Low molecular weight heparin and unfractionated heparin for prevention of thromboembolism in general surgery: a meta-analysis of randomised clinical trials

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Authors' objectives
To evaluate the efficacy and safety of low molecular weight heparin (LMWH) versus unfractionated heparin (UFH), in the prevention of thromboembolism in general surgery.

Searching
MEDLINE was searched for clinical trials assessing LMWH, UFH and warfarin as prophylaxis. In addition, studies cited in earlier reviews were assessed. Articles written in any language were considered.

Study selection
Study designs of evaluations included in the review
Randomised dose-ranging studies, open randomised studies, randomised single and double-blinded studies. Trials were included if they were randomised, open or controlled with dextran, UFH (alone or with dihydroergotamine), warfarin or placebo.

Specific interventions included in the review
LMWH versus dextran, UFH (alone or with dihydroergotamine), warfarin or placebo. The LMWH studied were: logiparin, Kabi 2165, CY216, enoxaparin, embolex, sandoparin, lovenox, clivarine, heparin NM, and dihydergot.

Participants included in the review
Patients who underwent general surgery and deep vein thrombosis (DVT) prophylaxis with LMWH, UFH or warfarin.

Outcomes assessed in the review
The outcomes assessed were DVT, pulmonary embolism (PE), and safety effects. DVT was diagnosed by phlebography, whilst PE was diagnosed by pulmonary angiography, ventilation or perfusion lung scan, or at autopsy. Safety effects were assessed by major or minor bleeding.

How were decisions on the relevance of primary studies made?
The trials were assessed independently by two physicians, and any disagreements were resolved by discussion.

Assessment of study quality
The authors do not state that they assessed validity.

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

Methods of synthesis
How were the studies combined?
Efficacy was assessed on the basis of a standard analysis where only those who completed the trial were included in the final analysis. Safety effects were assessed on an intention to treat basis.

The relative risks (RRs) calculated from each trial were combined using both fixed-effect (Bayes) and random-effects (DerSimonian and Laird) methods with Fast*Pro software.
How were differences between studies investigated?

Homogeneity was tested using the chi-squared test. The individual study duration was adjusted to a standard time period of 7 post-operative days.

Results of the review

Thirty-three randomised controlled trials, with 9,289 participants in the active treatment group and 8,800 in the control group, were included. However, there was a discrepancy in the table of included studies, which reported only 27 studies.

No significant differences between the LMWH- and UFH-treated groups were demonstrated for efficacy (DVT and PE) and major bleeding.

The RR of minor bleeding for LMWH versus UFH was 0.75 (95% confidence interval: 0.64, 0.88), which was significant (p<0.05).

The chi-squared test indicated there was no significant heterogeneity between the trials.

The study that had the greatest influence of any single trial on the results contained a relatively large number of patients (3,809).

Authors’ conclusions

LMWH and UFH did not differ significantly in terms of the prevention of thromboembolism, but LMWH had a significantly better safety profile. On this basis, LMWH may be preferable to UFH in the prevention of thromboembolism in general surgery.

CRD commentary

The authors searched MEDLINE (although the range of dates for the search was not stated). It is unclear how many relevant studies may have been excluded by restricting the search to one electronic database. In addition, the authors searched the bibliographies of the identified articles for additional studies. Publications in any language were included.

The inclusion and exclusion criteria were listed. One table cited the characteristics of the included studies, while a second listed the excluded studies and the reasons for their exclusion from the meta-analysis.

There was a discrepancy between the number of included studies reported in the text (33) and the number reported in the tables (27).

Although the authors found no significant heterogeneity, the results of this analysis should be treated with caution because there were several treatment variations. Furthermore, the authors’ conclusions that LMWH had a better safety profile than UFH should be treated with caution, as this was only the case for minor bleeding. There were no differences in major bleeding events.

Implications of the review for practice and research

No research recommendations were made.

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Bibliographic details

Other publications of related interest

This additional published commentary may also be of interest. Low molecular weight heparin and knee replacement. Bandolier 1999;63:7-8.

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