CLINICAL RESEARCH STUDY

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Home Therapy of Venous Thrombosis with Long-term LMWH versus Usual Care: Patient Satisfaction and Post-thrombotic Syndrome

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ABSTRACT

PURPOSE: Home-LITE compared long-term treatment at home with tinzaparin or usual care in terms of efficacy, safety, patients' treatment satisfaction, incidence of post-thrombotic syndrome, and associated venous leg ulcers.

METHODS: This multicenter, randomized, controlled trial enrolled 480 patients with documented, acute, proximal deep vein thrombosis. Patients received tinzaparin 175 IU/kg subcutaneously once daily for 12 weeks, or tinzaparin for ≥5 days plus oral warfarin, commenced on day 1, international normalized ratio-adjusted, and continued for ≥12 weeks ("usual care"). Patients received 1 in-clinic injection, then home treatment.

RESULTS: The rate of recurrent venous thromboembolism at 12 weeks was 3.3% in both groups (absolute difference 0%; 95% confidence interval −3.2-3.2), and at 1 year was 10.4%/8.3% in the tinzaparin/usual-care groups, respectively (difference 2.1%; 95% confidence interval −3.1-7.3). There were no between-group differences in deaths at 12 weeks or 1 year, or bleeding at 12 weeks. Patients in the tinzaparin group expressed significantly greater treatment satisfaction ($P = .0024$), particularly regarding freedom from the inconvenience of blood monitoring; were less likely to report signs/symptoms of post-thrombotic syndrome (individual odds ratios 0.66 to 0.91, overall odds ratio 0.77, $P = .001$); and reported fewer leg ulcers at 12 weeks: 1 (0.5%) versus 8 (4.1%) ($P = .02$) with usual care.

CONCLUSIONS: Long-term home treatment with tinzaparin or usual care resulted in similar rates of recurrent venous thromboembolism, death, and bleeding. The significantly lower incidence of post-thrombotic syndrome and leg ulcers observed in the tinzaparin group is a potentially important benefit and deserves further study.

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KEYWORDS: Deep vein thrombosis; Leg ulcer; Post-thrombotic syndrome; Tinzaparin; Warfarin

Patients with proximal deep vein thrombosis require long-term anticoagulant treatment to prevent symptomatic extension and/or recurrent venous thromboembolism.[1] Earlier guidelines for therapy of deep vein thrombosis and/or pulmonary embolism recommended unfractionated heparin or low-molecular-weight heparin for 5-7 days, initiating a vitamin K antagonist on day 1 and continuing for at least 3 months.[1] More recent guidelines recommend subcutaneous low-molecular-weight heparin, rather than unfractionated heparin, for initial treatment for deep vein thrombosis,[2] as it is at least as safe and effective as unfractionated heparin,

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and more convenient, not requiring intravenous infusion or frequent monitoring.

Home-LITE is one of 3 trials in the Long-term Innovations in TreatmEnt (LITE) program of studies, which were designed to evaluate long-term treatment of proximal deep vein thrombosis with low-molecular-weight heparin, at a time when few data were available to support this approach. The first 2 studies in the LITE series compared the efficacy and safety of the treatment of deep vein thrombosis using either the low-molecular-weight heparin tinzaparin (Innohep, LEO Pharma A/S Ltd., Ballerup, Denmark) given long-term, or unfractionated heparin therapy followed by vitamin K antagonist.[3,4] Long-term once-daily tinzaparin showed similar efficacy, but caused less bleeding than unfractionated heparin/vitamin K antagonist in a broad spectrum of patients (the Main-LITE study).[4] In cancer patients with deep vein thrombosis, long-term tinzaparin was more effective than unfractionated heparin/vitamin K antagonist in preventing recurrent venous thromboembolism, and bleeding was similar with both regimens (the Main-LITE Cancer study).[3] In these 2 studies, patients were hospitalized for as long as clinically required. The current study, Home-LITE, examined whether there are benefits to long-term once-daily low-molecular-weight heparin in patients with proximal deep vein thrombosis when treated at home from the outset, compared with low-molecular-weight heparin/warfarin.

CLINICAL SIGNIFICANCE

- Efficacy and safety were similar when patients with deep vein thrombosis were treated out of hospital with either once-daily subcutaneous tinzaparin 175 IU/kg, or tinzaparin for ≥5 days followed by warfarin, for 12 weeks.
- The occurrence of symptoms of the post-thrombotic syndrome and of leg ulcers was significantly lower with tinzaparin relative to Usual Care.
- Patients receiving long-term treatment with tinzaparin had significantly less interruption of work.

Home-LITE also addressed patients' satisfaction with their treatment, and the incidence of post-thrombotic syndrome. Post-thrombotic syndrome is a common sequela of deep vein thrombosis, occurring in 20%-60% of patients.[2,5-9] The pathophysiology of post-thrombotic syndrome is incompletely understood, but its development post deep vein thrombosis is believed to be related to the presence of persistent venous obstruction and/or reflux. It causes chronic lifestyle-limiting symptoms such as venous insufficiency, limb swelling, and pain. Post-thrombotic syndrome impacts negatively on patients' quality of life, can progress to leg ulcers, and is a large economic burden on society.[5,9] Adequate anticoagulation after a deep vein thrombosis is believed to reduce the development and severity of post-thrombotic syndrome.[5,7,9]

The objectives of Home-LITE were to compare long-term treatment at home with tinzaparin or usual care using the following outcomes: efficacy (venous thromboembolism recurrence, mortality), safety (bleeding, thrombocytopenia, bone fractures), patients' satisfaction; and the incidence of post-thrombotic syndrome and venous leg ulcers.

METHODS

Study Design

The study design, patient eligibility and allocation, treatment regimens, and procedures for surveillance and follow-up are shown in Table 3 (available online).[1,3,4,10-12]

Assessment of Outcomes

The primary efficacy outcome measure was the occurrence of objectively documented, symptomatic, recurrent venous thromboembolism at 12 weeks and 1 year. Other efficacy outcomes were: death rates at 12 weeks and 1 year; patients' self-reported treatment satisfaction during the treatment period; symptoms of post-thrombotic syndrome; and the incidence of venous leg ulcers as reported by patients. The primary safety outcome measure was the occurrence of bleeding (all, major or minor) during the 12-week treatment period. Additional safety outcomes were the incidence of thrombocytopenia and of bone fractures. The methods to assess venous thromboembolism and bleeding have been reported previously[3,4] and also are shown in the table available online.

Suspected recurrent deep vein thrombosis, pulmonary embolism, or bleeding was interpreted by a central, independent, adjudication committee without knowledge of the patient's treatment or the other outcome results. Adjudication was made by 2 committee members, and disputes were resolved independently by a third member.

Patients' quality of life was assessed using the Medical Outcome Study Short Form-20 (MOS-SF-20)[13,14] at baseline, and at 6 and 12 weeks. A questionnaire about parameters likely to affect the treatment satisfaction of post-thrombotic patients[15-17] also was administered at 12 weeks. The questionnaires for the 2 groups differed slightly but contained 11 questions in common, which could be compared between the groups. Responses were made on a 5-point Likert scale.

At 12 weeks, patients also completed a third questionnaire recording 8 symptoms or signs whose presence in combination is commonly used to diagnose the presence and severity of post-thrombotic syndrome,[6,7,18,19] additionally asking if an ulcer was present in the skin above the patient's ankle on the affected leg. All questionnaires were completed by the patients independently.

Statistical Analysis

The statistical analysis section can be found in the online table.