Dalteparin vs. enoxaparin as prophylaxis for deep-vein thrombosis after total hip or knee arthroplasty: a retrospective analysis

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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 anticoagulant switch from enoxaparin to dalteparin, as first-line prophylaxis for deep vein thrombosis (DVT) in patients undergoing inpatient rehabilitation following total hip or knee arthroplasty (THA or TKA), was examined.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients undergoing inpatient rehabilitation following THA or TKA. Patients were excluded if they received anticoagulant therapy other than dalteparin, enoxaparin or acetylsalicylic acid at the institution where their TKA or THA was performed. They were also excluded if they received therapies other than dalteparin and enoxaparin as DVT prophylaxis during their rehabilitation.

Setting
The setting was secondary care. The economic study was carried out in New Jersey, USA.

Dates to which data relate

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken retrospectively on the same sample as that used in the effectiveness analysis.

Study sample
No power calculations were performed. The patients were selected by a retrospective examination of medical records. Given the type of study, the initial sample appears to have been suitable for the study question. Out of 934 candidate patients, 461 met the inclusion criteria. The sample consisted of 161 patients on enoxaparin and 300 on dalteparin.

Study design
This was a retrospective cohort study (a before-and-after study) that was carried out in a single-centre rehabilitation setting. The length of follow-up was the length of rehabilitation stay.

**Analysis of effectiveness**

The primary health outcomes were the rates of DVT occurrence, as confirmed by ultrasonography, and bleeding events during the rehabilitation stay. Age-adjusted rates (per 100 persons) were also estimated. The number of events was compared using bivariate logistic regression.

There were some significant differences between the two treatment groups in terms of their body mass index (BMI) and the length of hospitalisation. The BMI was 30.3 kg/m² in the enoxaparin group and 28.9 kg/m² in the dalteparin group, (p<0.03). The length of hospitalisation (i.e. rehabilitation stay) was 1.5 days longer, on average, among patients treated with dalteparin, (p<0.002).

**Effectiveness results**

DVT events occurred at a rate of 1.9 per 100 patients in the enoxaparin group, compared with a rate of 0.3 per 100 patients in the dalteparin group.

The age-adjusted risk of a DVT event in patients receiving dalteparin was substantially less than that among patients treated with enoxaparin, although the difference was not statistically significant (odds ratio, OR=0.160, 95% confidence interval, CI: 0.016 - 1.570).

Bleeding events occurred at a rate of 3.7 per 100 patients receiving enoxaparin, and at a rate of 2.3 per 100 patients receiving dalteparin.

The age-adjusted risk of a bleeding event in patients receiving dalteparin was substantially less than that among patients treated with enoxaparin, although the difference was not statistically significant (OR 0.634, 95% CI: 0.209 - 1.922).

**Clinical conclusions**

The authors did not provide a clinical conclusion. Their results showed that dalteparin was as good as enoxaparin for first-line prophylaxis for DVT.

**Measure of benefits used in the economic analysis**

No summary health benefit was used in the analysis. In effect, a cost-consequences analysis was performed.

**Direct costs**

The perspective of the study was unclear, but it was likely to have been that of the hospital. The resource use quantities and the unit costs were not reported separately. The direct costs consisted only of those relating to the drugs used for prophylaxis (acquisition and dispensing) during the rehabilitation stay. The resource use data were obtained from the patients’ medical records and no model was used to extrapolate the data. The unit costs were derived from published pricing lists and were reported for each anticoagulant regimen. Discounting was not relevant and, appropriately, was not performed. The study reported the average costs.

**Statistical analysis of costs**

The costs were analysed using multivariate ordinary least-squares (OLS) regression. OLS is suitable for normally distributed data, whereas cost data are positive and typically right-skewed. Given a large enough sample size, the inference about the mean cost in each group should not have been affected by the fact that the cost data were not normally distributed, and so, given the sample size, the results may be robust. Age, gender, BMI, length of stay, prior DVT prophylaxis, and significant medical history were all included in the regression as covariates. The authors provided the mean costs with an adjusted 95% CI.
Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analyses were conducted.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The average cost was $364 for patients treated with enoxaparin and $273 for patients treated with dalteparin. The adjusted cost difference was -$129 (95% CI: -150 - -108).

Similar patterns favouring dalteparin were observed among THA patients (adjusted difference -$108, 95% CI: -138 - -77) and TKA patients (adjusted difference -$153, 95% CI: -181 - -126).

Knock-on costs and adverse events were not included in the analysis.

Synthesis of costs and benefits
Not relevant as the study was, in effect, a cost-consequences analysis.

Authors' conclusions
The switch to dalteparin as first-line prophylaxis for deep vein thrombosis (DVT) in the rehabilitation period after total hip or knee arthroplasty (THA or TKA) led to substantial cost-savings for the institute without compromising patient care.

CRD COMMENTARY - Selection of comparators
The chosen comparator was current practice in the study setting. You should consider whether this is a widely used health technology in your setting.

Validity of estimate of measure of effectiveness
The basis of the analysis was a before-and-after study. This allowed many other covariates to change, as well as the choice of treatment. Hence, the estimate of relative effectiveness might not be as accurate as one derived from a randomised controlled trial. The CIs around the estimated ORs were very wide, indicating a large degree of uncertainty in the study findings. The authors acknowledged that a larger sample size would have provided sufficient statistical power to permit the detection of differences in the outcomes. The study sample appears to have been representative of the study population, although the authors did not provide specific evidence of this. The patient groups were not shown to be comparable at analysis, and although many covariates were included in the cost analysis in order to adjust for this, only age was included in the effectiveness analysis.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit. The analysis was, in effect, a cost-consequences study.
Validity of estimate of costs

The study included a very limited amount of cost data in that it only assessed the cost of prophylaxis during the rehabilitation stay. The costs of DVT prophylaxis in the post-discharge period were excluded. This is particularly important as the length of rehabilitation stay was significantly higher in the dalteparin group, and the cost of inpatient stay is likely to exceed the cost of prophylaxis. Also excluded were the costs of treating DVT events or bleeding episodes. The authors acknowledged that the inclusion of any costs of complications would have favoured dalteparin. The costs and the quantities were not reported separately.

The resource use quantities were obtained from a review of medical records. The difference in cost was analysed using multivariate OLS regression, which is not suitable for non-normally distributed data such as costs, but the large sample size may mean that the results are robust. The prices were obtained from published sources in the authors’ setting or, where they were not available, were estimated to be 80% of the average wholesale price. A statistical analysis of the prices was not conducted and sensitivity analyses were not performed on the costs. This means that the uncertainty in the results of this study has not been assessed, thus the generalisability of the study is reduced. Discounting was not necessary since all the costs were incurred during less than one year.

Other issues

The authors made appropriate comparisons of their findings with those from other studies. They acknowledged that the small number of events observed in the study sample meant that the estimated ORs did not approach statistical significance. They also acknowledged that limiting the analysis to the period of rehabilitation stay excluded events and costs occurring post-discharge. The issue of generalisability to other settings was not addressed. Given the study type, the large uncertainty around the outcomes measured, and the concentration on a single institute, the results are probably not generalisable to other settings. The inclusion of more resource use items in the cost analysis might have improved the generalisability. The authors did not present their results selectively and their conclusions reflected the scope of the study.

Implications of the study

The authors did not make any recommendations for policy, practice or further research as a result of their study.

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