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DJ Anderson, AD Burrell & A Bearne

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DJ Anderson[1], AD Burrell[2], A Bearne[2]

Summary

The aim was to compare the costs of treating venous thromboembolism in three possible clinical settings, either in-hospital, or out-of-hospital, by means of an anticoagulation clinic or by treatment at home. Initial treatment of venous thromboembolism involves the initiation of anticoagulation and the provision of concomitant antithrombotic therapy for 5-7 days, consisting of monitored, dose-adjusted, unfractionated heparin, given in-hospital, or low molecular weight heparin, given in a once-daily weight-adjusted dose, either in- or out-of-hospital. The cost model assumes that outcomes do not vary relative to the treatment administered. Costs were categorised under drug costs, administration costs and costs associated with care, both in- and out-of-hospital. Our study showed that savings can be made using Clexane* (enoxaparin) treatment without hospital admission. Total expected costs of enoxaparin provided in the community, incorporating nurse visits, were £241.70. The anticoagulation clinic costs were £433.70, compared with in-hospital unfractionated heparin at £1,183.13. Acute venous thromboembolism treatment in the community reduces costs, providing an incentive to manage patients out-of-hospital.

Key words: venous thromboembolism, treatment, costs, low molecular weight heparin, unfractionated heparin, community, anticoagulation clinic

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[1] Pharmacy Department, St. Peter's Hospital, Chertsey, UK

[2] Outcomes Research, Aventis Pharma, West Malling, Kent, UK

Address for correspondence: : Andy Bearne, Outcomes Research, Aventis Pharma, Aventis House, 50 Kings Hill Avenue, Kings Hill, West Malling, Kent ME19 4AH, UK. Tel: + 44 (0)1732 584069, fax: +44 (0)1732 584404, e-mail: Andy.Bearne@Aventis.com.

* Clexane is a registered trademark of Aventis Pharma, UK.

Introduction

Venous thromboembolism (VTE) is a serious condition that is a major cause of morbidity and mortality in the UK population. VTE occurs in approximately one in 1,000 individuals in the developed world[1]. It is now widely accepted that VTE encompasses both pulmonary embolism (PE) and deep vein thrombosis (DVT), representing different facets of the same disease[2]. The treatment of both forms of VTE is effectively the same and involves anticoagulation, or less commonly, thrombolysis or mechanical disruption of the thrombus[3]. If VTE is either inadequately treated or left untreated, there is a high risk of developing late-stage complications such as recurrent venous thrombosis or post-thrombotic syndrome or life-threatening acute massive PE[3].

The initial management of VTE involves the initiation of oral anticoagulation in conjunction with heparin, either adjusted dose unfractionated (UFH), or fixed dose low molecular weight heparin (LMWH)[3]. The anticoagulant effect of UFH is influenced by non-specific binding to cells and plasma proteins, resulting in a variable anti-coagulant effect that provides the rationale for careful laboratory monitoring. LMWHs are fragments of heparin and demonstrate less non-specific binding, resulting in several attractive kinetic features including a better bioavailability and a longer half-life than UFH. LMWHs can, therefore, be given without the need for laboratory monitoring and dose adjustment. This is the most important factor that influenced the move to out-of-hospital administration of LMWH for the treatment of VTE[3]. Studies show that LMWHs can be effectively self-administered in the community and outpatient departments, something that is not feasible with UFH administration[4].

Several studies and meta-analyses have demonstrated that LMWHs are at least as effective and safe as UFH for the treatment of acute DVT[5-10]. In these trials, UFH was administered by intravenous infusion with the dose adjusted according to the activated partial-thromboplastin time (aPTT) while the LMWHs were administered subcutaneously and weight-adjusted without the need for laboratory monitoring. Additional studies have shown that LMWH in the outpatient setting has comparable safety and efficacy as UFH given in hospital[11,12] and that outpatient management may now be the standard of care[13,14]. Similarly, it has been shown that patients with sub-massive PE[15] who are haemodynamically stable can be treated with LMWHs as effectively as with UFH and there is now the suggestion that these patients can also be managed out-of-hospital[16-18]. Moving VTE care to the outpatient setting, either at an anticoagulation clinic or at home, largely eliminates in-hospital costs, and provides a relatively simple anticoagulation treatment[17,19].

