New DVT Recommendations for Cancer Patients

BY DIANA MAHONEY
New England Bureau

HOLLYWOOD, FLA. — Low-molecular-weight heparin should be the drug of choice for the initial treatment of deep vein thrombosis in cancer patients, according to new management recommendations developed by the National Comprehensive Cancer Network.

"In cancer patients, low-molecular-weight heparin results in lower risk of recurrence of venous thrombosis and a reduced risk of major bleeding, compared with warfarin," Mohammad Jahanzeb, M.D., reported at the annual conference of the NCCN.

Many studies have confirmed a strong association between cancer and venous thromboembolism (VTE), said Dr. Jahanzeb, chair of the NCCN panel on the management of deep vein thrombosis in cancer. Patients with cancer have a higher risk of progressive and recurrent VTE, as well as an increased risk of bleeding. The association between cancer and VTE is thought to be both a consequence of tumor growth and host inflammatory responses as well as an indirect result of cancer treatment, venous stasis, and direct vessel trauma.

Traditionally, long-term anticoagulation therapy with warfarin has been the standard treatment for cancer patients with VTE, but its use has many disadvantages in this population. Cancer patients being treated for VTE experience a higher failure rate of warfarin, compared with patients who do not have cancer, he said. Warfarin can exacerbate cancer-related bleeding problems, can be difficult to manage in the presence of cancer-related comorbidities and concurrent medications, and is associated with an increased risk of adverse events in cancer patients.

In contrast, results of a metaanalysis of studies conducted during the past 7 years suggest that low-molecular-weight heparins are associated with a lower risk of adverse events, compared with warfarin in patients with cancer, said Dr. Jahanzeb, chief of the division of hematology and oncology, University of Tennessee, Memphis.

The landmark CLOT study (Randomized Comparison of Low-Molecular-Weight Heparin Versus Oral Anticoagulant Therapy for the Prevention of Recurrent Venous Thromboembolism in Patients With Cancer) compared injection of the low-molecular-weight heparin dalteparin with intravenous warfarin therapy for treating cancer patients with symptomatic, newly diagnosed deep vein thrombosis and/or pulmonary embolism. The dalteparin group had 52% fewer recurrent clots over the 6-month study period, with no significant increase in the incidence of bleeding, Dr. Jahanzeb said.

Low-molecular-weight heparin has more predictable anticoagulant effects and thus does not require the same degree of monitoring as warfarin.

And in nine randomized controlled trials that examined 3-month mortality in cancer and noncancer patients, those who received low-molecular-weight heparin had a significantly greater survival benefit than those who did not.

Low-molecular-weight heparins also have practical advantages over warfarin. Warfarin requires frequent dose monitoring because of substantial variability between and within the same individuals (which is exaggerated in cancer patients). Low-molecular-weight heparin has more predictable anticoagulant effects and thus does not require the same degree of monitoring. Subcutaneous injections of low-molecular-weight heparin can be done in the outpatient setting, but intravenous warfarin treatment usually is done on an inpatient basis.

"The data consistently suggest that [low-molecular-weight heparin] is safe and effective for the treatment and secondary prevention of venous thrombosis in cancer patients," he said.

It also should be considered for prophylaxis in certain subgroups of cancer patients, such as those with extensive disease or poor vascular access. ■

Electronic Alerts Reduce Venous Thromboembolism

BY BRUCE JANCIN
Denver Bureau

NEW ORLEANS — An automated electronic alert program aimed at physicians responsible for high-risk patients not receiving prophylaxis against venous thromboembolism resulted in a substantial reduction in thromboembolic events in a large randomized trial, Nils Kucher, M.D., said at the annual scientific sessions of the American Heart Association.

"Our results suggest that hospitals with adequate information system resources should consider implementation of electronic alerts to increase the awareness of venous thromboembolism [VTE] risk, improve utilization of prophylaxis, and reduce rates of leg deep vein thrombosis and pulmonary embolism," said Dr. Kucher of Brigham and Women's Hospital, Boston.

Studies have consistently shown that mechanical as well as pharmacologic prophylaxis against VTE is underutilized in at-risk patients.

In an effort to rectify this situation, Dr. Kucher and coworkers developed a computer program to electronically search the medical records of in-hospital patients and identify those at increased risk for VTE who weren't receiving prophylaxis.

