

Outpatient treatment of venous thromboembolic disease based in an emergency department

PETER J. ZED, LYNE FILIATRAULT, AND JAMES R. BUSSER

Traditionally, patients diagnosed with venous thromboembolic disease (VTD) required hospitalization for five to seven days for initiation of treatment.^{1,2} In many cases these patients were otherwise healthy and clinically stable and were admitted for no other reason than to receive continuous infusion and monitoring of intravenous unfractionated heparin (UFH) therapy and for warfarin dosage adjustment. Low-molecular-weight heparins (LMWHs), derived from the chemical or enzymatic depolymerization of UFH, have a more predictable anticoagulant effect and a longer elimination half-life than UFH, allowing for single daily subcutaneous administration.^{3,4} Clinical trials have demonstrated outpatient LMWH to be as safe, effective, and economically attractive as inpatient UFH for the initial treatment of VTD.⁵⁻⁹ As a result, outpatient management of VTD has expanded to various settings and become the standard of care for eligible patients.¹⁰⁻¹²

Many models exist for the provision of outpatient care of patients

Purpose. The efficacy, safety, and patient satisfaction of an emergency department (ED)-based outpatient program providing treatment for venous thromboembolic disease (VTD) were studied.

Methods. A prospective cohort study of patients enrolled in a hospital outpatient VTD treatment program was conducted from June 1999 to September 2003. Endpoints included recurrent VTD at three and six months following discharge from the program, minor and major bleeding, and thrombocytopenia during the acute phase of therapy. Patient satisfaction was assessed with an 18-question survey that was mailed to all patients following discharge from the program.

Results. A total of 162 patients were included. Of the 142 evaluable patients, no patient experienced recurrent VTD at three months, while at six months, 2 patients (1.4%; 95% confidence interval [CI], 0.2–5.0%) had recurrence. No patient experi-

enced major bleeding or thrombocytopenia, while 4 (2.5%; 95% CI, 0.8–6.2%) had minor bleeding. Ninety-seven percent of the patients were comfortable having their condition treated on an outpatient basis, and 85.1% felt it was more convenient to return to the hospital daily for medications and assessment than to be admitted to the hospital. Overall, 97.7% of the respondents were satisfied or very satisfied with the treatment received in the outpatient program, and 94.0% said they would enroll again if future treatment was indicated.

Conclusion. An ED-based outpatient VTD treatment program was safe and effective and appeared to achieve a high level of patient satisfaction.

Index terms: Anticoagulants; Data collection; Hospitals; Patients; Thromboembolism; Toxicity

Am J Health-Syst Pharm. 2005; 62:616-9

with VTD. The most common programs involve either teaching patients to self-inject LMWHs at home or having patients return to an ambulatory care clinic or hospital for medication administration and monitoring. Both strategies have

merits, and in most cases the preferred strategy is based on available resources to ensure efficient and safe outpatient care.

In June 1999, Vancouver General Hospital (VGH) implemented an outpatient VTD treatment program.

PETER J. ZED, B.Sc., B.Sc.(PHARM.), PHARM.D., is Pharmacotherapeutic Specialist—Emergency Medicine, CSU Pharmaceutical Sciences, Vancouver General Hospital (VGH), and Clinical Associate Professor, Faculty of Pharmaceutical Sciences, and Associate Member, Division of Emergency Medicine, Department of Surgery, University of British Columbia (UBC), Vancouver, Canada. LYNE FILIATRAULT, M.D.C.M., FRCPC, FACEP, is Attending Physician, Department of Emergency Medicine, VGH, and Clinical Assistant Professor, Division of Emergency Medicine, Department of Surgery, UBC. JAMES R. BUSSER, M.D., FRCPC, M.H.Sc., is Attending Physician, Department of Medicine, VGH, and Clinical Assistant Profes-

sor, Division of General Internal Medicine, Department of Medicine, UBC.

Address correspondence to Dr. Zed at CSU Pharmaceutical Sciences, Vancouver General Hospital, 855 West 12th Avenue, Vancouver, British Columbia, Canada V5Z 1M9 (zed@interchange.ubc.ca).

