Low-molecular-weight heparin therapy for patients undergoing total knee replacement surgery: cost and outcomes


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 a formulary interchange of low molecular weight heparin (LMWH) products for prophylactic therapy in patients undergoing total knee replacement (TKR) surgery. The products compared were enoxaparin (Lovenox, Aventis) and dalteparin (Fragmin, Pharmacia).

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The population comprised adult patients of at least 18 years of age who underwent unilateral, primary knee replacement. Patients with previous knee replacement or with incomplete inpatient medical records were excluded from the study, as were those who belonged to a local health maintenance organisation.

Setting
The setting was secondary care. In particular, the study was carried out in three community hospitals that belonged to the Franciscan Health System in Tacoma (WA). The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were collected between 1 July 1996 and 31 December 1998. The interchange programme was introduced in October 1997. Data on resource use were collected for the same period, while unit costs of the year 2000 were assigned to resources used during the study period.

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

Link between effectiveness and cost data
The costing was carried out retrospectively on the same sample of patients as that used in the effectiveness study.

Study sample
The sample size was not determined in the planning phase of the study and power calculations were not performed retrospectively. Patients were selected from the computerised hospital billing records and decision support system by identifying the patients' International Classification of Disease (ICD-9) code for knee replacement. Of the 189 patients,
88 (28% male) were allocated to the enoxaparin group and 101 (46% male) to the dalteparin group. In the enoxaparin group, 2% were under 45 years of age, 27% were aged 45 to 64, and 71% were 65 years or older. In the dalteparin group, 5% were younger than 45 years, 33% were aged 45 to 64, and 62% were 65 years or older. Patients were consecutively and consistently allocated to each of the two groups according to their date of knee surgery; it was not up to the physician which patients received enoxaparin or dalteparin.

**Study design**
The analysis was based on a retrospective cohort study that was carried out in three community hospitals. Data on the interchange programme were collected from October 1997 until 31 December 1998: data were collected during the inpatient stay and for a 28-day period following discharge.

**Analysis of effectiveness**
The primary health outcomes used were:

the length of hospital stay and location of inpatient stay (e.g. general ward),

the incidence of deep vein thrombosis and pulmonary embolism, and

the incidence of bleeding-related adverse events (postsurgical blood transfusion, bleeding from any anatomical site, and reoperation due to bleeding wound haematoma).

The outcomes were extracted from computerised administrative records and written medical records using a standard case report form. In order to reduce potential information bias, three staff member (two RNs and 1 RA) abstracted the data. The patients were found to be comparable at baseline after analyses with regression models. In cases where the baseline characteristics differed, the authors evaluated potential confounding.

**Effectiveness results**
Almost all inpatient days were located in general wards. The length of inpatient hospital stay was equal in both groups and the median length of stay was 6 days. The rate of discharge changed by 1% after adjusting for gender and age using a Cox regression model (rate ratio 0.94, 95% confidence interval, CI: 0.7 to 1.26). No patient stayed in the hospital for more than 17 days.

Deep vein thrombosis or pulmonary embolism was experienced by 3.4% of the patients in the enoxaparin group and 4% in the dalteparin group had. Bleeding was experienced by 3% of the patients in the enoxaparin group and 0% in the dalteparin group. Multivariate regression analyses could not be performed because of the small number of events.

Post surgery transfusions were performed for 61% of the patients in the enoxaparin group and 39% in the dalteparin group. After performing statistical adjustments for age and gender and after excluding 10 patients for a history of bleeding, patients in the enoxaparin group were 42% more likely to need a blood transfusion (risk ratio 1.42, 95% CI, 0.92 to 2.18). Since the resultant CI was wide it means that the possibility of no increased risk was also included.

**Clinical conclusions**
The authors concluded that enoxaparin and dalteparin seemed equivalent in terms of their effectiveness and safety in patients who underwent primary, unilateral TKR surgery. Interchange to dalteparin was therefore thought to be successful.

