

Outpatient Treatment of Deep Vein Thrombosis and Pulmonary Embolism: a Hospital-Based Program

S. Jo-Anne Wilson, Lisa Gray, and David R. Anderson

ABSTRACT

Objective: To assess the effectiveness and safety of a hospital-based outpatient treatment model for venous thrombosis in terms of clinical outcomes, specifically recurrence of venous thromboembolism and occurrence of minor or major hemorrhage.

Methods: The authors performed a prospective cohort study of consecutive patients diagnosed with acute deep vein thrombosis or pulmonary embolism presenting to the emergency department of a tertiary care hospital in Nova Scotia. Patients were treated for a minimum of 5 days with dalteparin sodium, 200 U/kg subcutaneously once daily for deep vein thrombosis or 120 U/kg subcutaneously twice daily for pulmonary embolism; long-term warfarin sodium was also administered. Patients were followed for 3 months to determine rates of recurrence of venous thromboembolism and rates of hemorrhage.

Results: Eighty-three patients with objectively confirmed deep vein thrombosis or pulmonary embolism were eligible for this study. Of these, 81 were treated as outpatients through the outpatient treatment facility. Two patients were excluded and were treated in hospital; one of these had massive pulmonary embolism and the other lived out of province. During this study, 4% (95% confidence interval [CI] 1% to 6%) of the patients had recurrent venous thromboembolic events, 5% (95% CI 2% to 7%) had minor hemorrhage, and no patients had major hemorrhage. The mean duration of dalteparin treatment was 5.8 days (standard deviation 1.9 days). It was estimated that between 316 and 624 hospital days were saved for the 81 patients managed through the program.

Conclusion: Patients with acute venous thromboembolism can be safely and effectively treated as outpatients with a hospital-based treatment model of care.

Key Words: low-molecular-weight heparin, outpatient treatment, deep vein thrombosis, pulmonary embolism

RÉSUMÉ

Objectifs : Évaluer l'efficacité et l'innocuité du modèle de traitement ambulatoire hospitalocentrique de la thrombose veineuse, en termes de résultats cliniques, et particulièrement la récurrence de thromboembolie veineuse et la survenue d'hémorragies mineures ou majeures.

Méthodes : Les auteurs ont réalisé une étude prospective de cohorte chez une série consécutive de patients présentant une thrombose veineuse profonde ou une embolie pulmonaire diagnostiquées à l'urgence d'un hôpital de soins tertiaires de Nouvelle-Écosse. Les patients ont été traités pendant un minimum de cinq jours, à la daltéparine sodique, administrée à raison de 200 U/kg par voie s.-c., une fois par jour dans les cas de thrombose veineuse profonde ou à raison de 120 U/kg par voie s.-c., deux fois par jour dans les cas d'embolie pulmonaire; de la warfarine sodique a également été administrée à long terme. Les patients ont été suivis pendant trois mois pour déterminer les taux de récurrence de thromboembolie veineuse et d'hémorragies.

Résultats : Quatre-vingt-trois patients présentant une thrombose veineuse profonde ou une embolie pulmonaire confirmée objectivement étaient admissibles à cette étude. De ces patients, 81 ont reçu un traitement ambulatoire à la clinique de soins ambulatoires. Deux patients ont été exclus et traités à l'hôpital; l'un d'eux avait une embolie pulmonaire massive et l'autre vivait à l'extérieur de la province. Au cours de cette étude, 4 % (intervalle de confiance à 95 % [IC] 1 % à 6 %) des patients ont eu des récurrences de thromboembolie veineuse, 5 % (IC 95 %, de 2 % à 7 %) ont eu une hémorragie mineure, et aucun n'a présenté d'hémorragie majeure. La durée moyenne du traitement à la daltéparine était de 5,8 jours (écart type de 1,9 jour). On a estimé qu'entre 316 et 624 jours d'hospitalisation ont été évités pour les 81 patients soignés par le biais de ce programme.

Conclusion : Les patients présentant une thromboembolie veineuse profonde peuvent être traités efficacement et en sûreté en soins ambulatoires, en suivant un modèle de traitement ambulatoire hospitalocentrique.

