Journal Watch

Low-Molecular-Weight Heparin versus a Coumarin for the Prevention of Recurrent Venous Thromboembolism in Patients with Cancer.

Lee AYY, Levine MN, Baker RI, Bowden C, Kakkar AK, Prins M, et al. N Engl J Med 2003; 349(2):146-53.

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Received during: Journal Rounds on the Tertiary Palliative Care Unit, July 27, 2006

Abstract:

BACKGROUND: Patients with cancer have a substantial risk of recurrent thrombosis despite the use of oral anticoagulant therapy. We compared the efficacy of a low-molecular-weight heparin with that of an oral anticoagulant in preventing recurrent thrombosis in patients with cancer.
METHODS: Patients with cancer who had acute, symptomatic proximal deep-vein thrombosis, pulmonary embolism, or both were randomly assigned to receive low-molecular-weight heparin (dalteparin) at a dose of 200 IU per kilogram of body weight subcutaneously once daily for five to seven days and a coumarin derivative for six months (target international normalized ratio, 2.5) or dalteparin alone for six months (200 IU per kilogram once daily for one month, followed by a daily dose off approximately 150 IU per kilogram for five months).
RESULTS: During the six-month study period, 27 of 336 patients in the dalteparin group had recurrent venous thromboembolism, as compared with 53 of 336 patients in the oral-anticoagulant group (hazard ratio, 0.48; P=0.002). the probability of recurrent thromboembolism at six months was 17 percent in the oral-anticoagulant group and 9 percent in the dalteparin group. No significant difference between the dalteparin group and the oral-anticoagulant group was detected in the rate of major bleeding (6 percent and 4 percent, respectively) or any bleeding (14 percent and 19 percent, respectively). The mortality rate at six months was 39 percent in the dalteparin group and 41 percent in the oral-anticoagulant group.
CONCLUSIONS: In patients with cancer and acute venous thromboembolism, dalteparin was more effective than an oral anticoagulant in reducing the risk of recurrent thromboembolism without increasing the risk of bleeding.

Comments:

Strengths/uniqueness:
Well designed large multi-centered randomized clinical trial with wide applicability to almost all cancer patients with VTE. Both VTE recurrence as well as bleeding risk were assessed.

Weaknesses:
Potential biases include the open-label design. No assessment of whether additional therapies were used (eg. compression stockings).

Relevance to Palliative Care:
LMWH would likely improve morbidity by reducing recurrent VTE, but there is no evidence that it improves survival. Additional literature has also shown no improved survival. I would change my practice to offer both LMWH and oral a/c to patients, with an emphasis that LMWH is better at preventing recurrence. However, if patients are extremely adverse to daily subcutaneous injections, oral a/c is still a good option (with good INR monitoring, no exclusion criteria as in study).