Nowadays, health care managers are increasingly aware of the need to maximise health resources and are conscious of cost-effective patient care. This reflects awareness that healthcare decision-makers are placing increasing importance on value

for money from healthcare interventions. This cost minimisation analysis was undertaken to examine the economic arguments surrounding the treatment of VTE in a hospital setting, in the community setting or via the use of an anticoagulation clinic. The objective of the analysis was to compare the direct medical costs associated with the different treatment options available to patients in the UK, based on the assumption that all forms of administered treatment produce relatively similar clinical outcomes.

Methods

Study design and protocol

The costs were based on the theoretical management of confirmed VTE in three different treatment settings: in-hospital, home and an anticoagulation clinic (Figure 1). Each of the settings for the different treatment options involved the use of different resources and these were documented such that the relevant costings could be applied. The study was designed to assess the costs of VTE treatment using a LMWH (enoxaparin) compared with UFH and all costs were assessed from a UK National Health Service (NHS) perspective.

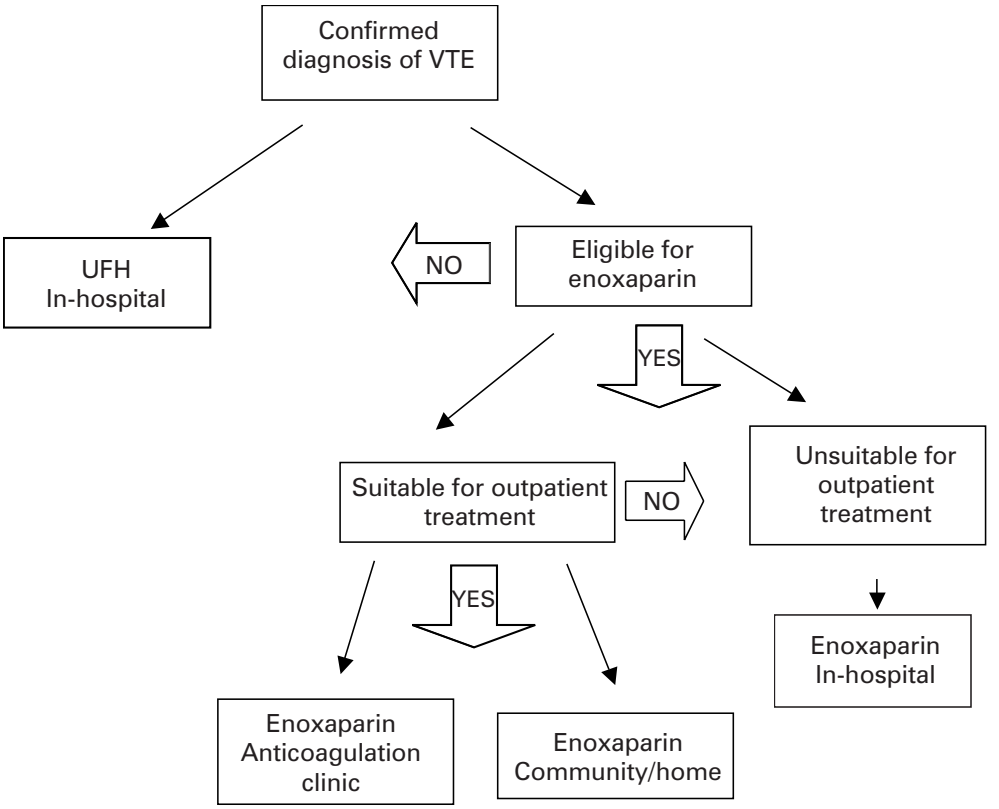
In the UK, three low molecular weight heparins are licensed to treat DVT and PE. Specifically, enoxaparin is licensed for the treatment of venous thromboembolic disease presenting with deep vein thrombosis, pulmonary embolism or both. Although LMWHs share similar properties, they differ in molecular weight distribution, plasma clearance times, and specific activities. Importantly, this is reflected in their different dosing regimens[20-22]. This analysis is based on enoxaparin as it is the most widely prescribed LMWH in the UK. Doses described are for an average (80 kg) person[23], though it should be noted that under real circumstances, the dosage is adjusted according to either weight (as in the case of LMWH) or aPTT (as in the case of UFH). Thus, the costs of an individual case may actually be higher or lower. UFH treatment, administered by continuous intravenous infusion in the inpatient setting (dosage: 5,000 IU loading dose followed by 1,000 IU/h) was compared to the cost of a LMWH, Clexane* (enoxaparin, 120 mg dose, once daily subcutaneous injection), administered in-hospital, in the community or at an anticoagulation clinic, based on a UK National Health Service perspective. In the UK, enoxaparin is available at two concentrations, 100 mg/ml and 150 mg/ml. For convenience, pre-filled syringes are available for 20, 40, 60, 80, 100, 120 and 150 mg injections[23]. We based our costs on a 120 mg pre-filled syringe.

