Enoxaparin for thromboprophylaxis after major trauma: potential cost implications
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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
The study compared the use of low molecular weight heparin (LMWH), in this case enoxaparin, with the use of low-dose heparin (LDH) for thromboprophylaxis after major trauma.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of 1,000 critically ill trauma patients requiring thromboprophylaxis. Specifically, the authors focused on those with an Injury Severity Score (ISS) above 9, as these patients have been shown to be at higher risk of venous thromboembolism.

Setting
The setting was secondary care. The economic study was carried out in Washington DC, USA.

Dates to which data relate
The effectiveness data were derived from a study published in 1996. The price year was not reported.

Source of effectiveness data
The evidence for the final outcomes was derived from a review of published studies.

Modelling
The authors modelled the outcomes of the study via a simple decision tree. The only decision node represented whether to employ LMWH or LDH.

Outcomes assessed in the review
The outcomes assessed were:

the baseline incidence of deep vein thrombosis (DVT);

the relative risk reduction (RRR) with LMWH compared with LDH; and

the magnitude of the risk of major bleeding with LMWH.
Study designs and other criteria for inclusion in the review
The authors aimed to identify all English-language randomised, controlled trials of LMWH for thromboprophylaxis in trauma.

Sources searched to identify primary studies
MEDLINE was searched for relevant literature.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Only literature published since 1994 was reviewed, as earlier articles might not have been applicable to present critical care and trauma practice.

Number of primary studies included
For comparisons of LMWH with LDH, four studies met several of the general search criteria. However, only one study (Geerts et al., see Other Publications of Related Interest) met all of the predefined search criteria. Hence, this double-blind, randomised controlled trial, which compared enoxaparin with LDH in trauma patients, was the only study included in the review.

Methods of combining primary studies
Not relevant.

Investigation of differences between primary studies
Not relevant.

Results of the review
The rate of DVT was 14.70% (no range) with LDH and 7.35% (range: 5.50 - 9.10) with enoxaparin.

The risk of major bleeding was 0.6% (no range) with LDH and 2.9% (range: 2.235 - 3.475) with enoxaparin.

For proximal DVT, the observed RRR was 57.8% with LMWH (no range).

Measure of benefits used in the economic analysis
The measure of benefit used was the number of venous thromboembolisms prevented.

Direct costs
The direct costs included in the study were those of the hospital. These were the costs associated with DVT and with major bleeding, and the costs of enoxaparin and LDH. The costs associated with DVT included the costs of any radiology studies, increased length of stay, and therapy. The costs for thromboprophylaxis were derived from the actual costs to the authors’ hospital for each of the two regimens, based on 10 days of therapy. To determine the diagnosis process of DVT, its treatment and the increased length of stay, the authors multiplied the component charges the hospital bills to third-party payers by a cost-to-charge ratio of 0.6. Resource use and the costs were not reported separately. Discounting was not relevant, as all the costs were incurred during a very short time, and was not conducted. The study reported the total costs. The price year was not reported.
Statistical analysis of costs
The costs were treated as point estimates (i.e. the data were deterministic).

Indirect Costs
The indirect costs were not included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was carried out to identify important model uncertainties and to assess the robustness of the authors' conclusions. The base-case estimates were varied by 25% individually to identify variables that substantially affected the results. The authors also adjusted all model inputs by 25% simultaneously to provide a multivariate assessment of a best- and worst-case scenario.

Estimated benefits used in the economic analysis
There were 73.5 DVTs when enoxaparin was employed, compared with 147 DVTs when standard LDH was used.

Major bleeding occurred in 29 patients treated with enoxaparin and complicated the course of 6 individuals treated with LDH.

Cost results
The total costs were $418,755.50 with enoxaparin and $444,511.00 with conventional LDH.

Overall, the costs with enoxaparin were $28,755.50 less than the costs incurred with LDH.

On a per patient basis, the use of enoxaparin yielded $28.76 in savings for each individual in the cohort.

