

Assessment of Outpatient Treatment of Deep-Vein Thrombosis With Low-Molecular-Weight Heparin

Linda Harrison, RN; Joanne McGinnis, RN; Mark Crowther, MD; Jeffrey Ginsberg, MD; Jack Hirsh, MD

Background: Low-molecular-weight (LMW) heparins are safe and effective for out-of-hospital treatment of acute deep-vein thrombosis (DVT) in a clinical trial setting. We examined the efficacy, safety, and feasibility of home treatment with LMW heparin of consecutive eligible patients with acute DVT in a routine care setting. In addition, we report our experience with patient compliance, acceptance, and satisfaction.

Methods: We performed a prospective cohort study of consecutive patients presenting to 2 thromboembolism clinics in a large Ontario city. Eligible patients were treated with LMW heparin for a minimum of 5 days and with long-term warfarin sodium. Outcomes included the incidences of bleeding and recurrence of DVT and pulmonary embolism and patient satisfaction as determined by a questionnaire.

Results: One hundred thirteen patients with objec-

tively confirmed DVT underwent screening; 89 patients were treated at home with LMW heparin. During the study, 1 patient died of a combination of pulmonary embolism and major bleeding, another patient required admission to the hospital for bleeding, and 5 patients with active malignant disease had recurrent DVT. Of the patients who completed the satisfaction questionnaire, 75 (91%) of 82 were pleased with home treatment; 44 (70%) of 63 felt comfortable self-injecting the LMW heparin; and 71 (92%) of 77 were satisfied with the support and instruction they received during the outpatient treatment.

Conclusions: Outpatient treatment of DVT with LMW heparin is safe, effective, and feasible for most patients and is associated with a high degree of patient satisfaction.

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TRADITIONALLY, patients with acute deep-vein thrombosis (DVT) have been treated in the hospital with intravenous unfractionated (UF) heparin for 5 to 7 days, followed by oral anticoagulants for 3 to 6 months.¹ Initial hospitalization was considered necessary to stabilize patients, to administer intravenous heparin, and to adjust the dose according to the results of the activated partial thromboplastin time. The need for hospitalization of most patients with DVT has been challenged by the results of 3 recent studies that evaluated low-molecular-weight (LMW) heparins.²⁻⁴ Two factors have enabled LMW heparins to be used in the home setting to treat patients with DVT. The first relates to the effectiveness and safety of LMW heparin when administered subcutaneously once or twice daily without laboratory monitoring, and the second, to the observation that many patients with DVT do not require hospital admission.⁵

We participated in 2 large clinical trials that compared the efficacy and safety of LMW heparin with that of UF heparin.^{2,3} In both studies, the LMW heparin was administered subcutaneously, twice daily on a weight-adjusted basis without laboratory monitoring,

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whereas the UF heparin was administered by continuous intravenous infusion with monitoring of activated partial thromboplastin time. In both studies, many patients allocated to receive LMW heparin were treated at home, whereas all of the patients treated with UF heparin were treated in the hospital. The results of these studies demonstrated that the LMW heparin preparations tested were as effective and safe as UF heparin. However, the feasibility of out-of-hospital administration of LMW heparin outside of a clinical trial setting and

From the Hamilton Health Sciences Corporation, Hamilton, Ontario.

Dr Ginsberg is a career investigator of the Heart and Stroke Foundation of Ontario, Toronto. Dr Crowther is a research fellow of the Medical Research Council of Canada, Ottawa, Ontario.

SUBJECTS AND METHODS

STUDY DESIGN

We conducted a prospective cohort study of consecutive outpatients referred to 2 thrombosis clinics at the Hamilton Health Sciences Corporation, Hamilton (McMaster Division and Henderson Division), from June 1, 1996, to June 1, 1997.

POPULATION

Patients who were referred to the clinics with suspected DVT and had the diagnosis confirmed by results of compression ultrasonography or venography were eligible. Patients were routinely treated as outpatients if they were not considered to have a high risk for bleeding, did not have additional medical conditions requiring hospital admission, and were considered capable of self-treatment at home. Because the outpatient clinics operate only between 9 AM and 5 PM on weekdays, 3 patients were initially admitted to the hospital for intravenous heparin therapy and then treated as outpatients. These patients were considered outpatients if they were hospitalized for less than 24 hours.