Cost analysis

For the analysis, costings were simply categorised under the broad headings of medication, administration, inpatient/outpatient costs and community nurse visits, as required. Administration included costs of equipment (syringes, needles, giving sets), laboratory costs (INR tests, aPTT tests), nursing time, and equipment depreciation (pump usage).

* Clexane is a registered trademark of Aventis Pharma, UK.

Figure 1. Study model showing venous thromboembolism treatment options



Adapted from Deitcher, Olin and Bartholomew[30]

Indirect costs, such as patient time off work, or buying meals in the hospital restaurant, were not included in the study. The data are limited to absolute direct costs of each treatment option, and other less definable direct costs, such as the community nurse's travel expenses, are not included. Therefore this is a conservative analysis of costs. As outpatient management of VTE can only be performed on confirmed cases, the costs of diagnosis (scans or other) have not been assessed for this analysis. The cost figures used in this analysis are taken from published sources and these include the *British National Formulary* (September 2001), and the *Unit Costs of Health and Social Care* (2000).

Results

The treatment strategy that resulted in the least cost per patient was LMWH (enoxaparin) provided out-of-hospital, either in the community setting (£241.70) or using an anticoagulation clinic (£433.70). The costs of in-hospital unfractionated heparin treatment were markedly more expensive (£1,183.13). The analysis shows

that in-hospital treatment of VTE accumulates the most costs, which is mainly due to the high cost of hospital admission. Both the anticoagulation clinic and the community setting with enoxaparin treatment resulted in substantial cost benefits when compared with in-patient VTE treatment. These cost benefits imply that there is sufficient spare capacity for a transition from one treatment setting to the other. The expected average costs per patient are shown in Table 1.

Discussion

This study shows that savings can be made if the treatment of an average (80 kg) person who presents with VTE is provided in the community setting with the LMWH, enoxaparin (120 mg, once daily subcutaneous injection), when compared with UFH. There are substantial savings if the treatment is at home or provided at an anticoagulation clinic. These savings are realised because enoxaparin given out-of-hospital, at the anticoagulation clinic or in the community, removes the need for an in-hospital stay. This is in contrast to the administration of UFH which requires patient admission, monitoring and dose adjustment. Enoxaparin can also be administered in the hospital setting, offering the health provider a wider range of treatment options.

Previous studies have demonstrated the safety and efficacy of LMWHs in the outpatient management of DVT and some economic analyses have been performed[19,28,29]. Tillman *et al* enrolled 91% of total patients presenting with DVT in their outpatient management program. This prospective study showed substantial economic benefits in moving DVT treatment of 391 patients from the hospital to an outpatient setting, with savings of more than US$1 million over a 2-year period. In the TASMAN cost-minimisation analysis, which was based on actual patient data, complete cost analysis including laboratory monitoring and in-hospital stays revealed a 64% reduction in overall costs associated with outpatient management of DVT compared with in-patient treatment with UFH. These savings were realised despite the higher purchase cost of the LMWH nadroparin.

In the past, conditions such as diabetes or asthma were treated in-hospital. Nowadays they are managed principally by the patients themselves, a clear shift from inpatient to outpatient management. Although subcutaneous administration of a LMWH may be somewhat daunting for a patient, the community nurse can provide instruction as to the correct procedure[11,30]. Family members can also be instructed if the patient is not comfortable with carrying out the procedure by themselves. In addition, training videos are available from the pharmaceutical companies detailing instructions on subcutaneous injection, which can be given to patients/family members. Reducing the need for continuous community nurse visits therefore will further reduce costs. Alternatively, patients can present at an anticoagulation clinic, and have the procedure carried out by a healthcare

