

New Directions in the Treatment and Prevention of Deep Vein Thrombosis

This supplement to *The American Journal of Managed Care* features the proceedings of a roundtable symposium, "New Directions in the Treatment and Prevention of Deep Vein Thrombosis," held August 24 and 25, 2001, in Chicago, Illinois. The faculty for the symposium was specifically chosen for its expertise in pulmonology, critical care medicine, internal medicine, vascular surgery, pharmacy, health economics, pharmacoeconomics, and managed care.

Highlights of 4 presentations, each followed by a substantive discussion, and an interview, are included in this supplement. The presentations explore several aspects of deep vein thrombosis (DVT), including:

- The clinical and economic burdens of DVT;
- The treatment of DVT with low-molecular-weight heparin (LMWH);
- Prophylaxis of DVT and why it is underused;
- Clinical and economic implications of current enrollment trends that are changing the patient population mix (with regard to DVT) in managed care health plans;
- The shift from inpatient treatment of DVT with unfractionated heparin to outpatient treatment with LMWH;
- Economic implications of this shift to managed care health plans, health plan members, hospitals, and the medical community as a whole;
- The use of pharmacoeconomics in formulary development and whether it can improve the way DVT is treated;
- The pharmacologic differences between

unfractionated heparin and LMWH and how they affect clinical outcome;

- Identification of patients at risk for recurrent venous thromboembolism; and
- The need for long-term studies to evaluate the impact of prophylactic therapy on long-term sequelae.

In the interview, Alex Spyropoulos, MD, discusses the outpatient DVT treatment program he championed and cowrote for Lovelace Health Systems in Albuquerque, New Mexico.

The need to recognize the risk for DVT and to manage DVT effectively is crucial because it is associated with considerable morbidity and mortality. DVT affects 2 million people in the United States and accounts for 800,000 cases of post-phlebotic syndrome as well as 600,000 cases of pulmonary embolism, 10% of which are fatal.¹ It is also a common cause of death in hospitalized patients.

All risk factors for DVT stem from the 3 components of Virchow's triad, which was first described in 1856 but still holds true today: stasis, hypercoagulability, and endothelial injury. Among the risk factors for DVT are previous DVT, malignancy, advancing age, obesity, prolonged bed rest, severe medical illness, pregnancy/postpartum, stroke, myocardial infarction, varicose veins, oral contraceptives, antipsychotic drugs, deficiencies of antithrombin III, protein C, protein S, heparin cofactors, activated protein C resistance, and elevated prothrombin levels.

Risk assessment is also crucial because, as suggested by current trends, managed

care organizations (MCOs) are enrolling more patients who are at risk for DVT.

Traditional in-hospital treatment of DVT with or without pulmonary embolism consists of an intravenous bolus of unfractionated heparin followed by a continuous infusion for several days and the concomitant administration of warfarin initiated within the first 24 hours after the heparin bolus. However, a review of the literature reveals that this treatment regimen is often subtherapeutic at 24 and 48 hours in many patients. This is a significant problem because the longer the patient remains on subtherapeutic therapy, the greater the risk of DVT recurrence. In some cases, treatment is subtherapeutic because warfarin therapy is not begun soon enough.

This raises several important questions about the use of LMWH as an alternative to unfractionated heparin. The most fundamental question, of course, is whether LMWH will make a difference in clinical outcome. The answer is yes, for several reasons.

First, the pharmacologic differences between unfractionated and LMWH favor the latter. With preferential binding to factor anti-Xa relative to anti-IIa or thrombin, lack of binding to endothelium, and greater bioavailability after subcutaneous injection, LMWH therapy is far less likely to be subtherapeutic. Because LMWH is given by subcutaneous injection, it can be administered on an outpatient basis, resulting in far shorter hospital stays and reduced hospitalization costs. In addition, a large meta-analysis has shown that LMWH is associated with significant reductions in mortality, major bleeding, and thrombocytopenia compared with unfractionated heparin.²

Although prophylaxis of DVT is not standard therapy, it is a major issue and an important new direction in management. The results of the Prophylaxis in Medical Patients with Enoxaparin (MED-ENOX) study demonstrate the efficacy of 6 to 14 days of therapy with the LMWH

enoxaparin in more than 1100 hospitalized medical patients who were acutely ill with conditions such as acute respiratory failure, acute infection, and congestive heart failure. At 14 days after randomization, the rate of symptomatic or radiographically confirmed DVT was considerably lower in patients treated with enoxaparin than in patients receiving placebo.³

Both the treatment and prevention of DVT raise a number of important economic issues, not only in terms of costs but also in terms of enrollment trends that are changing the patient population mix in MCOs. In addition, the shift from inpatient treatment with unfractionated heparin to outpatient treatment with LMWH shifts dollars and resources. For managed care health plans, it means cost savings, but for health plan members (ie, patients) it might mean increased out-of-pocket costs. The potential shift from inpatient prophylaxis with unfractionated heparin to outpatient prophylaxis with LMWH is also expected to raise the same and similar economic issues.

Although there is considerable information regarding the treatment of DVT, there is relatively little regarding prophylaxis. More studies in both areas are needed, including effectiveness studies (as opposed to efficacy studies), head-to-head comparisons, and studies evaluating the long-term efficacy of prophylactic treatment.

... REFERENCES ...

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3. Samama MM, Cohen AT, Darmon JY, et al. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. Prophylaxis in Medical Patients with Enoxaparin Study Group. *N Engl J Med* 1999; 341:793-800.