Whenever possible, the first dose of LMW heparin (dalteparin sodium [Fragmin, Pharmacia and Upjohn, Toronto, Ontario], 100 IU/kg every 12 hours; or tinzaparin sodium [Innohep, Leo Laboratories, Ajax, Ontario], 175 IU/kg per day) was given by the patient or family member in the thrombosis unit. Subcutaneous injections of LMW heparin were continued for a minimum of 5 days and until the international normalized ratio (INR) was within the therapeutic range (2.0-3.0) for 2 consecutive days. Warfarin sodium therapy was commenced in a dose of 5 or 7.5 mg on the day of diagnosis or on the following day. Dosage adjustments were then made to maintain an INR of 2.0 to 3.0, and treatment was continued for a minimum of 3 months.

In the outpatient clinic, each patient was given an explanation of their disease and the treatment plan, was taught to self-inject, and had baseline blood work performed. In addition, arrangements were made for the purchase of medications and for required laboratory monitoring of warfarin therapy. In total, this required from 30 to 45 minutes for a nurse clinician.

SURVEILLANCE AND FOLLOW-UP

Patients were contacted on a regular basis, usually as part of oral anticoagulant therapy monitoring. All patients were asked to report any new symptoms suggestive of thromboembolic disease and any bleeding episodes. They were again contacted, by telephone or at a clinic visit, 3 months after their initial diagnosis, at which time they were questioned about new symptoms of recurrence or bleeding. Most treatment assessment forms were completed after LMW heparin therapy was discontinued, whereas the remainder were completed throughout the 3 months of warfarin therapy.

ASSESSMENTS

Recurrent thromboembolic disease was diagnosed if new symptoms developed that were confirmed as a new thrombus or an extension of the previous thrombus by results of compression ultrasound or venography. If test results were inconclusive, new or increasing symptoms were considered evidence of recurrent disease. Bleeding episodes were recorded and considered major complications if hospitalization or transfusions were required. Patient satisfaction and comfort with home treatment were assessed using a questionnaire based on a 5-point Likert scale, with 1 indicating very dissatisfied and 5, very satisfied. Patients were asked if they (1) preferred outpatient treatment; (2) felt comfortable giving their own injections; and (3) received sufficient support and instruction from the thrombosis unit.

the proportion of patients with DVT who are suitable for out-of-hospital treatment are unknown.

Based on our experience in these clinical trials, we decided to establish a program of home treatment for suitable patients with DVT. We herein report our experience with the home-treatment program in consecutive patients referred to 2 hospitals affiliated with McMaster University, Hamilton, Ontario.

RESULTS

POPULATION

During the 12-month study, 113 outpatients received a diagnosis of DVT at 1 of the 2 participating hospitals. Of the 113 patients, 11 required admission to the hospital. Reasons for admission included high risk for bleeding (brain metastases [$n = 2$] and neurosurgery within 3 weeks [$n = 1$]), pain control ($n = 1$), underlying medical problems requiring hospital treatment ($n = 4$), weekend admission ($n = 2$), and inability to cope at home ($n = 1$). One 19-year-old patient with DVT of the calf refused subcu-

aneous injections and admission to the hospital. Another 4 patients returned to their referring hospitals following diagnostic testing and consultation and were not followed up for the 3 months. Of the remaining 97 patients, 8 were treated at home with UF heparin due to cost considerations (unable to pay for LMW heparin, which is covered by insurance if the patient is admitted to the hospital) or inability to obtain LMW heparin. These patients were not included in our analysis.

The remaining 89 patients were treated at home with LMW heparin. Of these, 69 (78%) had proximal vein thrombosis (which extended into the iliac veins in 2 patients), 11 (12%) had isolated calf vein thrombosis, 7 (8%) had upper-extremity thrombi (superior vena cava thrombosis in 1 patient), and 2 (2%) had confirmed pulmonary embolism in addition to DVT.

Patients ranged in age from 18 to 92 years (average, 61.4 years), and 58 (65%) were female. Sixty-four patients (72%) received dalteparin, and 25 (28%) received tinzaparin.

Risk factors for thromboembolic disease included underlying malignant neoplasms ($n = 41$), recent sur-

Questionnaire Results*

Questionnaire Items	Responses, No. (%)				
	5	4	3	2	1
Preferred outpatient treatment	75 (91)	3 (5)	2 (2)	2 (2)	0
Comfort with self-injections	44 (70)	8 (13)	7 (11)	1 (2)	3 (5)
Comfort with level of support and instruction	71 (92)	4 (5)	1 (1)	0	1 (1)

*Five indicates very satisfied; 1, very dissatisfied.

gery (n = 17), no identified cause (n = 12), immobility (n = 6), inherited thrombophilia (n = 5), and other risk factors (n = 8).