Synthesis of costs and benefits
The authors calculated the marginal cost-effectiveness of enoxaparin as the additional costs associated with enoxaparin, less any cost-savings resulting from the use of enoxaparin, divided by the cases of venous thromboembolism prevented. Hence, the use of enoxaparin compared with LDH was associated with a net saving of $391.23 per DVT prevented.

The results of the one-way sensitivity analysis showed that the total cost-savings with enoxaparin were most sensitive to the cost of a DVT. The authors also found that when the RRR of enoxaparin fell below 43.1%, or when the cost of a DVT was below $2,421.77, its use resulted in additional net expenditures. A two-way sensitivity analysis of the RRR and the costs of DVT showed that when the costs of a DVT was low and enoxaparin was assumed to be minimally effective, this resulted in an outlay of $59.84 per patient in the cohort. However, as enoxaparin became more effective and DVT more costly, more net savings were reaped.

Authors' conclusions
The economic analysis of enoxaparin for thromboprophylaxis after trauma demonstrated that reliance on a low molecular weight heparin (LMWH) might produce significant savings, irrespective of the increased costs of LMWH.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used. Low-dose heparin is a well-validated approach for seriously ill medical and general surgery patients. You should decide if this is a widely used health technology in your own setting.
Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been undertaken to identify relevant research and minimise bias. Nevertheless, the review seems to have been conducted in a clear, proper way. The authors appropriately reported the sources searched to identify randomised controlled trials, the inclusion criteria, the keywords used, and the reasons why three potentially relevant studies were excluded from the review. Further, the study from which the effectiveness data were derived was a double-blinded randomised controlled trial (RCTs), which was appropriate for the study question as properly conducted RCTs are the ‘gold’ standard study design when comparing health interventions. However, the authors elected to search only one source for studies to be included. This does not constitute a systematic review, which would have represented the best source of evidence.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. The instrument used to derive a measure of health benefit was a decision tree, which was appropriate. However, the authors reported that the model did not investigate the impact of pulmonary embolism or mortality on the outcomes. Hence, the model was likely to be conservative, as a reduction in DVT rate would alter the incidence of pulmonary embolism and, in turn, lower mortality.

Validity of estimate of costs
All the categories of cost relevant to the hospital perspective adopted were included in the analysis. In addition, for each category of cost, all the relevant costs appear to have been included. The authors did not report the costs and the quantities separately, which will limit the generalisability of their results. The authors derived the unit costs from their own setting and from published sources. Appropriate sensitivity analyses of the prices and costs were conducted, using ranges that appear to have been appropriate. Since all the costs were incurred during a short time, discounting was unnecessary and was not performed. Charges were used to proxy prices. However, a cost-to-charge ratio of 0.6 was used to derive the inpatient cost accounting. The price year was not reported, thus hampering any possible inflation exercises.

Other issues
The authors made appropriate comparisons of their findings with those from other studies that found LMWH to be more expensive than the comparator. However, one study compared LMWH with no prophylaxis and the other used a societal perspective, rather than an institutional one. The issue of generalisability to other settings was partially addressed through the sensitivity analysis. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis.

The authors reported a number of further limitations to their study. First, they assumed that the sensitivity of venography and duplex ultrasound scanning for the detection of DVT were equivalent, hence overestimating the baseline rate of DVTs in trauma patients. Second, they relied only upon the findings of one study for their effectiveness assumptions although, as they pointed out, this study was methodologically sound, focused on objective end points, and reported a complete accounting for all patients enrolled. Finally, the uncertainty around the actual costs to trauma patients of developing a DVT represented another limitation.

Implications of the study
The authors concluded that apprehension about either elevated rates of bleeding, or the monetary ramifications of significant haemorrhage, should not dissuade clinicians from adopting enoxaparin for the prevention of venous thromboembolism in trauma patients. The authors also pointed out that if future studies confirmed that daily dosing of enoxaparin is equally effective as twice-a-day use, economic factors would clearly favour the routine employment of LMWH in the trauma population.

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Other publications of related interest


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MeSH
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