The program sent an e-mail alert to the physician in charge of the patient's care that included mention of the full range of prophylactic options, such as compression stockings, low-molecular-weight heparin, unfractionated heparin, warfarin, and pneumatic compression boots.

The physician was forced to acknowledge the alert but could then choose to order or withhold prophylaxis.

The randomized trial involved 2,506 consecutive hospitalized patients at high risk for VTE who were not on prophylaxis. Physicians responsible for those in the intervention arm were issued an electronic alert. The alert was withheld from physicians caring for patients in the control group.

Use of the computerized electronic alert program resulted in more than a doubling of orders for prophylaxis, from 14.5% in the control group to 33.5% in the intervention group.

The primary study end point was the overall VTE rate at 90 days, which was 4.9% in the intervention arm and 8.2% among controls. This translated into a highly significant 41% relative risk reduction.

Pulmonary embolism was reduced by 60% in the intervention group, while proximal leg deep venous thromboembolism was decreased by 53%.

These benefits were achieved without an increase in major hemorrhage, which occurred in 1.5% of patients in both the intervention and control arms; 90-day mortality was 22% in each group as well.

The computer program identified patients as being at increased risk for VTE by using a scoring system that assigned 3 points each for prior VTE, cancer, or hypercoagulability; 2 points each for major surgery or a bed-rest order; and 1 point each for acute trauma, obesity, hormone therapy, or use of an OC. Patients with 4 or more points were defined as high-risk.

The reduction in VTE events seen with use of the electronic alert system was equally robust in patients with or without cancer, in both young and elderly patients, in men and women, and in those with or without a history of VTE.

Venous thromboembolism is said to be the No. 1 cause of unexpected in-hospital death. ■

DVT Prophylaxis Underused in Acutely Ill Patients, Study Finds

BY DOUG BRUNK
San Diego Bureau

SAN DIEGO — Deep vein thrombosis prophylaxis practice in hospitalized, acutely ill patients is clearly underused in the United States and Europe, results from a large international trial suggest.

"Despite the [American College of Chest Physicians] consensus guideline recommendations of 2001 and 2002 and evidence from clinical studies showing the benefits of DVT prophylaxis in acutely ill medical patients, only 44% received in-hospital prophylaxis," Victor F. Tapson, M.D., reported in a poster session at the annual meeting of the American Society of Hematology.

The finding is part of the International Medical Prevention Registry on Venous Thromboembolism (IMPROVE). Funded by an unrestricted grant from Aventis Pharmaceuticals Inc., the purpose of the multicenter registry is to assess routine clinical practices for providing hospitalized, acutely ill patients with venous thromboembolism prophylaxis and to test predictive models of the relationship between patient characteristics, prophylaxis use, and key clinical end points.

For the trial, patients aged 18 years and older who were hospitalized for at least 3 days were enrolled consecutively. Data were recorded at discharge and 3 months after discharge.

Dr. Tapson reported on 4,315 patients from 37 hospitals in 11 countries who were enrolled between Jan. 1, 2002, and June 30, 2004. Half were female and the mean age was 69.

Less than half of the patients (44%) received in-hospital DVT prophylaxis, said Dr. Tapson, of Duke University Medical Center, Durham, N.C. Low-molecular-weight heparin and unfractionated heparin were used most often. Low-molecular-weight heparin regimens were usually given once daily.

Unfractionated heparin regimens varied. Outside of the United States, most regimens (85%) were given every 12 hours. In the United States a similar number of patients received unfractionated heparin every 12 hours (55%) or every 8 hours (40%). Aspirin was given as DVT prophylaxis to 7% of patients in the United States and 3% to patients in other countries.

"Unfractionated heparin is used more for medical patient prophylaxis than low-molecular-weight heparin in the United States while the reverse is true in Europe and certain other parts of the world," Dr. Tapson said in an interview. "Low-molecular-weight heparin has considerable advantages including once-daily injection and, for example, a lower risk of heparin-induced thrombocytopenia This is very relevant to the primary care physician, particularly those that do inpatient work. They need to consider prophylaxis for every medical patient admitted, as most need it."

As for mechanical methods of DVT prophylaxis, U.S. clinicians used pneumatic compression more often, compared with those in other countries (19% vs. 0.3%). Foreign clinicians used elastic stockings more often, than U.S. doctors (8% vs. 2%). ■