Effect of enoxaparin on death rates in acute care

Pharmacological thromboprophylaxis when used in addition to compression stockings does not reduce death rates, when compared with compression stockings alone. However, prophylaxis is still useful in reducing venous thromboembolism, unless there is a high risk of bleeding.

Overview: Venous thromboembolism (VTE) is an important cause of death in patients admitted to hospital, and treatment of non-fatal symptomatic VTE and related long-term morbidities is associated with considerable cost to the health service. It is estimated that 25,000 people die in the UK every year from preventable hospital-acquired VTE. The inconsistent use of prophylactic measures for VTE in patients admitted to hospital has been widely reported. A UK survey suggested that 71% of patients assessed to be at medium or high risk of developing deep vein thrombosis did not receive any form of mechanical or pharmacological VTE prophylaxis (that is, anticoagulant medicine) (Rashid et al. 2005).

Current treatment: NICE recommends that all patients be assessed on admission to identify those who are at increased risk of VTE. Pharmacological VTE prophylaxis should be offered as soon as possible after a risk assessment has been completed. This is to be continued until the patient is no longer at increased risk of VTE. However, patients with risk factors for bleeding should not be offered this medication unless the risk of VTE outweighs the risk of bleeding.

Ensuring that the provision of VTE prophylaxis is in accordance with NICE guidance is a statement of the VTE NICE Quality Standard.

New evidence: A double-blind, placebo-controlled, randomised trial evaluated the effect of pharmacological thromboprophylaxis on the rate of death from any cause in patients hospitalised for an acute cause (Kakkar et al. 2011).

A total of 8307 patients from 193 sites in China, India, Korea, Malaysia, Mexico, the Philippines, and Tunisia were randomly assigned to receive the low-molecular-weight heparin (LMWH), enoxaparin or placebo, with both groups assigned to wear elastic stockings with graduated compression.

Inclusion criteria were an age of at least 40 years and hospitalisation for acute decompensated heart failure, severe systemic infection with at least one risk factor for venous thromboembolism, or active cancer. The primary efficacy outcome was the rate of death from any cause at 30 days after randomisation. The primary safety outcome was the rate of major bleeding during and up to 48 hours after the treatment period.

Results showed the rate of death from any cause at day 30 was 4.9% in the enoxaparin group as compared with 4.8% in the placebo group. The rate of major bleeding was 0.4% in the enoxaparin group and 0.3% in the placebo group. Pharmacological prophylaxis was not associated with increased rates of major bleeding but was associated with increased rates of total bleeding. The use of enoxaparin plus elastic stockings with graduated compression, as compared with elastic stockings with graduated compression alone, was not associated with a reduction in the rate of death from any cause among hospitalised, acutely ill patients.

Commentary: This is an interesting study of VTE prophylaxis in acute medical patients performed in several non-European countries. It should be noted that in both study groups graduated compression stockings were worn and the study was not designed to compare these directly with the LMWH enoxaparin. Current NICE guidance suggests LMWH prophylaxis for acute medical patients at VTE risk unless there is a high bleeding risk.
when mechanical methods are preferred. It is also of note that the study was underpowered to assess the main endpoint of mortality, due to an unexpectedly low mortality rate in both groups, perhaps making it less relevant for an NHS setting. The main message from this study is probably that more research is needed in this area and that for most patients one modality of VTE prophylaxis is sufficient in line with current guidance. It is also worth stressing that graduated compression stockings should be used with caution, especially in people who have had a stroke, and LMWH may be risky if there is a bleeding tendency present. So in practice, and in line with current guidance, clinicians need to fully assess and then balance the VTE risk against the bleeding risk for each patient.” — Gerard Stansby, Professor of Vascular Surgery, Freeman Hospital, Newcastle upon Tyne.

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