Authors' objectives
To determine the efficacy and safety of subcutaneous low molecular weight heparins (LMWHs) in the initial treatment of proximal deep vein thrombosis (DVT).

Searching
MEDLINE and Current Contents were searched from 1966 to 30 November 1998 in French and English, using a range of keywords that were included in the report. In addition, the reviewers examined the reference lists of included articles, meta-analyses and reviews, and contacted experts in the field. Abstracts and unpublished reports were not eligible for inclusion.

Study selection
Study designs of evaluations included in the review
All of the included studies were randomised controlled trials (RCTs).

Specific interventions included in the review
The included studies needed to evaluate subcutaneous LMWHs versus standard intravenous unfractionated heparin. The LMWHs assessed were enoxaparin, dalteparin and nadroparin (the doses were listed in the paper).

Participants included in the review
Patients with DVT, as diagnosed by phlebography or ultrasound, were eligible. Studies of patients with symptoms of pulmonary embolism or thrombosis of veins in the arms were excluded. In five of the included trials all patients had proximal DVT, while in the remaining four this group represented 57 to 79% of the participants. The dose was always related to patient weight and varied from 175 to 240 UI/kg per day, administered as one or two doses. LMWH was given for 5 to 10 days.

Outcomes assessed in the review
Efficacy was examined in terms of survival and resolution of DVT. The adverse events assessed included thrombocytopenia, major and minor bleeding, and recurrence of DVT. Both early and late adverse events were examined. Early events were defined as occurring during heparin treatment or up to 48 hours after the cessation of heparin treatment.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

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

Data extraction
The numbers and percentages of events in the intervention and control groups were presented in the paper. The risk of an adverse event in the LMWH group was stated to be expressed as an odds ratio of the standard heparin group, but this information was not presented in the text.
Methods of synthesis
How were the studies combined?
The studies were combined narratively. Efficacy and adverse events were grouped within the text and the results compared to existing meta-analyses (see Other Publications of Related Interest nos.1-4).

How were differences between studies investigated?
Differences in the definition of DVT, drugs and dosage were described in the report.

Results of the review
The review included 9 RCTs with 2,185 participants.

The mortality rate was 0 to 1.2% for LMWH groups versus 0 to 1% in the standard heparin groups. The incidence of recurrent venous thromboembolism was 0 to 2% versus 0 to 4.7%, respectively, while major bleeding rates were 0 to 2.4% versus 0 to 4.9%. Such events were linked to a high mortality rate (9 to 16%). Thrombocytopenia occurred in 0 to 2.5% of cases in the LMWH groups versus 0 to 3.5% in the standard heparin groups. None of the included studies could demonstrate a statistically-significant difference between the treatments.

In the two studies assessing ambulatory treatment with LMWHs, this was possible for 36 to 49% of the patients. In these studies, home administration of the treatment was as safe and effective as hospital standard heparin treatment.

Cost information
The authors commented that LMWHs are between four and six times as expensive as standard heparin, but they can be more cost-effective due to lower administrative and laboratory costs. They quoted a pharmacoeconomic study showing a saving of 230 Swiss francs per patient and two other studies describing a saving of between 25 and 35% of per patient costs.

Authors' conclusions
LMWHs are of equivalent or greater efficacy and safety when compared to standard intravenous unfractionated heparins in the initial treatment of proximal DVT.

CRD commentary
The review addressed a clear research question. The inclusion criteria were broadly defined in terms of the study design, participants and intervention. Eligible outcomes were not explicitly stated, but those included were defined appropriately. The search was limited to two electronic databases, but this was followed up by reference checking and contacting experts in the field. There is a risk of publication bias since unpublished material was not included in the review. No validity assessment was performed and it cannot be assumed that all the included RCTs were of a high quality. While there was evidence of some clinical heterogeneity, it may have been appropriate to pool the data statistically in a series of meta-analyses. The reviewers’ conclusions appear to follow from their results and the reviewers were careful to compare them with the results of other meta-analyses.

Implications of the review for practice and research
Practice: The authors state that the use of fixed doses of LMWH adapted to the patient's weight for a minimum of 5 days, until two clear scans 24 hours apart are obtained, is to be recommended. Early mobilisation of the patient and a compressing bandage are supported in several studies. Ambulatory treatment is possible for certain patients (patients without post-thrombotic syndrome or symptoms of pulmonary embolism, first or second episode of DVT, adequate support) whose DVT occurs below the inguinal ligament. Otherwise, 2 to 3 days of hospitalisation is likely.

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

PubMedID
10407944

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Heparin /administration & dosage /adverse effects; Heparin, Low-Molecular-Weight /administration & dosage /adverse effects; Humans; Injections, Subcutaneous; Randomized Controlled Trials as Topic; Thrombophlebitis /drug therapy; Treatment Outcome

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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.