**Measure of benefits used in the economic analysis**
No summary measure of benefit was used in the economic analysis. The study was, in effect, a cost-consequences analysis.
Direct costs
Health service or hospital costs were included. These comprised the costs of hospitalisation, associated medications, laboratory tests, nursing, physical therapy and medical procedures (e.g. venous Doppler, lung scan X-ray). It was reported that overheads and administrative costs were included. The quantities of resources used were derived from a combination of billing and written medical records. Medication costs were derived from a published source (Average Wholesale Price). Hospital-related costs were based on actual data and were derived from sources published by the hospitals using a "step-down" accounting method. Discounting was not carried out, which was appropriate as the costs were incurred during a short time. All costs were reported as the median cost per patient and related to the year 2000.

Statistical analysis of costs
The authors calculated the median cost-difference with 95% CI between the two groups using Confidence Interval Analysis software.

Indirect Costs
No indirect costs were included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was carried out.

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

Cost results
The median total cost per patient was $2,962 in the enoxaparin group and $2,675 in the dalteparin group.

The results remained unchanged even after adjusting for age and gender using a linear regression model (i.e. approximately 1% change).

After these adjustments it was found that patients in the enoxaparin group had a higher total cost (by 6%) than patients in the dalteparin group (95% CI: -2% to +15%). However, the wide CI implies that there is the possibility of there being no cost-difference.

Synthesis of costs and benefits
The costs and benefits were not combined.

Authors' conclusions
Based on their retrospective analysis, the authors concluded that the change of the low weight molecular heparin (LMWH) product on formulary from enoxaparin to dalteparin was successful and that the costs were almost equivalent for both groups.

CRD COMMENTARY - Selection of comparators
A justification was provided for the interventions under study. The American College of Chest Physicians recommends both LMWH products after TKR surgery for the prevention of deep vein thrombosis and pulmonary embolism. You
should decide if this represents a widely used technology in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a retrospective cohort study. The study is associated with some limitations, in particular, the use of observational data which may result in confounding between the two groups. In addition, the retrospective nature of the study represents a limitation to the internal validity. However, appropriate statistical analyses were undertaken to take potential biases and confounding factors into consideration. The study sample was representative of the study population and the two groups were shown to be comparable at analysis. No power calculations were performed, which makes it difficult to decide whether the sample size was appropriate.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of benefit. In effect, a cost-consequences analysis was performed. The comments under ‘Validity of estimate of measure of effectiveness’ field (above) therefore apply.

Validity of estimate of costs
The analysis of the costs was performed from the perspective of the health care provider (hospital). All the relevant categories of costs appear to have been included in the analysis. The costs and the quantities were reported separately, thus enhancing the reproducibility of the study. The resource quantities were obtained from medical records and an appropriate statistical analysis was performed. Kaplan-Meier techniques were also used to estimate the length of inpatient stay. The costs were based on actual data and were derived from published sources. However, although the costs were treated stochastically, no sensitivity analysis of the prices was conducted, which may limit the generalisability of the findings to other settings. Discounting was not necessary since the costs were incurred during less than 2 years. The price year was reported.

Other issues
The authors compared their results with published studies and, despite differences in the study designs and the patients’ baseline characteristics, they reported consistency in their findings. The issue of the generalisability of the results to other settings was not discussed. The authors pointed out further limitations of their study. For example, the weaker character of a retrospective study design versus a prospective study design in relation to data recording methods, which could not be controlled. The authors also referred to the restricted statistical precision of their study since the limited number of adverse events observed resulted in wide CIs.

Implications of the study
The authors did not make any explicit recommendations for policy change or practice. However, they stressed the need for future research, particularly the requirement for larger studies that will demonstrate statistically more robust findings, and the need for a head-to-head randomised controlled trial evaluating LMWH protocols for patients undergoing TKR surgery.

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Bibliographic details

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