The assistance and statistical analysis of Dr. Riyad Abu-Laban are acknowledged.

Copyright © 2005, American Society of Health-System Pharmacists, Inc. All rights reserved. 1079-2082/05/0302-0616\$06.00.

This program was unique in that it was an emergency department (ED)-based program in which most patients were enrolled by emergency physicians without ever requiring hospitalization. Patients returned to the hospital each day for LMWH administration and monitoring and were telephoned by a pharmacist for warfarin dosage adjustment. As our program involved a different setting than most outpatient programs, it was important to ensure that efficacy, safety, and patient satisfaction were maintained. Patient satisfaction is an aspect of outpatient VTD programs that has not been adequately studied.

The purpose of this study was to evaluate the efficacy, safety, and patient satisfaction of an ED-based outpatient VTD treatment program.

Methods

VGH is a tertiary care teaching hospital and referral center in British Columbia. The ED treats 50,000 patients annually, of whom 20% require hospital admission. The VGH outpatient VTD treatment program is an ED-based program that enrolls patients seven days a week, 24 hours a day.

The study protocol was approved by the University of British Columbia behavioral research ethics board and the research advisory committee at VGH. We conducted a prospective cohort study of patients enrolled in the VGH outpatient VTD treatment program over a 52-month period between June 1999 and September 2003.

All patients accepted into the outpatient VTD treatment program were eligible. A majority of the patients were enrolled in the ED by emergency physicians without spending any time in the hospital. Patients were deemed eligible for outpatient treatment if they had radiographically confirmed deep-vein thrombosis (DVT) by compression ultrasonography or stable pulmo-

nary embolism (PE) confirmed by ventilation-perfusion scanning or spiral computed tomography (CT). In addition, patients had to agree to return to the hospital each day for LMWH injection and laboratory monitoring and to be reachable at home for instructions on warfarin administration each day. Patients were not accepted if they had active bleeding, recent gastrointestinal or genitourinary bleeding, recent trauma or major surgery, recent hemorrhagic stroke or intracranial bleeding, renal dysfunction (creatinine clearance, ≤ 30 mL/min), severe uncontrolled hypertension (systolic blood pressure of >180 mm Hg or diastolic blood pressure of >110 mm Hg), a platelet count of $<50,000$ cells/mm³, an allergy to heparin, a history of heparin-induced thrombocytopenia, known thrombophilia, or pregnancy.

Once deemed eligible for outpatient therapy, patients received baseline blood work, followed by administration by a nurse of tinzaparin 175 units/kg s.c. and warfarin sodium 10 mg orally. At the time of enrollment, each patient was provided with written information about VTD, tinzaparin, and warfarin. Within 24 hours of enrollment, an educational session was conducted by a pharmacist outlining information in the package and answering any questions. In addition, each patient was seen by an internist, who determined if further investigations were warranted, provided information on compression stockings, and determined the duration of warfarin therapy on the basis of current guidelines.¹³

Patients returned to the hospital daily for tinzaparin administration, laboratory monitoring (complete blood count and International Normalized Ratio [INR]), and bleeding assessment. After the first day, subsequent warfarin doses were determined by the pharmacist until the INR was within the targeted range (2.0–3.0). Tinzaparin injections continued daily for a minimum of five

days and until the INR was within the targeted range for two consecutive days. At the time of discharge from the program, care was transferred both orally and by discharge letter to the family physician, who continued to monitor patients' anticoagulation and clinical progress for the duration of their treatment. Patients were informed that they would receive a patient-satisfaction survey by mail within seven days and be contacted by telephone three and six months after discharge to determine disease recurrence.

