Authors' objectives
To compare the efficacy and safety of different low molecular weight heparins (LMWH) in the treatment of patients with venous thromboembolism (VTE).

Searching
EMBASE, MEDLINE, and Current Contents were searched. In addition, the references from recently published meta-analyses were examined. The search terms and dates were not stated.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion if it were possible to extract clinical data.

Specific interventions included in the review
Studies that compared dose-adjusted unfractionated heparins (UFH, either subcutaneous or intravenous) with fixed-dose subcutaneous LMWH were eligible for inclusion. Studies using non-therapeutic doses of UFH or LMWH and dose-finding studies were excluded. The doses of UFH ranged from 87.5 to 114 a-Xa U/kg twice daily and from 175 to 200 a-Xa U/kg once daily. The LMWHs used were reviparin, enoxaparin, nadroparin, CY 222, dalteparin, certoparin and tinzaparin with a-Xa to A-IIa ratios (where given) ranging from 1.9 to 5.0.

Participants included in the review
Studies of patients with objectively confirmed VTE (either deep venous thrombosis and/or pulmonary embolism) were eligible for inclusion. The studies had to be of the initial treatment of these patients.

Outcomes assessed in the review
Studies had to present data on at least one of the following outcomes to be included in the review: symptomatic and objectively confirmed recurrent VTE during 3 months' follow-up; major haemorrhage during the initial treatment period; or mortality during the first 3 months after the first VTE episode.

How were decisions on the relevance of primary studies made?
Two authors independently screened identified papers for inclusion and resolved disagreements by reaching consensus.

Assessment of study quality
The authors did 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 reviewers performed the data extraction. The tabulated information included the year of publication, sample size, and details of the intervention and control regimens. The odds ratio (OR) and 95% confidence interval (CI) were calculated for each outcome for each study.

Methods of synthesis
How were the studies combined?
Where an adequate number of well-conducted similar studies were available, the pooled OR and 95% CI were estimated using the Mantel-Haenszel method for all LMWH combined in comparison with UFH. The relationship between efficacy and safety for the different LMWH drugs was assessed by plotting the log OR of bleeding against the
log OR of recurrent VTE for the different LMWHs with UFH control.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared statistic.

Results of the review
Sixteen RCTs (6,055 patients) were included.

Mortality (12 RCTs, 5,364 patients): LMWH significantly reduced mortality in comparison with UFH; the OR was 0.68 (95% CI: 0.53, 0.88). No significant heterogeneity was found (P=0.75).

Recurrent VTE (13 RCTs, 5,568 patients): LMWH significantly reduced recurrent VTE in comparison with UFH; the OR was 0.66 (95% CI: 0.51, 0.86). No significant heterogeneity was found (P=0.1).

Major bleeding (16 RCTs, 6,055 patients): LMWH significantly reduced major bleeding in comparison with UFH; the OR was 0.56 (95% CI: 0.38, 0.83). No significant heterogeneity was found (P=0.3).

Different LMWHs: the scatter plot indicated that most LMWHs had greater efficacy and safety than standard UFH treatment. However, there was considerable variation between different LMWHs and also between studies using a single LMWH. The log OR of major bleeding ranged from 0.23 to -0.89 and the log OR of recurrent VTE ranged from 0.88 to -0.89.

Authors' conclusions
LMWHs had increased efficacy and safety in comparison with UFH. There was no definitive evidence that LMWHs differed in their efficacy and safety.

CRD commentary
The review question was clear in terms of the study design, intervention, participants and outcomes. Three relevant databases were searched, but no details of the dates searched, keywords or any language limitations were reported. No attempt was made to locate unpublished studies, thus raising the possibility of publication bias. Two reviewers selected the studies, but the methods used to assess validity and extract the data were not described. Hence, the adequacy of the methods used cannot be judged. Only RCTs were included, but no formal validity assessment was performed. The studies were appropriately combined in a meta-analysis and statistical heterogeneity was assessed. The comparison of different LMWH was not based on direct comparisons, hence, as the authors correctly stated, definitive conclusions cannot be reached. The evidence presented appears to support the authors' conclusions.

Implications of the review for practice and research
The authors did not state any implications for further research and practice.

Bibliographic details

Indexing Status
Subject indexing assigned by NLM

MeSH
Anticoagulants /administration & dosage /adverse effects /classification /therapeutic use; Clinical Trials as Topic; Hemorrhage /chemically induced /epidemiology; Heparin, Low-Molecular-Weight /administration & dosage /adverse effects /classification /therapeutic use; Postoperative Complications /drug therapy /prevention & control; Pulmonary
Embolism /drug therapy /prevention & control; Randomized Controlled Trials as Topic; Safety; Treatment Outcome; Venous Thrombosis /drug therapy /prevention & control

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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.