Anticoagulant prophylaxis to prevent asymptomatic deep vein thrombosis in hospitalized medical patients: a systematic review and meta-analysis

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CRD summary
This review concluded that anticoagulant prophylaxis in hospitalised at-risk medical patients reduced the risk of asymptomatic deep vein thrombosis, but increased the risk of major bleeding, in comparison with placebo. Although the authors’ conclusions were based on only a small number of studies, this was a well-conducted review and its findings were supported by the data presented.

Authors' objectives
To compare the risk of asymptomatic deep vein thrombosis (DVT) in at-risk hospital medical patients treated with anticoagulant prophylaxis versus no prophylaxis.

Searching
MEDLINE (1950 to March 2007), EMBASE (1980 to week 11, 2007) and the Cochrane Library (first quarter, 2007) were searched using reported search terms. The United States National Institute of Health Registry of Clinical Trials was searched for ongoing trials and the reference lists of retrieved trials and reviews checked for further studies. Topic experts were approached for information about unpublished studies. No language restrictions were applied.

Study selection
Randomised controlled trials (RCTs) comparing the incidence of asymptomatic DVT in hospitalised medical patients receiving anticoagulant prophylaxis versus no prophylaxis were eligible for inclusion in the review. Studies had to assess all patients using a reliable screening method for DVT, such as venography or venous ultrasound. Studies were excluded if they assessed mechanical methods of prophylaxis (including compression stockings) or if patients received co-administered prophylactic antithrombotic drugs such as aspirin. Other eligible outcomes included the incidence of proximal DVT, all-cause mortality and major bleeding.

Included studies assessed commonly used single daily subcutaneous doses of low molecular weight heparins (LMWH; dalteparin, nadroparin and enoxaparin) or fondaparinux compared with subcutaneously administered placebo. The majority of included patients had various acute medical conditions. One study included only patients with acute decompensated chronic obstructive pulmonary disease (COPD). Another study included patients with congestive heart failure. Treatment periods were mainly between six and 14 days in duration, with follow-up periods lasting between 21 and 110 days.

Two reviewers independently assessed each study for inclusion.

Assessment of study quality
Multiple reviewers (number not stated) assessed the quality of each study using the 5-point Jadad scale, which assesses randomisation, blinding and loss to follow-up. Inter-reviewer agreement was assessed using the kappa statistic.

Data extraction
Two reviewers independently extracted the study data. Disagreements were resolved by a third reviewer. Intention-to-treat (ITT) data were extracted for each outcome and any risk factors and co-morbidities were recorded.

Methods of synthesis
Studies were combined and pooled relative risks (RRs) with 95% confidence intervals (CIs) were calculated using the random effects model. Statistical heterogeneity was assessed using the $I^2$ statistic and data were pooled only in the absence of heterogeneity or where any statistical heterogeneity could not be explained.

Results of the review
Four RCTs (n=5,516) were included in the review. All of the studies were of good quality: three studies scored 4 out of 5 points and one study scored the maximum 5 points. The three studies that scored 4 points all failed to report the method of randomisation used.

The pooled data showed that compared with placebo, anticoagulant prophylaxis was associated with a statistically significant lower risk of asymptomatic DVT (RR 0.51; 95% CI: 0.39, 0.67) and asymptomatic proximal DVT (RR 0.45; 95% CI: 0.31, 0.65), but a significantly higher risk of major bleeding (RR 2.00; 95% CI: 1.05, 3.79). There were no significant differences in all-cause mortality. No significant statistical heterogeneity was detected.

Authors’ conclusions
Anticoagulant prophylaxis in at-risk hospital medical patients was effective at reducing the risk of DVT, but was associated with an increase risk of bleeding.

CRD commentary
This review answered a clearly defined research question and searched a number of sources for both published and unpublished data without any restriction on language. Multiple reviewers were involved at each stage of the review process to reduce the risk of reviewer error and bias. The assessment of study quality showed that all the studies were rated as very good. An assessment of statistical heterogeneity prior to data pooling detected no significant heterogeneity. In addition, a conservative estimate of outcome effect sizes was reported using a random effects analysis of intention to treat data. Although the authors’ conclusions are based on only a small number of studies, this was a well-conducted review and its findings were supported by the data presented.

Implications of the review for practice and research
Practice: the authors stated that the therapeutic benefits of anticoagulant prophylaxis outweighed the increased risk of bleeding and should be considered in at-risk hospital medical patients.

Research: the authors stated that further research was required to identify in which specific patient groups prophylaxis was most effective and to identify any barriers to the implementation of prophylaxis that may exist.

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**Record Status**
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