Low molecular weight versus unfractionated heparin: a clinical and economic appraisal

Heaton D, Pearce N

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Using low molecular weight heparin (LMWH) in the prevention and treatment of deep venous thrombosis (DVT).

Type of intervention

Economic study type
Cost-effectiveness analysis.

Study population
Patients at risk from postoperative thrombosis or established deep venous thrombosis (DVT).

Setting
Hospital. The economic study was carried out in Christchurch, New Zealand.

Dates to which data relate
The effectiveness and resource use data were obtained from studies published between 1992 and 1994. The price year was not explicitly specified.

Source of effectiveness data
Effectiveness data were derived from a review of previously completed studies.

Outcomes assessed in the review
For preoperative DVT prophylaxis, the outcomes measured were the prevention of postoperative venous thromboembolism, thromboembolic complications and hemorrhagic complications. For DVT treatment, the relevant outcomes were reduction in thrombus extension, improvement in quantitative venographic assessment, and risk reduction in symptomatic thromboembolic complications and hemorrhagic complications.

Study designs and other criteria for inclusion in the review
Meta-analyses, and other non-specified studies were included in the review.

Sources searched to identify primary studies
Not stated.
Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
For preoperative DVT prophylaxis, two meta-analyses containing the results of 62 studies in which patients underwent general and orthopaedic surgery, and a multicentre study of 3,809 patients undergoing abdominal surgery were used. For DVT treatment, 2 meta-analyses containing the results of 16 studies and 2 other single studies were used.

Methods of combining primary studies
The results were directly reported from previously completed meta-analysis studies.

Investigation of differences between primary studies
No investigation of differences between primary studies was carried out.

Results of the review
With respect to preoperative DVT prophylaxis, the first analysis found that the relative risks of DVT were similar for both subgroups (general and orthopaedic surgery). For all surgical studies the calculated relative risk of DVT and pulmonary embolism with LMWHs versus UFH was 0.74 (95% CI: 0.65 - 0.86), and 0.43 (95% CI: 0.26 - 0.72), respectively. The second analysis found an odds ratio for DVT of 0.85 (95% CI: 0.74 - 0.97) and for pulmonary embolism of 0.59 (95% CI: 0.37 - 0.93), in favour of LMWH. The relative risk was similar for both surgical subgroups. Bleeding rates were not significantly different (both analyses). Two meta-analyses concluded that LMWH was at least as effective as UFH for the prevention of postoperative thrombosis in general and orthopaedic surgery. In the multicentre study of 3,809 patients undergoing abdominal surgery, the incidence of DVT and pulmonary embolism was reported to be 0.6% and 0.7% for both LMWH and UFH groups with a non-statistically significant reduction in major bleeding in the LMWH group (RR 0.77; 95% CI: 0.56 - 1.04). In the case of DVT treatment, one meta-analysis of 9 randomised trials found better outcomes for LMWH relative to UFH in terms of reduction in thrombus size (64% versus 50%), increase in thrombus size (6% versus 12%), thromboembolic complications (2.7% versus 7%), and hemorrhagic complications (0.9% versus 3.2%). Another study (used for cost analysis) showed that LMWH given once daily at a body-weight-determined dose without laboratory monitoring was as effective as UFH given by IV infusion.

Measure of benefits used in the economic analysis
No summary benefit measure was identified in the economic study, and only separate clinical outcomes were reported.

Direct costs
Costs were not discounted. Quantities of resource use were not systematically reported separately from the costs. Treatment costs (costs of drug, administration, and laboratory) and costs of complications were taken into account. The costs included were those of the hospital and the health service. The cost data were obtained from the study institution. The price dates were not explicitly specified.

Indirect Costs
Not considered.

Currency
NHS Economic Evaluation Database (NHS EED)
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New Zealand dollars (NZ$). The exchange rate at the time of the study was NZ$1 = US$0.60.

**Sensitivity analysis**
No sensitivity analysis was conducted.

**Estimated benefits used in the economic analysis**
Not applicable.

**Cost results**
For surgical prophylaxis of DVT, the average cost for each general surgery patient is NZ$285 for LMWH therapy and NZ$305 for UFH therapy. In orthopaedic surgery the average patient cost was NZ$806 compared with NZ$1,128, again in favour of LMWH. In the case of treatment of established DVT, the average cost of the treatment with once daily administered LMWH, taking into account the associated complications, was NZ$291 per patient compared with NZ$692 for intravenous infusion of UFH. The corresponding values for twice daily SC LMWH and UFH were NZ$313 and NZ$340, respectively.

**Synthesis of costs and benefits**
Costs and benefits were not combined since the use of LMWH was the dominant strategy.

**Authors’ conclusions**
LMWHs are more cost-effective in surgical prophylaxis of DVT if the costs of failed prophylaxis are considered. The costs of using subcutaneous LMWH as therapy for established DVT are lower than those of UFH administered by intravenous infusion. The difference becomes greater when the rates of antithrombotic failure and bleeding complications are incorporated. According to the authors, “if current trials demonstrate that LMWH treatment can be given on an ambulatory outpatient basis, the economic advantages of LMWH will be considerable”.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of the comparator is clear.

**Validity of estimate of measure of benefit**
The estimates of benefits are likely to be internally valid given the inclusion of large meta-analyses. In view of the lack of an explicit summary benefit measure, the study may be regarded as a cost-consequences analysis.

**Validity of estimate of costs**
Quantities of resource use were not systematically reported separately from the costs. Adequate details of the methods of cost estimation were given.

**Other issues**
The issue of generalisability to other settings or countries was not systematically addressed, the authors merely acknowledging that "these results are dependent on actual costs and clinical response, which may vary from country to country".

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