Mots clés : héparine de faible poids moléculaire, traitement ambulatoire, thrombose veineuse profonde, embolie pulmonaire

INTRODUCTION

Venous thromboembolism, comprising deep vein thrombosis and pulmonary embolism, is a common medical condition that can result in significant morbidity and mortality if not treated effectively.¹ Until recently, the standard treatment for these disorders was admission to hospital for the intravenous administration (over a period of 5 to 10 days) of unfractionated heparin at a dose adjusted to maintain the activated partial thromboplastin time in the desired range, followed by oral anticoagulant therapy for at least 3 months.²

After nearly 2 decades of research, low-molecular-weight heparins have become an important class of antithrombotic agents in the treatment of venous thromboembolism. Controlled trials have demonstrated that low-molecular-weight heparins administered subcutaneously are at least as effective and safe as adjusted intravenous doses of unfractionated heparin for the treatment of acute venous thromboembolism.³⁻¹¹

Two recent randomized clinical trials have demonstrated that, for the initial treatment of deep vein thrombosis, low-molecular-weight heparins administered subcutaneously on an outpatient basis are as effective and safe as in-hospital intravenous therapy with unfractionated heparin.^{12,13} However, the patients in these 2 trials were carefully selected, and 30% to 70% of patients with acute venous thromboembolism were excluded from the outpatient therapy.^{12,13} The study patients were also carefully managed within the confines of a highly supervised research trial. Clinicians may therefore be concerned that the benefits seen in these outpatient clinical trials may not translate to their own clinical practice.

Regardless of these concerns, many clinicians are striving to develop safe and effective outpatient treatment models for venous thromboembolism. Several such models have been developed for outpatient low-molecular-weight heparin therapy, including teaching self-injection to patients, arranging for home-care nurses to administer the injections, and using an ambulatory care clinic such as a medical day unit or an anticoagulation clinic as the base for outpatient therapy.

To date, 2 studies have examined the feasibility, safety, and efficacy of outpatient treatment models.^{14,15} These studies also expanded the eligibility for outpatient care to include patients who had been excluded from previous studies, such as patients with pulmonary embolism, previous deep vein thrombosis, and other comorbid conditions. The patients in these outpatient studies were taught to perform self-injections at home or

injections were given by home-care nurses. Both studies reported overall rates of recurrent venous thromboembolism and bleeding that were at least as favourable as those obtained in controlled clinical trials.

At our centre, we have developed a hospital-based outpatient treatment model for venous thromboembolism. Patients with acute deep vein thrombosis or pulmonary embolism are referred to the program, which is administered through an outpatient treatment facility, the Medical Day Unit. The purpose of this study was to evaluate the effectiveness and safety of our outpatient treatment model.

METHODS

Patients

All patients with objectively diagnosed deep vein thrombosis or pulmonary embolism who presented to the Emergency Department of the Queen Elizabeth II Health Sciences Centre in Halifax, NS, between August 1, 1997, and August 31, 1998, were considered eligible for outpatient treatment. We excluded patients with the following characteristics: (i) medical illness unrelated to deep vein thrombosis or pulmonary embolism for which the patient would require admission to hospital; (ii) recent major bleeding episode; (iii) active peptic ulcer disease; (iv) renal insufficiency (serum creatinine greater than 200 $\mu\text{mol/L}$); (v) massive pulmonary embolism as evidenced by hypotension, tachycardia, severe pain, or requirement for oxygen; (vi) geographic inaccessibility for follow-up; and (vii) likelihood of poor compliance (as for patients who were unable to care for themselves, lacked adequate home support, or were unwilling to comply with the treatment care plan).

Treatment Program

Potentially eligible patients were evaluated by a physician (D.R.A.), and those who were eligible were enrolled in the outpatient treatment program. Standardized physician orders were completed (Figure 1), and the overall care plan was discussed with the patient.

Patients with deep vein thrombosis received 200 U/kg of dalteparin subcutaneously once daily, and patients with pulmonary embolism received 120 U/kg of dalteparin subcutaneously twice daily for a minimum of 5 days. The dosage for pulmonary embolism was based on a previously published study,¹⁶ and was higher than the approved dosage of 100 U/kg of dalteparin twice daily. The first dose of dalteparin was usually administered in the Emergency Department and then patients

Figure 1. Standing order for outpatient management of deep vein thrombosis and pulmonary embolism.