The primary endpoint was recurrent DVT or PE three and six months after discharge from the program. Recurrent DVT or PE was diagnosed if new clinical symptoms developed and were confirmed on compression ultrasonography, ventilation-perfusion scanning, or spiral CT as representing a new thrombus or extension of the previous thrombus. Safety evaluation included major or minor bleeding or thrombocytopenia during the period of treatment in the program. Major bleeding was defined as intracranial or retroperitoneal bleeding or bleeding resulting in a decline in the hemoglobin concentration of greater than 2 g/dL or requiring the transfusion of 2 or more units of blood. Thrombocytopenia was defined as a reduction in platelets of 50% from baseline or to less than 50,000 cells/mm³.

The secondary endpoint was patient satisfaction as assessed with an 18-item survey. Patients were provided with a self-addressed, stamped envelope and asked to anonymously complete and return the survey. In addition to determining overall satisfaction with the outpatient program, the survey was designed to evaluate specific aspects, including the convenience of having the condition treated at home, the care and education provided by the hospital staff, and the efficiency of hospital visits.

All data were entered into an Excel database (Microsoft, Redmond, WA)

for analysis. Standard descriptive statistics were generated for all variables. Binomial 95% confidence intervals (CIs) for proportions were calculated by using Stata (version 5.0, StataCorp, College Station, TX 77845).

Results

One hundred sixty-two patients were enrolled in the outpatient VTD treatment program and were included in the study. Direct enrollment into the program occurred for 150 patients (92.6%), while 12 (7.4%) received initial inpatient treatment prior to enrollment for localized thrombolysis for upper-extremity DVT or iliofemoral DVT ($n = 7$), stabilization of symptomatic PE ($n = 3$), or additional diagnostic testing ($n = 2$). The mean \pm S.D. age of the subjects was 54.8 ± 18.3 years, and 46% were women. One hundred twenty-one patients (74.7%) experienced lower-extremity proximal-vein thrombosis, 12 (7.4%) had upper-extremity thrombosis, 4 (2.5%) had isolated calf-vein thrombosis, and 25 (15.4%) had PE. Risk factors for VTD were present in 103 patients (63.6%) and included injury or recent orthopedic surgery ($n = 36$), malignancy ($n = 23$), previous DVT or PE ($n = 22$), hormone replacement or oral contraceptive therapy ($n = 11$), and immobilization ($n = 11$). The mean \pm S.D. duration of treatment in the outpatient program was 5.6 ± 0.9 days.

For the efficacy evaluation, follow-up was achieved for 142 (87.7%) of the 162 patients. Twenty patients were lost to follow-up (19 could not be reached by telephone, and 1 patient had died of cancer). Of the evaluable patients, 0 patients (95% CI, 0–2.6%) experienced recurrent DVT or PE at three months after discharge from the program. At six months, 2 patients (1.4%; 95% CI, 0.2–5.0%) had recurrence. In both cases, warfarin therapy had been discontinued after three months of therapy.

All 162 patients were included in the safety assessment. No patients (95% CI, 0–2.3%) had major bleeding or thrombocytopenia, and 4 patients (2.5%; 95% CI, 0.8–6.2%) had minor bleeding. Minor bleeding included epistaxis ($n = 1$), bleeding gums ($n = 1$), hematuria ($n = 1$), and injection-site hematoma ($n = 1$). All minor bleeding episodes occurred in patients whose INR was within or below the targeted range.

Satisfaction surveys were returned by 134 patients, resulting in an 82.7% response rate. Overall, 130 respondents (97.0%) were comfortable having their condition treated on an outpatient basis, and 114 (85.1%) agreed or strongly agreed that it was more convenient to return to the hospital daily for medications and assessment than to be admitted to the hospital. Most respondents (129 [96.3%]) felt that the nursing staff was courteous and understanding and were satisfied or very satisfied with the education provided by the pharmacist (131 [97.8%]). Overall, 131 patients (97.8%) were satisfied or very satisfied with the treatment received in the outpatient program, and 126 (94.0%) said they would enroll again if future treatment was indicated. Seventy-one respondents (53.0%) indicated willingness to self-inject LMWHs at home if future treatment was indicated and if training was provided.

