Preoperative vs postoperative initiation of low-molecular-weight heparin prophylaxis against venous thromboembolism in patients undergoing elective hip replacement

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Authors' objectives
To assess the effectiveness of pre-operative versus post-operative initiation of low-molecular-weight-heparin (LMWH) prophylaxis against venous thromboembolism (DVT) in patients undergoing elective hip replacement.

Searching
The authors searched the MEDLINE electronic database (1986 to 1997) using the key subject headings 'thrombophlebitis', 'pulmonary embolism', LMWH', 'enoxaparin', 'hip prosthesis', 'prevention', and prophylaxis'. The authors also scanned the bibliographies of published articles and their personal reference files for additional relevant publications.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) (level 1 trials, defined as a randomised trial in which the lower limit of the confidence interval for the treatment effect exceeded the minimal clinically important benefit) (RCTs) that were double-blind, and which had objective documentation of the frequencies of DVT by ascending contrast venography which was performed before or at the time of discharge from the hospital. The mean duration of treatment was 12.7 days and the mean interval, operation to venography, was 12.1 days.

Specific interventions included in the review
Low-molecular-weight-heparin (LMWH) (enoxaparin given pre-operatively at 40 mg/day, or post-operatively at 30 mg/12 hours or 40 mg/day) where the same LMWH was initiated pre-operatively or post-operatively.

Participants included in the review
Patients undergoing elective hip replacement surgery. In the pre-operative group, the mean age of participants was 65.4 years and the proportion of males was 49% and females 51%. In the post-operative group, the mean age of participants was 65.8 years and the proportion of males was 55% and females 45%.

Outcomes assessed in the review
The effectiveness outcome was the relative frequencies of venographically documented DVT. The safety outcome was the objectively documented episodes of minor and major bleeding.

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 authors performed the selection.

Assessment of study quality
No formal assessment of quality was undertaken.

Data extraction
The authors do not state who, or how many of the authors, performed the data extraction. Data were extracted for patient characteristics, trial and year identification, duration of treatment and the interval between operation and venography.
Methods of synthesis
How were the studies combined?
The results from pre-operative and post-operative treatment arms of the included trials were pooled. The Fischer exact test was used to compare the incidence of DVT and the incidence of bleeding of the two treatment arms. 95% confidence intervals (CIs) were also calculated.

How were differences between studies investigated?
There were no tests for homogeneity. The authors state that since it was not feasible to stratify by trial in the analysis, it was not possible to assess the potential effect of between-trial variation in patient populations, protocols, and outcome evaluations.

Results of the review
Six RCTs were included in the review with 759 participants (101 in the intervention group and 658 in the control group).

Treatment with LMWH initiated pre-operatively was associated with a DVT frequency of 10.0% (95% CI: 7.0, 13.8) compared with a frequency of 15.3% (95% CI: 12.7, 18.3) when the LMWH was initiated post-operatively (p = 0.02).

Major bleeding was less frequent in patients receiving pre-operatively initiated LMWH (0.9%, 95% CI: 0.2, 2.5) than in patients receiving post-operatively initiated LMWH (3.5%, 95% CI: 2.4, 5.0).

Minor bleeding was less frequent in patients receiving pre-operatively initiated LMWH (0.6%, 95% CI: 0.1, 2.1) than in patients receiving post-operatively initiated LMWH (4.6%, 95% CI: 3.2, 6.3).

Authors’ conclusions
The authors state that their findings support the European view that optimal protection against surgically induced DVT is provided by pre-operatively initiated DVT prophylaxis.

CRD commentary
The authors have clearly stated their research question and their inclusion and exclusion criteria. The literature search is very good but the authors may have missed additional relevant studies by searching only one database. It was also not reported whether the authors restricted their search to English language publications.

The quality of the included studies was not formally assessed and the authors have not reported how the articles were selected, or how many of the reviewers were involved in the process of data extraction. The data extraction is reported in tables and text and the statistical methods used to pool the studies was appropriate.

Although no tests for heterogeneity were carried out the authors did discuss the limitations of their review. The authors stated that other factors may have influenced the outcomes as the comparisons were made across trials rather than direct randomised comparisons. This was due to differences between the study centres and clinical practices and because co-morbidity factors were not consistently reported. Their conclusions appear to follow from the results but should be viewed with caution because of the stated methodological limitations of the review.

Implications of the review for practice and research
Practice: The authors state that the results should not be used to determine the care of patients because of the methodological limitations of this review.

Research: The authors state that their findings support the need for a randomised comparison of pre-operative and post-operative initiation of pharmacological prophylaxis of DVT. Such a trial would resolve the divergent practices between European and the North American countries, and would affect the treatment for thousands of patients on both continents.
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