Physician Standing Order
Department of Medicine/Medical Day Unit
Outpatient Management of DVT and PE

Patient: _____

Allergies: _____

Date (YYYY/MM/DD) _____ Time (24hr/hh:mm) _____

1. The following orders may be used in any patient care area.
2. The following orders will be carried out by a nurse **ONLY** on the **AUTHORITY OF A PHYSICIAN**.
3. All orders to be carried out must be **circled/checked** as appropriate.
4. **Vital Signs:** Temp, Pulse, Resp Rate, BP, once a day, prior to administration of Low Molecular Weight Heparin (LMWH).
5. **Baseline Investigations:** CBC, INR, BUN, Creatinine, ALT, AST, ALK Phosphate, GGT, bilirubin, glucose. **(DAY 1)**
6. **Other Investigations:** INR and CBC on day 3 and 5. Notify physician if a platelet count is less than 100,000. Daily anti-Xa level to be drawn prior to LMWH injection for patients weighing >120 kg or creatinine >150 µmol/L.
7. **Low Molecular Weight Heparin Regimens for Deep Vein Thrombosis or Pulmonary Embolism:**

For Deep Vein Thrombosis:

- Choose one only: Dalteparin 200 u/kg (Day 1-5) _____ u (total dose) SC OD

OR

- 100 u/kg (Day 1-5) _____ u (total dose) SC q12h

For Pulmonary Embolism:

- Choose one only: Dalteparin 120 u/kg (Day 1-5) _____ u (total dose) SC q12h
 - Discontinue Dalteparin after Day 5 injection on (YYYY/MM/DD) _____ if INR ≥ 2.5.
 - If Day 5 INR is <2.5, continue daily Dalteparin injections, daily INR, and CBC every second day. Dalteparin may be discontinued once INR >2.0 for 2 consecutive days.
8. **Warfarin Regimen:** Give prescription for Warfarin, 5 mg tabs x 100. If baseline INR < 1.4, instruct patient to take 10 mg on Day 1, and Day 2. Warfarin doses for Day 3 and Day 4 are based on Day 3 INR.
 9. **Orders on the Weekend or Holidays:** The hematologist-on-call is responsible for the medical care of the patient. Warfarin dose should be adjusted using the nomogram unless otherwise indicated. The Medical Day Unit nurse will call the patient at home with the daily warfarin dose, if appropriate. If unable to contact the patient, the Medical Day Unit nurse will notify the hematologist on call.

Date (YYYY/MM/DD) _____

Physician's Signature _____

College of Physicians/Surgeons Number _____

Physician's Name - Print _____



were referred to the outpatient treatment program. Dalteparin was chosen for this program because at the time of the study it was the only low-molecular-weight heparin approved in Canada for treatment of deep vein thrombosis. A nurse (L.G.) coordinated patient care for the first 5 days. Patients were instructed to return to the outpatient clinic facility (the Medical Day Unit) within 24 h of diagnosis to receive their dalteparin injections and to have samples taken for blood work. All patients underwent baseline blood testing that included a complete blood count and determination of serum level of creatinine and international normalized ratio (INR). The complete blood count and the INR determination were repeated every 48 h while the patients remained on dalteparin therapy. Patients who were not mobile or lived too far away to commute were taught self-injection, or home care was arranged by a nurse. All patients were given a 24-h emergency number to call if problems with bleeding or worsening clot symptoms occurred. In the event of worsening or severe symptoms, patients were advised to report to their local emergency department.

Patients with normal baseline INR levels usually received a 10-mg dose of warfarin on days 1 and 2 of dalteparin therapy. The warfarin dose for days 3 and 4 was based on the day 3 INR according to a warfarin nomogram from another centre that was used with permission. A version of this nomogram was previously published,¹⁷ but the nomogram has since been modified and has not yet been published in its modified form. A nurse contacted the patient by telephone to communicate the dosage of warfarin for days 3 and 4. Dalteparin was discontinued after the day 5 injection if the INR was 2.5 or higher. If the INR was less than 2.5, the INR determination was repeated daily and dalteparin injections were continued until the INR was greater than 2.0 for 2 consecutive days.

After completion of the treatment with low-molecular-weight heparin, patients were referred to an oral anticoagulation clinic directed by a pharmacist (S.J.W.) for more detailed education and subsequent warfarin dosing. An ongoing education program was provided to each patient to deal with the goals and risks of therapy, the signs and symptoms of bleeding or worsening thromboembolic symptoms, laboratory monitoring, and the importance of compliance and follow-up.

