Drug Monitor

ONLINE EDITION

Long-Term LMWH vs. Usual Care in Home Therapy for DVT

For patients being treated for deep vein thrombosis (DVT) at home, long-term therapy with the low molecular weight heparin (LMWH) tinzaparin is as effective as the traditional combination of short-term tinzaparin and long-term warfarin—and may be safer and more acceptable to patients. These were the conclusions researchers from University of Calgary, Calgary, Canada; University of British Columbia, Vancouver, Canada; McGill University, Montreal, Canada; and University of Oklahoma, Oklahoma City arrived at after conducting a multicenter, randomized, controlled trial.

Part of the Long-Term Innovations in Treatment (LITE) program, the Home-LITE study enrolled 240 patients with documented acute, proximal DVT and assigned them randomly to receive either tinzaparin 175 IU/kg SC once daily for 12 weeks (long-term tinzaparin) or tinzaparin 175 IU/kg SC once daily for at least five days plus oral warfarin for at least 12 weeks (usual care). In the usual care group, the warfarin dose was adjusted according to daily international normalized ratio (INR) monitoring until a stable response was achieved. Short-term tinzaparin was stopped once the patient had maintained an INR of 2 to 3 for two consecutive days. In both groups, the first tinzaparin injection was administered in the clinic, with subsequent doses administered at home.

The rates of recurrent venous thromboembolism were similar between the two groups at 12 weeks (3.3% in each group) and at one year (10.4% in the long-term tinzaparin group and 8.3% in the usual care group). Death rates also were similar at both time points.

The safety analysis revealed similar rates of bleeding for both groups during the 12 weeks of the study (9.2% overall for both groups). Patients in the long-term tinzaparin group, however, had a lower risk of developing symptoms of postthrombotic syndrome, had fewer leg ulcers after 12 weeks, and had significantly less interruption of work. Additionally, long-term tinzaparin was associated with significantly greater patient satisfaction—particularly with regard to freedom from the inconvenience of blood monitoring.

To the researchers' knowledge, their study was the first to compare long-term LMWH treatment with usual care in patients treated at home from the outset. Moreover, since Home-LITE had fewer exclusion criteria than previous trials, they say, it enrolled a population closer to the mix of patients likely to be seen in routine clinical practice, such as those with renal impairment.

Source: *Am J Med.* 2009;122(8):762–769. doi:10.1016/j.amjmed.2008.12.023.

Easing into Efavirenz

More than half of patients starting the antiretroviral drug efavirenz experience neuropsychiatric adverse events (NPAEs). These events include dizziness, a feeling of drunkenness or hangover, nightmares, and sleep disorders; impaired concentration, mood changes, and severe psychiatric symptoms also have been reported. While NPAEs usually do not require efavirenz withdrawal, they are sometimes intense or long-lasting enough to necessitate treatment interruption.

To address this problem, researchers for the Sociedad Andaluza de Enfermedades Infecciosas set out to determine whether stepped dosing during the first two weeks of efavirenz treatment could reduce the incidence and severity of NPAEs while maintaining the drug's effectiveness. In their 24-week study, they randomly assigned 114 patients with HIV, who were treated at seven clinics in Spain, to a full-dose group or a stepped-dose group. The 54 patients in the full-dose group received the standard dose of efavirenz 600 mg/day from day one. The 60 patients in the stepped-dose group received efavirenz 200 mg/day on days one through six, 400 mg/day on days seven through 13, and 600 mg/day on day 14 and thereafter. All patients were asked at baseline and at days seven, 14, and 30 whether they had experienced NPAEs. To gauge the treatment regimens' effectiveness, blood samples were collected from the patients at baseline and at weeks one, two, four, 12, and 24.

The two regimens resulted in no apparent differences with regard to immunovirologic efficacy. Both groups showed similar percentages of patients with undetectable viral loads at all follow-up points and similar increases in CD4+ cell counts at week 24.

During the first week of treatment, however, 66% of patients in the full-dose group versus 47% of patients in the stepped-dose group developed efavirenz-related NPAEs, and patients in the full-dose group experienced more severe NPAEs. During the second week, 58% of patients in the full-dose group and 49% of those in the stepped-dose group experienced NPAEs; although this difference was

statistically nonsignificant, patients in the full-dose group continued to experience more severe NPAEs.

The researchers conclude that stepped dosing of efavirenz over two weeks "significantly decreases the incidence and severity of NPAEs while apparently maintaining the same efficacy as the standard schedule." They note, however, that their study's small sample size prevents them from drawing definitive conclusions about the virologic efficacy of stepped dosing. ●

Source: *Ann Intern Med.* 2009;151(3):149–156.