Long-term treatment of deep venous thrombosis with a low molecular weight heparin (tinzaparin): a prospective randomized trial

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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 use of a low molecular weight heparin (LMWH), tinzaparin, in the treatment of proximal deep venous thrombosis (DVT). Tinzaparin was administered at a daily dose of 175 anti Xa IU/kg bodyweight for 6 months.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients aged over 18 years with less than 1 week of symptoms of acute proximal DVT of the lower limbs, confirmed by colour duplex ultrasound scan. Twenty-one exclusion criteria were reported. For example, segmental DVT restricted to infrapopliteal deep veins or calf muscles as determined by duplex ultrasonography, and symptomatic or clinically suspected pulmonary embolism (PE). Full details were provided in the paper.

Setting
The setting was a hospital. The economic study was carried out in a district hospital in Greece.

Dates to which data relate
The authors did not report the dates of the clinical effectiveness data and resource use information. The price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was conducted prospectively on the same sample of patients as that used in the effectiveness analysis.

Study sample
Power calculations were not reported. All consecutive patients presenting during the study period were evaluated for eligibility. A total of 108 patients were selected, but 6 (5 from the LMWH group and 1 from the OA group) were excluded from the study because they withdrew their consent before the treatment was initiated. Of the remaining 102 patients, 50 (31 females) were randomly allocated to the LMWH group and 52 (30 females) to the OA group. The mean
age of the patients was 59 years in the LMWH group and 58.2 years in OA group.

**Study design**
This was a prospective randomised controlled trial that was carried out at a single centre. Randomisation was performed using a computer. The patients were followed up at 4 weeks and 3, 6 and 12 months after discharge. No patient was lost to the follow-up assessment.

**Analysis of effectiveness**
It appears that all the patients included in the initial study have been accounted for in the clinical analysis. The primary outcomes used were the reduction in quantitative ultrasonographic score and the vein reflux score. The secondary outcomes were the incidence of major and minor haemorrhagic complications, mortality, and the incidence of recurrent DVT and PE. The study groups were well balanced in terms of the patient demographics and baseline characteristics.

**Effectiveness results**
The LMWH group produced a significantly lower Marder score than the OA group from 3 months onwards. In the LMWH group versus the OA group, the median Marder scores were 9 (range: 7 - 10) versus 10 (range: 8 - 15), (p=0.017) at 3 months, 6.5 (range: 4 - 9) versus 8 (range: 6 - 12), (p=0.013) at 6 months, and 5 (range: 3 - 7) versus 7 (range: 5 - 10), (p=0.011) at 12 months.

When patients were divided into sub-groups, thrombus regression was significantly in favour of tinzaparin for the following sub-group and times.

For common femoral vein, the median Marder scores in the LMWH versus OA group were 1 (range: 1 - 3) versus 2 (range: 2 - 3), (p=0.025) at 6 months, and 1 (range: 1 - 2.25) versus 2 (range: 2 - 3), (p=0.008) at 12 months.

For superficial femoral vein, the median Marder scores in the LMWH versus OA group were 4 (range: 2 - 6) versus 5 (range: 3.25 - 6), (p=0.035) at 3 months, 3 (range: 2 - 5) versus 5 (range: 3 - 6), (p=0.013) at 6 months, and 13 (range: 2 - 5) versus 4 (range: 3 - 5.25), (p=0.032) at 12 months.

For popliteal vein, the median Marder scores in the LMWH versus OA group were 2 (range: 2 - 3) versus 3 (range: 2 - 4), (p=0.021) at 3 months, 2 (range: 1 - 3) versus 2 (range: 2 - 3), (p=0.027) at 6 months, and 1 (range: 1 - 2) versus 2 (range: 1 - 3), (p=0.018) at 12 months.

The mean scores were also presented.

The overall incidence of major events was 14% in the LMWH group and 32.7% in the OA group, (p=0.0354).

Only those results achieving statistical significance have been reported here. Full results were presented in the paper.

**Clinical conclusions**
The effectiveness study showed that treatment with tinzaparin was at least as effective and safe as that of UFH and acenocoumarol. In terms of major events and recanalisation, there was a significant benefit in favour of tinzaparin.