All patients returned 1 week after initial diagnosis and then again in 3 months for reevaluation by a physician. Patients with signs and symptoms of recurrent deep vein thrombosis or pulmonary embolism during the 3-month study period were assessed by a

physician and underwent appropriate diagnostic testing, including duplex ultrasonography or ventilation perfusion lung scanning (or both).

To minimize the cost of drug therapy to the patient, the dalteparin therapy was charged to the patient's third-party insurer by a community pharmacy. For patients without third-party insurance, a social worker evaluated the patient's situation for payment alternatives. For patients without social assistance options, the hospital covered the cost of the dalteparin therapy.

Analysis

Rates of recurrent deep vein thrombosis, pulmonary embolism, and minor or major bleeding events occurring in the 3-month period after diagnosis were determined, along with the associated 95% confidence intervals. Bleeding was defined as major if it was overt and associated with either a decrease in the hemoglobin level of at least 20 g/L or a need for the transfusion of 2 or more units of blood. Bleeding was defined as minor if it was overt but did not meet the other criteria for major bleeding.¹⁸ Unscheduled visits for signs and symptoms of recurrent thrombosis were recorded, as were the number of hospital days potentially saved with the outpatient program. Method of payment for the dalteparin therapy was also recorded.

RESULTS

Between August 1, 1997, and August 31, 1998, 83 potentially eligible patients presented to the Emergency Department and were referred to the outpatient treatment program. Of these, 2 were excluded from receiving outpatient therapy. One of these had unstable pulmonary embolism and the other resided in another province; both were treated in hospital. The median age of the 81 eligible patients was 56 (range 18 to 86) years. Forty-three (53%) were female and thirty-eight (47%) were male. Seventy-two patients had deep vein thrombosis and were treated with dalteparin once daily. Nine patients had pulmonary embolism and were treated with dalteparin twice daily. Total daily dalteparin doses ranged from 9000 to 27 000 U. The mean (\pm standard deviation [SD]) duration of dalteparin treatment was 5.8 ± 1.9 days. On the basis of the mean (\pm SD) duration of treatment, it is estimated that between 316 and 624 hospital days were potentially saved for the 81 patients managed through the outpatient program.

Sixty-nine of the patients were treated in our outpatient treatment facility, the Medical Day Unit, 5 patients were taught self-injection, and 7 patients

Table 1. Baseline characteristics of 81 patients* enrolled in outpatient treatment program for deep vein thrombosis (DVT) and pulmonary embolism during study period

Characteristic	No. of patients
With proximal DVT	64
With pulmonary embolism	9
With subclavian DVT	8
Idiopathic	29
With DVT due to risk factors	52

*Median age was 56 (range 18 to 86) years.

received their injections from home-care nurses.

The characteristics of the patients with deep vein thrombosis and pulmonary embolism are outlined in Table 1.

Five percent (95% confidence interval [CI], 2% to 7%) of the patients had minor hemorrhage (hematuria), and no patients had major hemorrhage. At or before the 1-week follow-up visit, 4% (95% CI 1% to 6%) of the patients had recurrence of their thromboembolic disorder. One patient's deep vein thrombosis had extended, and another patient had recurrence of pleuritic chest pain secondary to pulmonary embolic disease. Both patients were treated with low-molecular-weight heparin for an additional 7 to 10 days on an outpatient basis. Another patient was admitted to hospital for suspected pulmonary embolism 2 days after being enrolled in the outpatient program for treatment of deep vein thrombosis. Although investigations for pulmonary embolism yielded negative results, she remained in hospital for treatment with unfractionated heparin before resuming warfarin therapy.

There were 11 unscheduled visits (all in different patients) for suspected recurrence during the 3-month follow-up period. Two of these unscheduled visits occurred within the first 7 days of treatment. None of the 11 patients was found to have recurrent deep vein thrombosis or pulmonary embolism.

Sixty-nine (85%) of the 81 patients had third-party insurance to cover the low-molecular-weight heparin, and 12 (15%) patients received dalteparin therapy through either social assistance or the hospital.

DISCUSSION

The management of patients with acute venous thromboembolism is changing in Canada, and outpatient treatment with low-molecular-weight heparin is gradually replacing in-hospital treatment with unfractionated

heparin. Low-molecular-weight heparins offer several advantages over unfractionated heparin, including better bioavailability after subcutaneous injection, a longer plasma half-life, and more predictable anticoagulant activity.^{19,21} These properties allow low-molecular-weight heparins to be administered subcutaneously once daily in fixed doses based on a patient's body weight, without the need for routine monitoring of their anticoagulant effect.

