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Clinical Guide - Initial Treatment of VTE (May 2004)

Principal Developer: G. Pineo
Secondary Developers: M. Mant, S. Robinson, P. Wells

Heparin and Low Molecular Weight Heparin for the Initial Treatment of Venous Thromboembolism

The objectives of treatment for patients with venous thromboembolism (VTE) (deep venous thrombosis and/or pulmonary embolism) are 1) to prevent death from pulmonary embolism, 2) to relieve symptoms and prevent extension of deep venous thrombosis, 3) to prevent recurrent VTE, and 4) to prevent the post thrombotic syndrome. The anticoagulant drugs heparin, low molecular weight heparin (LMWH) and warfarin constitute the mainstay of treatment of VTE. In selected cases the use of thrombolytic agents and/or the insertion of an inferior vena cava filter may be indicated. The use of graduated compression stockings following an episode of deep venous thrombosis has been shown to decrease the incidence of the post thrombotic syndrome. For further information on the use of heparin and warfarin, please refer to the guidelines located elsewhere on the TIG web site.

Heparin therapy

Unfractionated heparin, delivered by a constant intravenous infusion, and monitored by the APTT has been used for the initial anticoagulant treatment of VTE for a number of years. More recently, low molecular weight heparin has replaced unfractionated heparin for most patients. However intravenous heparin continues to be the agent of choice in patients who are at high risk of bleeding, who may require urgent interruption of anticoagulant treatment for surgical intervention or thrombolysis, who require hospitalization, or for a combination of reasons such as patients in critical care units. The fact that intravenous heparin therapy can be rapidly reversed by stopping the intravenous infusion or administering protamine sulfate favours its use in such circumstances. When intravenous unfractionated heparin is used it is very important to control therapy with one of the validated heparin nomograms to ensure that patients receive adequate therapy. The platelet count should be monitored every one to two days during initial therapy. In most cases warfarin should be started on day 1 with the heparin being continued until the INR is therapeutic on two consecutive days and until the patient has received at least five days of intravenous heparin.

Low Molecular Weight Heparin Therapy

The LMWHs have a number of advantages over unfractionated heparin. Of particular importance are the following: increased bioavailability (more than 90% after subcutaneous injection), prolonged half-life and predictable clearance enabling once or twice daily s.c. injection and predictable antithrombotic response based on body weight permitting treatment without laboratory monitoring. These features also permit the out of hospital use of LMWH for the initial treatment of VTE. LMWHs may cause less major bleeding and have a decreased incidence of heparin induced thrombocytopenia and osteoporosis.

A number of randomized clinical trials have compared the efficacy and safety of LMWH with intravenous unfractionated heparin in the initial treatment of deep venous thrombosis and pulmonary embolism. Meta-analysis of the methodologically strong studies indicates a reduction in recurrent VTE, major bleeding and mortality with the use of LMWH. Studies comparing the use of LMWH out of hospital with intravenous unfractionated heparin in hospital have shown the LMWHs to be of equal efficacy and safety. Cohort studies in patients with venous thrombosis, pulmonary embolism and upper extremity venous thrombosis continue to show the feasibility and safety of treating the majority of such patients out of hospital. LMWH, either in hospital or out of hospital, has been shown to be cost effective in comparison with intravenous unfractionated heparin treatment.

There are now four LMWHs available for use in Canada. The CPS or the local hospital pharmacy should be consulted for prescribing instructions. Monitoring of Factor Xa is usually not required although, depending on the LMWH being used, Xa monitoring may be useful in patients with significant renal impairment. The other option

is to use unfractionated heparin in such cases. As with unfractionated heparin, the platelet count should be measured every one to two days during initial treatment, and warfarin should be commenced on day one, with LMWH continued until the INR is therapeutic on two consecutive days and a minimum of five days treatment has been given.

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