Discussion

Outpatient management of VTD has become the standard of care for stable patients in many institutions. Despite the existence of different models for the provision of outpatient care, it is important to ensure that efficacy, safety, and patient satisfaction can be maintained in all practice settings. This study demonstrated that an ED-based outpatient program was safe and effective and achieved a high level of patient satisfaction. Our efficacy and safety outcomes are consistent with reported rates from larg-

er randomized trials and assure us that we can provide safe and effective care within the current structure of our program.^{5,6,14}

To our knowledge, this study is the first to evaluate patient satisfaction with an ED-based program for VTD. Harrison et al.¹⁵ evaluated satisfaction in 89 patients treated at home with LMWHs for DVT. Of patients who completed the survey, 91% were pleased with home treatment, and 92% were satisfied with the support and instruction they received regarding outpatient treatment. Seventy percent of the patients were comfortable with self-injecting LMWHs at home. Despite the different setting in our study, patient satisfaction with our program was also high.

In addition to the small sample, our study has other limitations. First, the use of clinical features of recurrent DVT or PE to dictate the need for radiographic imaging to confirm recurrence may underrepresent the rate of recurrence. A higher rate of DVT or PE recurrence may have been seen had all patients been imaged at three and six months. However, it could be argued that symptom-directed investigations for recurrence more closely reflect clinical practice. Second, the patient-satisfaction survey was an unvalidated assessment tool. No validated survey was identified for outpatient VTD treatment, so we developed our own. Still, we are confident that the survey results accurately reflect patient satisfaction.

Conclusion

An ED-based outpatient VTD treatment program was safe and effective and appeared to achieve a high level of patient satisfaction.

References

1. Hyers TM, Hull RD, Weg JG. Antithrombotic therapy for venous thromboembolic disease. *Chest*. 1995; 108(4, suppl): 335S-51S.
2. Weinman EE, Salzman EW. Deep-vein thrombosis. *N Engl J Med*. 1995; 331: 1630-41.

3. Hirsch J, Levine MN. Low molecular weight heparin. *Blood*. 1992; 79:1-17.
4. Weitz JI. Low-molecular-weight heparins. *N Engl J Med*. 1997; 337:688-98.
5. Koopman MM, 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; 334:682-7.
6. Levine M, Gent M, Hirsch 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.
7. Boccalon H, Elias A, Chale JJ et al. Clinical outcomes and cost of hospital vs home treatment of proximal vein thrombosis with low-molecular-weight heparin. *Arch Intern Med*. 2000; 160: 1769-73.
8. Dolovich LR, Ginsberg JS, Douketis JD et al. A meta-analysis comparing low-molecular-weight heparins with unfractionated heparin in the treatment of venous thromboembolism. *Arch Intern Med*. 2000; 160:181-8.
9. Boucher M, Rodger M, Johnson JA et al. Shifting from inpatient to outpatient treatment of deep vein thrombosis in a tertiary care center: a cost-minimization analysis. *Pharmacotherapy*. 2003; 23:301-9.
10. Wells PS, Kovacs MJ, Bormanis J et al. Expanding the eligibility for outpatient treatment of deep vein thrombosis and pulmonary embolism with low-molecular-weight heparin. *Arch Intern Med*. 1998; 158:1809-12.
11. Chiquette E, Amato MG, Bussey HL. Comparison of an anticoagulation clinic with usual medical care. *Arch Intern Med*. 1998; 158:1641-7.
12. Vinson DR, Berman DA. Outpatient treatment of deep vein thrombosis: a clinical care pathway managed by the emergency department. *Ann Emerg Med*. 2001; 37:251-8.
13. Hyers TM, Agnelli G, Hull RD et al. Antithrombotic therapy for venous thromboembolic disease. *Chest*. 2001; 119 (suppl):176S-93S.
14. Hull RD, Raskob GE, Pineo GF 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.
15. Harrison L, McGinnis J, Crowther M et al. Assessment of outpatient treatment of deep vein thrombosis with low-molecular weight heparin. *Arch Intern Med*. 1998; 158:2001-3.

Copyright of American Journal of Health-System Pharmacy is the property of American Society of Health System Pharmacists and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.