Controlled clinical trials have demonstrated that low-molecular-weight heparins are as effective and safe as unfractionated heparin for the acute treatment of venous thromboembolism.^{3,11} Two further controlled trials reported similar results when low-molecular-weight heparin was given mainly on an outpatient basis to patients with proximal deep vein thrombosis.^{12,13} Extrapolation of these results to routine clinical practice is challenging, as patients were carefully selected and cared for in these outpatient clinical trials. Nevertheless, many institutions have developed and implemented various outpatient treatment models for deep vein thrombosis and pulmonary embolism. Several treatment models exist for outpatient therapy with low-molecular-weight heparin, including teaching patients self-injection, arranging for home-care nurses to administer the injections, and using a hospital-based ambulatory facility, such as a medical day unit, to administer therapy. Models based on teaching patients self-injection or arranging for home-care nurses to administer injections usually involve one initial visit. During this visit, patients receive the necessary education and skills (specifically the self-injection technique) to permit outpatient treatment. Follow-up involves daily telephone contact to assess the patient's progress and to ensure compliance with both low-molecular-weight heparin and warfarin therapy. For patients taught self-injection, one drawback is that the daily assessment is limited to the patient's interpretation of the situation. The benefit of this treatment model is that it is convenient for patients and consumes the least amount of hospital resources. The benefits of home-care nurses administering therapy are convenience for patients and minimization of potential errors in injections. However, this model of care is costly, as home-care nurses must be consulted to provide this service.

The third treatment model involves using a hospital-based facility to deliver outpatient treatment. Medical day unit treatment programs have the advantage of availability of space for daily nursing assessment, patient counselling, and treatment.²² Because patients return daily, any potential problems can be addressed

immediately. Furthermore, patients diagnosed on the weekend can still start their treatment immediately, because many medical day units are open 7 days a week. Despite the virtues of this treatment model, it can be both inconvenient and costly for patients in terms of commuting and parking.

The selection of a treatment model will depend on an institution's available resources and clinical expertise.²² For continuity of care, it is necessary to have a core group of clinicians involved in facilitating outpatient therapy. Regardless of the treatment model chosen, it is imperative to follow a clearly defined protocol that outlines all aspects of treatment to minimize potential errors.

To date, 2 studies have evaluated the safety and efficacy of different outpatient treatment models.^{14,15} Wells and colleagues¹⁴ compared 2 models of care. In one model 95 patients were taught self-injection and in the other model home-care nurses administered low-molecular-weight heparin injections to 99 patients. There was no significant difference in the rate of recurrent venous thromboembolism between the 2 groups (3/95 and 4/99 respectively; $p > 0.99$). Similarly, there were no significant differences in rates of major hemorrhage (2/95 and 2/99 respectively; $p > 0.99$) and minor hemorrhage (8/95 and 2/99 respectively; $p = 0.06$). When the results from the 2 models were combined, the overall rate of recurrence was 3.6% (95% CI, 1.5% to 7.4%) and that of major hemorrhage was 2.0% (95% CI, 0.6% to 5.2%). Despite the expansion of the indications for treatment to include patients with more critical conditions, such as pulmonary embolism (34 patients), the results were similar to those reported in controlled clinical trials.^{12,13}

In the second study, by Harrison and colleagues,¹⁵ 67 patients were taught self-injection, whereas the other 22 patients required assistance from a visiting nurse or through nursing-home nurses. A similar low rate of recurrent venous thromboembolism and major bleeding was observed. Patients also reported a high degree of satisfaction with the level of support and instruction they received.

Our results demonstrate that patients can be safely and effectively treated through a hospital-based treatment model. In our study, 85% (69/81) of the patients were treated through our Medical Day Unit and the remaining 15% (12/81) were taught self-injection or received injections from home-care nurses. During the 3-month follow-up period, only 4% (95% CI, 1% to 6%) of patients had recurrent venous thromboembolic events, 5% (95% CI, 2% to 7%) of patients had minor bleeding,

and no patients had major bleeding events. Despite this study's small sample size, our event rates concur with previous outpatient studies and clinical trials.¹²⁻¹⁵

