Treatment and Secondary Prophylaxis of VTE in the Cancer Patient: Current Status

Agnes Y.Y. Lee

Hamilton Civic Hospitals Research Center, Hamilton, Canada

Based on a number of large randomized clinical trials and well-designed prospective studies, outpatient therapy with low molecular weight heparin (LMWH) is now established as a safe and effective option for initial treatment in patients with acute deep vein thrombosis and selected patients with pulmonary embolism [1]. This advance is particularly important for cancer patients, in whom quality of life is an important issue. Although cancer patients represented a small subgroup of the patients that were included in the clinical trials evaluating initial antithrombotic therapy, the available data suggest that LMWH and heparin have comparable efficacy in this complex patient population.

For long-term treatment or secondary prophylaxis of VTE, vitamin K antagonists have been the mainstay of therapy for decades. However, the narrow therapeutic window and inconvenience of laboratory monitoring make these agents particularly problematic in cancer patients. Furthermore, studies have shown that, while on oral anticoagulants, cancer patients have a 2- to 3-fold risk of recurrent thrombosis and 3- to 6-fold risk of major bleeding compared to patients without cancer [2]. Warfarin failure despite therapeutic dosing has also been reported in cancer patients. Consequently, long-term LMWH has been evaluated as an alternative to oral anticoagulant therapy. Although once- or twice-daily injections are required for the administration of LMWHs, the elimination of laboratory monitoring and the predictable anticoagulant effect of LMWHs make them an attractive option to cancer patients who have difficult venous access, limited mobility, a high risk of bleeding, or are taking multiple concurrent medications.

Randomized controlled trials in patients without cancer have failed to show a significant difference in the risk of recurrent thrombosis and major bleeding between LMWH and standard intensity oral anticoagulation, but a recent multicenter trial in cancer patients showed a 52% risk reduction in recurrent thrombosis in those who received long-term dalteparin compared to oral anticoagulants [3]. This benefit was achieved without an associated increase in major bleeding. Injections were well tolerated and no excess adverse events were reported with long-term dalteparin. The cost of LMWHs, however, makes the extended use of these agents prohibitive for the majority of patients.

Further questions to be addressed in the treatment of thrombosis in cancer patients include duration of therapy. To-date, the optimal duration of anticoagulant therapy in cancer patients has not been examined. Since most cancer patients have advanced disease at the time of their thrombotic event and, thereby, are considered to have an ongoing risk factor for recurrent thrombosis, the usual practice is to continue ‘indefinite’ anticoagulation in these patients [4]. In patients without any evidence of residual cancer and who are not receiving antineoplastic treatment, anticoagulant therapy is sometimes stopped after of 3–6 months. When deciding on the duration of anticoagulant therapy, it remains prudent to weigh the risk of recurrent thrombosis against the risk of anticoagulant-related bleeding and the patient’s quality of life. In patients with a high risk of bleeding or who are in the terminal stages of their cancer, the benefits of anticoagulation is unlikely to outweigh the risk of fatal hemorrhage or improve quality of life.

References

- 1 van den Belt AG, Prins MH, Lensing AW, et al: Fixed dose subcutaneous low molecular weight heparins versus adjusted dose unfractionated heparin for venous thromboembolism. *Cochrane Database Syst Rev* 2000;CD001100.
- 2 Prandoni P, Lensing AW, Piccioli A, et al: Recurrent venous thromboembolism and bleeding complications during anticoagulant treatment in patients with cancer and venous thrombosis. *Blood* 2002;100:3484–3488.
- 3 Lee AYY, Levine MN, Baker RI, Bowden C, Kakkar AK, Prins M, et al: Low-molecular-weight heparin versus a coumarin for the prevention of recurrent venous thromboembolism in patients with cancer. *N Engl J Med* 2003;349:146–153.
- 4 Lee AY, Levine MN: Management of venous thromboembolism in cancer patients. *Oncology* 2000;14:409–417, 421.