Table 1. Summary of venous thromboembolism treatment costs

	UFH (hospital)	*Enoxaparin (A-C clinic)*	*Enoxaparin (community)*	*Enoxaparin (hospital)*
Drug cost[23,24]				
Daily treatment dose	£0.92	£10.51	£10.51	£10.51
Loading dose	£0.37	£0.00	£0.00	£0.00
Warfarin 3 mg/day[24]	£0.06	£0.06	£0.06	£0.06
Treatment for 5 days	*£5.27*	*£52.85*	*£52.85*	*£52.85*
Administration costs				
Cost of sundries[25]				
Luer-lock syringe	£0.37	£0.00	£0.00	£0.00
Plain needle	£0.02	£0.00	£0.00	£0.00
Vygon 3-way tap	£0.28	£0.00	£0.00	£0.00
Ivac standard set	£1.37	£0.00	£0.00	£0.00
Letro-cath	£1.81	£0.00	£0.00	£0.00
Laboratory costs				
APTT cost per test[25]	£2.80	£0.00	£0.00	£0.00
INR test[26]	£7.13	£7.13	£7.13	£7.13
Nursing time[a] £0.174/min[25]	£1.22	£1.04	£1.04	£1.04
Pump costs Graseby 3400 infusion pump (depreciation per day)[25]	£0.34	£0.00	£0.00	£0.00
Summed daily cost	£11.49	£8.17	£8.17	£8.17
Treatment for 5 days	*£62.86*	*£40.85*	*£40.85*	*£40.85*
Outpatient/inpatient visits[27]				
Outpatient visits (£68 each visit)	£0.00	£340.00	£68.00	£0.00
In-patient stays (average 5)	£1,115.00	£0.00	£0.00	£1,115.00
Community nurse visits (average 5)	£0.00	£0.00	£80.00	£0.00
Treatment for 5 days	*£1,115.00*	*£340.00*	*£148.00*	*£1,115.00*
Summary of costs				
Drug costs	£5.27	£52.85	£52.85	£52.85
Administration costs	£62.86	£40.85	£40.85	£40.85
Inpatient/outpatient costs	£1,115.00	£340.00	£148.00	£1,115.00
TOTAL	*£1,183.13*	*£433.70*	*£241.70*	*£1,208.70*

[a] Nursing time has been adjusted according to inflation index[27]

professional. Both processes circumvent the costs of hospital admission.

Home treatment of VTE has obvious advantages for the patient, potentially improving their quality of life, and providing a more efficient healthcare delivery. Many trials have shown the safety and benefit of outpatient DVT treatment[11,29-34] although these and other

trials have highlighted the need for careful patient selection[34,35], and the actual number of patients eligible for outpatient treatment varies from trial to trial[11,13,36]. Of course, not all patients are suitable for at home management of DVT, such as those with inherited thrombophilias, evidence of current active bleeding, previous VTE, or pregnancy[11-13]. In such circumstances, these higher-risk patients are usually admitted to hospital for closer monitoring. Pharmacokinetic and pharmacodynamic studies show that enoxaparin dosage does not need to be adjusted for obesity[37]. However, the dose may need to be reduced in cases of severe renal impairment[38]. As with DVT, not all patients with confirmed PE are suitable for outpatient treatment. Patients that should be excluded from a home-treatment program include those with haemodynamic instability, co-morbidity, oxygen requirements and active or high risk of bleeding[16].

A weakness of this analysis rests on the assumption that each of the treatment options produces the same outcome, when there is evidence that LMWHs are actually superior to UFH[10]. Meta-analysis of VTE treatment trials has suggested that the efficacy of LMWH may be superior to UFH, with an equivalent incidence of bleeding complications. This suggests that LMWH may be more efficacious in terms of lives saved. However, it is beyond the scope of this analysis to pursue these issues. A cost-benefit or cost-utility analysis, although a more complex investigation, would provide a greater evaluation of the savings not only in monetary value, but also in less measurable quantities such as patient well being, or quality of life.

Pharmaceutical companies may provide a volume-related pricing scheme, helping reduce the cost of drug and making the outpatient procedure even more attractive. Given that the LWMH analysed in this study (enoxaparin) has been licensed for a broad range of indications that is not matched by any other LMWH[39] and includes the prevention and treatment of venous thromboembolism in medical and surgical patients and the treatment of patients presenting with an acute coronary syndrome, further savings may be realised by the use of one LMWH across all therapeutic (arterial and venous) indications. Rationalisation may have other advantages, such as helping to minimise prescribing errors and may facilitate the implementation of a single anticoagulation protocol.

This study provides a guide to the setting which, wherever feasible, realises the greatest cost saving for the treatment of VTE, It does not take into account local issues such as availability of an anticoagulation clinic (opening hours, only 5 days per week) or community nurse visits. This study provides a strong cost rationale for moving the treatment of VTE from secondary to primary care. Although such a setting shift may incur additional costs according to local service provision, it seems likely that the shift from inpatient to outpatient care would still prove cost saving irrespective of the local cost structures. In summary, acute VTE treated in the community with LMWH reduces costs for the health service and increases convenience for the patient.

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