



## Home treatment of deep vein thrombosis: a two-years experience of a single institution

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### ABSTRACT

**Background and Objective.** Low molecular weight heparin (LMWH) is known to be safe and effective for the initial treatment of patients with acute deep-vein thrombosis (DVT). Moreover, LMWH allows patients to be treated at home. However, only limited data are available on the feasibility of LMWH treatment at home in daily clinical practice.

**Design and Methods.** We evaluated the feasibility, efficacy and safety of home treatment of DVT in a consecutive series of outpatients using LMWH over a two year period. The two main reasons for exclusion were concomitant pulmonary embolism and a high hemorrhagic risk. Patients were treated with 95 IU/kg bid of nadroparin for a minimum of 7 days. The study design allowed patients to go home immediately after diagnosis or to be discharged after a short hospital stay. Anticoagulation with acenocoumarol was started 2 days before discontinuing nadroparin.

**Results.** From 1995 to 1997, 71 consecutive outpatients with DVT were treated with nadroparin. Ambulatory treatment was feasible in 39 patients (24 patients did not require admission and 15 patients were discharged in less than 48 hours). The remaining 32 patients were treated in hospital. The main causes for admission were the presence of serious comorbid conditions, the severity of symptoms in the involved leg and the inability to obtain a diagnosis. None of the patients had clinical recurrent venous thromboembolism during the initial treatment with nadroparin. One patient receiving nadroparin at home had a non-fatal major bleeding. None of the patients to whom the possibility of home therapy was offered wished to remain at hospital. However, only 26% of the home-treated patients injected the drug by themselves.

**Interpretation and Conclusions.** Home therapy of DVT with LMWH bid at doses adjusted to patient's body weight is feasible, efficient and safe. Over 50% of outpatients with DVT can be treated at home, either entirely or after a short stay in hospital. Nevertheless, before using this therapeutic alternative as a standard of practice, an adequate assessment of embolic and hemorrhagic risks, and comorbid conditions, should be made.

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Key words: home treatment, deep-vein thrombosis, low molecular weight heparin

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In Western countries, each year 1 to 3 persons per 1000 require anticoagulant therapy for symptomatic deep-vein thrombosis (DVT) or pulmonary embolism (PE).<sup>1,2</sup> The standard treatment of patients with DVT is hospital admission, with unfractionated heparin (UFH) given by intravenous infusion for 5 to 10 days, followed by oral anticoagulant therapy for 3 to 6 months.<sup>3,4</sup> During admission frequent laboratory monitoring with appropriate dose adjustment is needed to keep their level of anticoagulation in the therapeutic range.<sup>5,6</sup>

Trials in hospitalized patients with DVT showed that LMWH in a dose determined by body weight alone is at least as effective and safe as UFH.<sup>7-13</sup> In addition, LMWH has a longer half-life and a more predictable anticoagulant response to a fixed dose than does UFH making it suitable for subcutaneous administration without laboratory monitoring.<sup>14,15</sup> The simplicity of treatment of DVT with LMWH makes it attractive for home use. Two recent multi-institutional randomized trials showed that about half of all patients with DVT can be safely treated with LMWH without hospital admission.<sup>16,17</sup>

We report the results of a prospective cohort study designed to determine if LMWH can be used safely and effectively to treat patients with DVT at home.

### Patients and Methods

#### Patients

Consecutive outpatients with acute, symptomatic DVT referred to the emergency department of our institution were eligible for the study. Patients were excluded from the study if they were less than 18 years, concurrent symptomatic PE, high hemorrhagic risk (intracranial bleeding within the previous month, gastrointestinal bleeding within the previous 2 weeks, known hemorrhagic disorder, and renal or hepatic insufficiency), allergy to nadroparin or if they were already receiving full-dose UFH for more than 24 hours.

