were given in the paper. Concomitant treatments included aspirin, eptifibatide, clopidogrel, abciximab and ticlopidine.

Participants included in the review
Studies on people undergoing PCI were eligible for inclusion. The participants in the included studies had stable or unstable angina and some had complex coronary lesions. PCI was elective or urgent. Men and women were included.

Outcomes assessed in the review
The primary outcome of clinical efficacy was a composite end point of ischaemic events, as defined in the individual studies (combinations of death, myocardial infarction, re-PCI, stenting, coronary artery bypass graft or bailout use of glycoprotein IIb/IIIa inhibitors). Safety was expressed as adverse event rates (major bleeding, minor bleeding, or a combination of all bleeding). The duration of follow-up, where reported, ranged from 3 to 30 days.

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.

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

Relative risks (RRs) were calculated for composite outcomes in the individual studies, using the inverse variance weighted RRs.

**Methods of synthesis**

**How were the studies combined?**
Pooled RRs and 95% confidence intervals (CIs) were calculated for the RCTs, using a fixed-effect model. The efficacy of LMWH compared with UFH was assessed using a chi-squared test on the pooled RRs. Mean event rates were calculated for all RCTs and non-RCTs combined.

**How were differences between studies investigated?**
A chi-squared test was used to assess heterogeneity between the RCTs, and to compare event rates in non-RCTs with those in RCTs.

**Results of the review**

Eight RCTs (2,015 participants) and 7 non-RCTs (2,750 participants) were included.

No heterogeneity was found between the RCTs included in the meta-analysis.

Data from RCTs showed that LMWH was not significantly different from UFH: the RR was 0.90 (95% CI: 0.65, 1.23, P=0.5) for the composite outcome, 0.63 (95% CI: 0.29, 1.37, P=0.25) for major bleeding and 1.35 (95% CI: 0.84, 2.16, P=0.21) for minor bleeding (4 trials).

No outcome measure observed in the non-RCTs was significantly different from that observed for LMWH groups in the RCTs.

When data from RCTs and non-RCTs were pooled together, composite outcomes and major bleeding events were significantly less for patients in the LMWH group than for those in the UFH group (composite outcome P=0.03, major bleeding P=0.0001).

**Authors' conclusions**

For people not already receiving anticoagulation, a single intravenous injection of LMWH immediately before PCI has the potential to be as safe and effective as UFH.

**CRD commentary**

The aims and inclusion criteria for this review were clearly stated. The database search was limited to MEDLINE, although efforts were made to identify other published or unpublished studies. However, it is possible that studies were missed and this could affect the results. The methods of the review (study selection, data extraction) were not described and there was no mention of any quality assessment. It is possible for decisions made during a review, and the quality of primary studies included in a review, to influence its results through the introduction of bias or error. These issues cannot be assessed where no methodology is reported.

There was little detail about the participants in the included studies and this may affect the generalisability of the results. The authors have, appropriately, presented pooled data from the RCTs alone; they have also combined data from RCTs and non-RCTs. Evidence from non-RCTs is less reliable than that from RCTs and, therefore, as the authors commented, these combined results should be interpreted with caution. However, bearing these comments in mind, the authors' conclusions seem suitably cautious.

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

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

Research: The authors stated that an adequately powered trial is needed to assess the effects of LMWH versus UFH during PCI.

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