**Measure of benefits used in the economic analysis**
No summary measure of health benefits was used in the economic analysis. In effect, a cost-consequences analysis was performed.

**Direct costs**
This economic study adopted the cost/quantity boundary of a health care system. The costs of hospitalisation, laboratory tests and drug therapy were included in the economic analysis. The costs of tests performed equally in both groups were
excluded from the study. The unit costs were reported separately from the quantities of resources used. The cost data were obtained from hospital charges. No cost-to-charge ratio appears to have been used. The source of the costs and resources used was unclear. Discounting was not reported as it was irrelevant. The price year was not reported.

**Statistical analysis of costs**
A statistical analysis was performed to test the significance of differences in the estimated costs.

**Indirect Costs**
In line with the stated perspective, the indirect costs were not included in this analysis.

**Currency**
Euros (Euro).

**Sensitivity analysis**
Sensitivity analyses were not performed.

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

**Cost results**
The total costs in the LMWH group (Euro 2,432.7) were slightly lower than those in the OA group (Euro 2,504.56).

**Synthesis of costs and benefits**
A synthesis of the costs and benefits was not relevant.

**Authors’ conclusions**
Based on clinical and economic evidence, the long-term treatment of deep venous thrombosis (DVT) with tinzaparin could be an appropriate alternative to conventional treatment.

**CRD COMMENTARY - Selection of comparators**
The justification for the choice of the comparator was clear. UFH followed by OAs in DVT represented the traditional practice. You should decide whether this is a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**
The effective evidence was derived from a prospective, randomised controlled trial. This was appropriate for the study question as it provided a robust assessment of the clinical implications of the two treatment approaches. The study groups were shown to be comparable at baseline. The patients were identified at a single centre, which may reduce the transferability of the results to other settings. Power calculations were not used to decide the sample size, which means that the possibility that the study lacked sufficient power to obtain significant results cannot be ruled out.

**Validity of estimate of measure of benefit**
No summary measure of benefit was used in the study. The reader is referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above).
Validity of estimate of costs

The authors stated that a national health system perspective was adopted in the study. It appears that all the relevant categories of costs have been included in the analysis. Details of inpatient and outpatient costs, including those of laboratory tests and drug therapy, were provided. A breakdown of the cost items was given, in addition to information on the unit costs and quantities of resources used. This increases the possibility of replicating the study. However, a cost-to-charge ratio was not used to evaluate the true cost of the resources used. The authors acknowledged that the cost of hospitalisation for some major events was not included on the study, and this additional cost would apparently be attributed to the OA group. The exclusion of this cost impacts greatly on the cost results obtained for the OA group and the results of any comparison. The price year was not reported, which makes reflation exercises difficult.

Other issues

The authors made extensive comparisons of their findings with those from other studies. They did not present their results selectively and their conclusions reflected the scope of the analysis. The issue of the generalisability of the study results to other settings was not addressed and sensitivity analyses were not conducted. This reduces the external validity of the analysis.

Implications of the study

The study results suggested that the LMWH tinzaparin should be used in patients with DVT.

Source of funding

Supported by Leo Pharmaceutical Products Hellas Ltd, Athens.

Bibliographic details


PubMedID

15878544

DOI

10.1016/j.ejvs.2004.02.029

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Acenocoumarol /administration & dosage /adverse effects; Administration, Oral; Adult; Aged; Aged, 80 and over; Drug Therapy, Combination; Female; Follow-Up Studies; Heparin /administration & dosage /adverse effects; Heparin, Low-Molecular-Weight /administration & dosage /adverse effects; Humans; Infusions, Intravenous; Injections, Subcutaneous; Long-Term Care; Male; Middle Aged; Partial Thromboplastin Time; Pulmonary Embolism /drug therapy /ultrasonography; Recurrence; Ultrasonography, Doppler, Duplex; Vascular Patency /drug effects; Venous Thrombosis /drug therapy /ultrasonography

AccessionNumber
22005000793

Date bibliographic record published
31/03/2006

Date abstract record published
31/03/2006