#### Study design

Once DVT was suspected, 95 IU/kg of Nadroparin-Ca (Laboratoires Choay, Paris, France) was given subcutaneously twice daily. Patients weighing less than 50 kg received a total daily dose of 8200 International Factor Xa Inhibitory Units per liter; those weighing between 50 and 60 kg, 10,000 IU; those

weighing between 60-70 kg, 12,300 IU; those weighing between 70-80 kg, 14,500 IU; and those weighing over 80 kg, 16,400 IU. Diagnosis of DVT was confirmed by venography or ultrasonography in all cases. After the patients gave their consent, they were allowed to go home immediately after diagnosis or to be discharged after a short hospital stay. Two home treatment models were offered to patients: a self-injection model or a nurse-coordinated care model. There was no laboratory monitoring. Whenever possible, patients were allowed to ambulate after 48 hours of nadroparin treatment. All patients received nadroparin treatment for at least 7 days, but for no longer than 10 days. Treatment with acenocoumarol was begun 2 days before discontinuing nadroparin. It was continued for a total of 6 months, unless the persistence of risk factor required its continuation beyond that period. The dose was adjusted to achieve an international normalized ratio of 2.0 to 4.0.

### Follow-up

All patients were contacted daily during the initial treatment with nadroparin. All patients were instructed to report to our clinical center on an emergency basis if any new symptoms developed that were suggestive of progression of DVT or PE. In addition, they were instructed to report all clinically unusual episodes of bleeding. The patients were assessed monthly for 6 months. Each visit included a history taking and physical examination. Hemoglobin and platelet counts were measured, at base line and after 1 week.

### Results

From July 1995 to July 1997, a total of 93 consecutive outpatients met the eligibility criteria. Of these, 22 were excluded. The most common reason for the exclusion of patients was concurrent symptomatic PE (18 patients). Four patients were excluded because they were already receiving full-dose UFH for more than 24 hours. The remaining 71 patients were treated with nadroparin. No patient was lost to follow-up. Table 1 summarizes the clinical characteristics of this group of patients. Data on the initial treatment and hospitalization are shown in Table 2. Ambulatory treatment was feasible in 39 patients (55%) either entirely or after a short stay in hospital. Among those who was treated at home, 24 patients (34%) were not hospitalized at all and another 15 patients (21%) were discharged during the first two days of treatment (Table 2). The remaining 32 patients (45%) received treatment with nadroparin in hospital. None of the 39 patients to whom the possibility of home therapy was offered desired to remain at hospital. Only 1 patient treated at home with nadroparin required admission because of persistence of symptoms in the involved limb. Venography did not show thrombus progression and that patient continued treatment with nadroparin in hospital with favorable evolution. The

**Table 1. Clinical characteristics of the study patients (n=71).**

Demographic variables		
Age (yrs)(median, range)	64 (22-90)	
Sex (M/F)	39/32	
Risk factors for DVT		
	no. of patients	(%)
Previous DVT/PE	9	(13)
Surgery within previous 3 months	14	(20)
Trauma within previous 3 months	8	(11)
Known cancer	7	(10)
None	19	(20)
Diagnosis at presentation		
Method of diagnosis		
Ultrasonography	62	(87)
Venography	9	(13)
Extent of thrombosis		
Calf only	15	(21)
Proximal ± calf	56	(79)

**Table 2. Data on the initial nadroparin treatment, and hospitalization.**

Data on the initial nadroparin treatment, and hospitalization		
	no. of patients	(%)
Nadroparin daily dosage		
8200 IU	3	(4)
10,000 IU	2	(3)
12,300 IU	50	(70)
14,500 IU	6	(8)
16,400 IU	10	(14)
Hospitalization		
Not admitted to hospital	24	(34)
Admitted to hospital	15	(21)
Early discharge (<48 hours)	32	(45)
Treated in hospital		
Main reasons for hospitalization		
Inability to obtain a diagnosis	10	(21)
Comorbid conditions	18	(38)
Phlegmasia	11	(23)
High embolic risk	4	(9)
Another reasons	4	(9)

most frequent reasons for hospitalization were the presence of serious comorbid conditions, phlegmasia and the inability to obtain a diagnosis (Table 2). Most of the patients hospitalized for severe symptoms in the involved leg or for diagnostic procedures could be discharged from the hospital before completion of initial treatment and continued their treatment at home. Only 15 patients (26%) of the home-treated group of patients injected themselves or were assist-

ed by a family member, whereas homecare was needed for the remaining 74% of patients.

None of the 71 patients treated with nadroparin had venous thromboembolic recurrence during the 6 months of follow-up.