Although 98% of the patients referred to our program could be treated as outpatients, one limitation of our study is that the Emergency Department may not have referred all potentially eligible patients, and some of these patients may in turn have been admitted to hospital. In addition, only a few patients in our study had pulmonary embolism. To date, there have been no randomized controlled trials comparing outpatient with in-hospital treatment for patients with pulmonary embolism. However, evidence is accumulating that patients with symptomatic pulmonary embolism who are hemodynamically stable can be managed with low-molecular-weight heparin on an outpatient basis.^{14,15,23}

Moving the initial treatment of patients with deep vein thrombosis and pulmonary embolism to an outpatient setting represents a dramatic change in practice but is in keeping with the general trends in health care today. To realize the potential benefits of outpatient treatment of venous thromboembolism (decreased hospital admissions and costs of management, along with increased patient comfort), careful selection of a treatment model and the formation of a multidisciplinary team including medicine, pharmacy, and nursing are essential.

Pharmacists can play a fundamental role in the development and implementation of an outpatient treatment model. To ensure a smooth treatment process for patients, pharmacists can develop standardized physician orders and arrange financial coverage for the low-molecular-weight heparin therapy, as well as communicating the treatment plan to the referring physician or the primary provider (or both). Furthermore, pharmacists can also be directly involved in educating patients by providing medication counselling, monitoring for side effects, teaching administration of low-molecular-weight heparin, and providing information on the signs and symptoms of clot recurrence. Our program presently employs 0.6 of a full-time equivalent pharmacist, which represents new resources specifically for the program.

Our study results have demonstrated that for the treatment of acute venous thromboembolism, a hospital-based model of care appears at least as favourable as either teaching patients self-injection or having home-care nurses administer therapy and provides another approach for outpatient therapy that can be adapted by a wide range of institutions.