One patient died of an autopsy-proven combination of pulmonary embolism and a major bleeding episode 4 hours after the first injection of LMW heparin. No other patient died of thromboembolic disease or bleeding during the 3-month follow-up. Eight patients died of nonthromboembolic causes before completing 3 months of anticoagulant therapy (6 deaths were cancer related; 1 death was due to nonhemorrhagic stroke; and 1 death, heart failure). There was 1 bleeding episode (into the arm) requiring admission to the hospital. There were no other bleeding episodes that required interruption of anticoagulant therapy. There were 5 cases of recurrent DVT (6%) (3 confirmed and 2 suspected) within the 3-month follow-up (1 case at 2 weeks, 2 cases at 5 weeks, 1 case at 8 weeks, and 1 case at 12 weeks). All 5 patients had active malignant disease.

Of the 89 patients, 67 (75%) managed self-injection or had a family member perform the injections, whereas 17 (19%) required the assistance of a visiting nurse, and 5 (6%) returned to nursing homes where nurses administered the subcutaneous injections. All surviving patients were followed up in clinic or by telephone 3 months after their initial diagnosis of acute DVT. Clinical outcomes (bleeding and recurrent thromboembolism) were assessed at this follow-up. Patients completed a follow-up questionnaire that assessed their satisfaction with outpatient treatment. The satisfaction questionnaire was not completed by patients who returned to nursing homes for treatment or by 1 mentally handicapped patient. Patients who required assistance with injections were not asked if they felt comfortable with self-injection, and those who had the services of visiting nurses or were too ill to respond did not complete the questionnaire. We did not ask family members of those who died to comment on how they felt about home treatment.

Of the patients who completed each question (**Table**), 75 (91%) of 82 were very pleased to be treated at home, 44 (70%) of 63 felt very satisfied self-injecting LMW heparin, and 71 (92%) of 77 were very satisfied

with the level of support and instruction they received from the thrombosis clinic.

COMMENT

We have confirmed that outpatient treatment with LMW heparin is safe and effective for DVT and for selected patients with pulmonary embolism. In addition, we have shown that more than 75% of patients with proven DVT referred to 2 tertiary care centers could be treated at home. Most of our patients had proximal DVT. The event rates were similar to those reported in other contemporary studies. Thus, the rate of fatal embolism was 1%, and the rate of proven recurrent DVT or pulmonary embolism was no higher than 6%. All of the recurrences occurred during oral anticoagulant therapy in patients with active malignant disease. The incidence of major bleeding was low at 1%.

Our questionnaire shows that most patients with DVT prefer out-of-hospital treatment and are comfortable giving their own injections. We had no reason to doubt that patients took their medications as prescribed.

The organization of an outpatient treatment program requires an efficient diagnostic service to confirm or refute the diagnosis of DVT in a timely manner and a commitment from the institution and certain members of the medical staff. We use dedicated, experienced nurse clinicians to educate the patients about DVT and its complications, to teach the patients how to administer LMW heparin subcutaneously, and, if necessary, to help them procure the LMW heparin. This educational process takes an average of 30 minutes. Experienced medical staff must be available on a 24-hour basis to provide support (usually by telephone) to patients who have concerns about self-injection or symptoms compatible with recurrence or side effects of treatment.

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Reprints: Linda Harrison, RN, Hamilton Health Sciences Corporation, Henderson Division, 711 Concession St, Hamilton, Ontario, Canada L8V 1C3.

REFERENCES

1. Hirsh J. Oral anticoagulant drugs. *N Engl J Med.* 1991;324:1865-1875.
2. Koopman MMW, Prandoni P, Piovella F, et al. Treatment of venous thrombosis with intravenous unfractionated heparin administered in the hospital as compared with subcutaneous low-molecular-weight heparin administered at home. *N Engl J Med.* 1996;334:682-687.
3. Levine M, Gent M, Hirsh 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;334:677-681.
4. The Columbus Investigators. Low-molecular-weight heparin in the treatment of patients with venous thromboembolism. *N Engl J Med.* 1997;337:657-662.
5. Crowther M, Hirsh J. Low-molecular-weight heparin for the out-of-hospital treatment of venous thrombosis: rationale and clinical results. *Semin Thromb Hemost.* 1997;23:77-81.