A nonfatal major bleeding occurred in one patient during initial treatment with nadroparin at home: a gastrointestinal bleeding in a patient also receiving non-steroidal drugs. That patient was admitted to hospital and nadroparin was stopped. There were not minor bleeding episodes during initial treatment. No patient develop a major heparin-induced thrombocytopenia, however, two patients had platelet counts below  $120 \times 10^9/L$  after a week of treatment with nadroparin.

No patient died during initial treatment. Three patients died during the six-month study period. The causes of death included cancer (2 patients) and cardiovascular disease (1 patient). After 6 months of follow-up, most of the patients presented minimal pretibial edema, and 4 patients (6%) presented mild to moderate post-thrombotic syndrome.<sup>18</sup> Three of these four patients had a history of previous ipsilateral DVT before enrollment in our study.

## Discussion

Two recent randomized trials have shown that home treatment with LMWH in patients with DVT is as safe and effective as in-hospital treatment with UFH.<sup>16,17</sup> However, because in these trials about two thirds and one third of patients, respectively, were excluded for reasons such as comorbid conditions or history of past venous thromboembolism, it is difficult to translate these findings into the daily clinical practice.<sup>19</sup>

During 2-year period, we studied a broad range of consecutive outpatients with DVT. Indeed, among the 93 patients who met the criteria for enrollment, 19% were excluded because they had concurrent PE and only 4% were excluded for other reasons. Thus, the demographic and clinical characteristics of our patients are comparable to other series of outpatients with symptomatic DVT.<sup>20,21</sup>

LMWH (administered twice daily by subcutaneous injection in fixed doses adjusted to the patient's body weight, without laboratory monitoring) was shown to be an effective and safe treatment in patients with confirmed DVT and permitted approximately 60 percent of patients to be treated as outpatients or discharged early from the hospital.

This study confirms previous observations that recurrent, life-threatening pulmonary embolism is exceedingly rare during initial treatment with LMWH. However, it would seem prudent to begin LMWH therapy in the hospital in patients with high thromboembolic risks such as cancer, or free-floating thrombus.

The incidence of post-thrombotic syndrome after 6 months of follow-up was comparable to that

obtained in large series of patients with DVT treated with UFH in hospital, in spite that wearing elastic support was not systematic in our patients.<sup>18,22,23</sup> As expected the development of ipsilateral recurrent DVT increased the risk of developing post-thrombotic syndrome.<sup>18</sup> However, the duration of follow-up in our study was probably too short to give valid estimate of its overall incidence.<sup>18,22,23</sup>

Major, life-threatening bleeding complications are also likewise rare during the initial treatment. The patient who presented a major bleeding episode during home treatment also had a coexisting risk factor for hemorrhage. We believe that patients with a known hemorrhagic risk, should be treated at least partially in hospital.

This study suggests that home treatment of patients with DVT is feasible in daily clinical practice. The great majority of patients were very satisfied with this therapeutic approach. However, the ambulatory care of these patients increases the burden on primary care teams. Home care was needed in a high proportion of patients and only a minority injected themselves. This contrasts the results of a previous study.<sup>17</sup> Nevertheless, most of our patients treated at home started walking after three days of treatment and received further nadroparin injections on their health primary centers. In some studies, once-daily subcutaneous LMWH or shorter course of LMWH treatment (4 to 5 days) seem to be as effective and safe as intravenous UFH in the initial treatment of DVT.<sup>9,10,16,17</sup> Although LMWH given once daily and for a short course may be the most convenient and cost-effective treatment of DVT, there are few studies comparing this regimen with LMWH given twice daily and for a long course in large series of patients with DVT.

We conclude that home therapy of DVT with LMWH is feasible, efficient and safe. Many patients with acute DVT can be treated entirely at home or after a short stay in hospital with subcutaneous LMWH, increasing the convenience for the patient and reducing the cost to the health care system. Nevertheless, before using this therapeutic alternative on a wider scale, a series of factors should be considered which include the severity of clinical presentation, the embolic and hemorrhagic risks, and the presence of associated diseases.

## Contributions and Acknowledgments

*EG was responsible for the conception of the study, interpretation, and the writing of the paper. ER and EP collected the clinical data and contributed to the execution of the study. VV and JA were responsible for the clinical assessment of the patients.*

*The order of authorship has been made according to the substantial contribution given to the study.*

## Disclosures

*Conflict of interest: none.*

*Redundant publications: no substantial overlapping with previous papers.*

### Manuscript processing

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