References

1. Anderson FA Jr, Wheeler HB, Goldberg RJ, Hosmer DW, Patwardhan NA, Jovanovic B, et al. A population-based perspective of the hospital incidence and case-fatality rates of deep vein thrombosis and pulmonary embolism: the Worcester DVT Study. *Arch Intern Med* 1991;151:1933-8.
2. Hull RD, Raskob GE, Rosenbloom D, Panju AA, Brill-Edwards P, Ginsberg JS, et al. Heparin for 5 days as compared with 10 days in the initial treatment of proximal venous thrombosis. *N Engl J Med* 1990;322:1260-4.
3. Leizorovicz A, Simonneau G, Decousus H, Boissel JP. Comparison of efficacy and safety of low molecular weight heparin and unfractionated heparin in initial treatment of deep vein thrombosis: a meta-analysis. *BMJ* 1994;309:299-304.
4. Lensing AWA, Prins MH, Davidson BL, Hirsh J. Treatment of deep vein thrombosis with low molecular weight heparins: a meta analysis. *Arch Intern Med* 1995;166:601-7.
5. Siragusa S, Cusmi B, Piovela F, Hirsh J, Ginsberg JS. Low molecular weight heparin and unfractionated heparin in the treatment of patients with acute venous thromboembolism: results of a meta-analysis. *Am J Med* 1996;100:269-77.
6. Prandoni L, Lensing AWA, Buller HR, Carta M, Cogo A, Viso M, et al. Comparison of subcutaneous low molecular weight heparin with intravenous standard heparin in proximal deep vein thrombosis. *Lancet* 1992;339:441-5.
7. Hull RD, Raskob GE, Pineo GF, Green D, Trowbridge AA, Elliott GG, et al. Subcutaneous low molecular weight heparin compared with continuous intravenous heparin in the treatment of proximal vein thrombosis. *N Engl J Med* 1992;326:975-82.
8. Hull RD, Raskob GE, Rosenbloom D, Graham FP, Lerner RG, Gafni A, et al. Treatment of proximal vein thrombosis with subcutaneous low molecular weight heparin versus intravenous heparin: an economic perspective. *Arch Intern Med* 1997; 157:259-94.
9. Simonneau G, Sors H, Charbonnier B, Page Y, Laaban JP, Azarian R, et al. A comparison of low molecular weight heparin compared with continuous intravenous heparin in the treatment of proximal deep vein thrombosis. *Arch Intern Med* 1993;153:1541-6.
10. Lindmarker P, Holmstrom M, Granqvist S, Johnsson H, Lockner D. Comparison of once-daily subcutaneous Fragmin with continuous intravenous unfractionated heparin in the treatment of deep vein thrombosis. *Thromb Haemost* 1994;72:186-90.
11. Luomanmaki K, Granqvist S, Hallert C, Jauro I, Ketola K, Kim HC, et al. A multicentre comparison of once-daily subcutaneous dalteparin and continuous infusion heparin in the treatment of deep vein thrombosis. *J Intern Med* 1996;240:85-92.
12. Levine M, Gent M, Hirsh J, Leclerc J, Anderson D, Weitz J, et al. A comparison of low molecular weight heparin administered primarily at home with unfractionated heparin administered in the hospital for proximal deep vein thrombosis. *N Engl J Med* 1996;334:677-81.
13. Koopman M, Prandoni L, Piovela F, Ockelford PA, Brandjes DPM, Meer JVD, et al. Treatment of venous thromboembolism with intravenous unfractionated heparin administered in the hospital as compared with subcutaneous low molecular weight heparin administered at home. *N Engl J Med* 1996;334:682-7.
14. Wells PS, Kovacs MJ, Bovmanis J, Forgie MA, Goudie D, Marrow B, et al. Expanding eligibility for outpatient treatment of deep vein thrombosis and pulmonary embolism with low-molecular-weight heparin. *Arch Intern Med* 1998;158:1809-12.
15. Harrison L, McGinnis J, Crowther M, Ginsberg J, Hirsh J. Assessment of outpatient treatment of deep vein thrombosis with low-molecular-weight heparin. *Arch Intern Med* 1998;158:2001-3.
16. Meyer G, Brenot F, Pacouret G, Simonneau G, Juvin KG, Charbonnier B, et al. Subcutaneous low molecular weight heparin Fragmin versus intravenous unfractionated heparin in the treatment of acute non massive pulmonary embolism: an open randomized pilot study. *Thromb Haemost* 1995;74:1432-5.
17. Kovacs MJ, Cruickshank M, Wells PS, Kim H, Chin-Yee I, et al. Randomized assessment of a warfarin nomogram for initial oral anticoagulation after venous thromboembolism disease. *Haemostasis* 1998;28:62-9.
18. Anderson DR, Levine M, Gent M, Hirsh J. Validation of a new criteria for the evaluation of bleeding during antithrombotic therapy. *Thromb Haemost* 1993;69:650.
19. Weitz JL. Low molecular weight heparin. *N Engl J Med* 1997; 337:688-98.
20. Martineau P, Tawil N. Low molecular weight heparins in the treatment of deep vein thrombosis. *Ann Pharmacother* 1998; 32:588-98,601.
21. Thompson-Ford JK. Low molecular weight heparin for the treatment of deep vein thrombosis. *Pharmacotherapy* 1998;18:748-58.
22. Leong W. Outpatient deep vein thrombosis treatment: implementation of an outpatient deep vein thrombosis treatment program using low molecular weight heparin. *Hosp Pharm Pract* 1998;6:23-31.
23. Columbus Investigators. Low molecular weight heparin in the treatment of patients with venous thromboembolism. *N Engl J Med* 1997;337:657-62.

S. Jo-Anne Wilson, BSc(Pharm), PharmD, is a Clinical Pharmacy Specialist, Thrombosis Anticoagulation Program and Department of Pharmacy, Queen Elizabeth II Health Sciences Centre, and an Assistant Professor of Pharmacy, Faculty of Health Professions, Dalhousie University, Halifax, NS.

Lisa Gray, BScN, is a Thrombosis Nurse, Thrombosis Anticoagulation Program and Department of Nursing, Queen Elizabeth II Health Sciences Centre, Halifax, NS.

David R. Anderson, MD, FRCPC, is Medical Director, Thrombosis Anticoagulation Program and Department of Medicine, Queen Elizabeth II Health Sciences Centre, and an Associate Professor of Medicine and Pathology, Faculty of Medicine, Dalhousie University, Halifax, NS.

Address correspondence to:

Dr. S. Jo-Anne Wilson
Thrombosis Anticoagulation Program
Pharmacy Department
Victoria General Hospital
Room 2043
1278 Tower Road
Halifax NS
B3H 2Y9
e-mail: RXJSW@qe2-hsc.ns.ca

Acknowledgement

The authors would like to acknowledge Ms. Jennifer Blundell, pharmacy student, College of Pharmacy, Dalhousie University, Halifax, NS, for her assistance.

