Efficacy and safety of anticoagulant prophylaxis to prevent venous thromboembolism in acutely ill medical inpatients: a meta-analysis
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CRD summary
This review assessed anticoagulants (low-molecular-weight heparin or fondaparinux) for preventing venous thromboembolism in medical inpatients and concluded that anticoagulants reduced the risk of venous thromboembolism by approximately half. Risk assessment should be undertaken to decide who was likely to benefit from anticoagulation. Some methods of the review were not well described, but the conclusions are likely to be reasonable.

Authors' objectives
To assess the effects of anticoagulants for preventing venous thromboembolism in acutely ill medical inpatients.

Searching
MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from 1980 to October 2006. Abstracts from three major meetings and reference lists of identified papers were checked.

Study selection
Published blinded randomised controlled trials (RCTs) that compared the prophylactic effects of a fixed dose of unfractionated heparin, low molecular weight heparin (LMWH) or fondaparinux to placebo in acutely medically ill inpatients were sought. Studies had to report on venous thromboembolism as assessed by objective diagnostic testing. Treatment and follow-up had to be at least one week.

Participants in studies included people with cardiac and respiratory conditions. Where stated, studies only included participants aged 40 and over, aged 60 and over or aged 65 and over. Treatment included pharmuka, enoxaparin, nadroparin, dalteparin and fondaparinux (details of doses are given in the paper). Treatment duration was until hospital discharge and until discontinued from mechanical ventilation and ranged from six to 24 days. Duration of follow-up ranged from 10 to 90 days. Primary outcomes were symptomatic venous thromboembolism (deep-vein thrombosis (DVT) and pulmonary embolism) and major bleeding, intracranial bleeding or fatal bleeding. Definitions of major bleeding were taken as those in the individual included studies (see paper for details) and objectively confirmed intracranial bleeding. Other outcomes reported included asymptomatic DVT and all-cause mortality. DVT was diagnosed by fibrinogen update test, venography, ultrasound or autopsy. Where evaluated, pulmonary embolism was diagnosed by scintigraphy, angiography, computed tomography (CT) or autopsy.

Three reviewers performed the study selection independently. Disagreements were resolved by discussion.

Assessment of study quality
The authors stated that three reviewers independently extracted data (no other details were provided).

Data extraction
Data extracted included numbers and percentages of outcome events, and risk ratios (RR).

Three reviewers extracted data independently.

Methods of synthesis
Summary relative risks were calculated using a fixed-effect and random-effects models. Pooled risk ratios (RR) and 95% confidence intervals (CI) were calculated as well as numbers need to treat (NNT) or numbers needed to harm (NNH). Heterogeneity was assessed using the X² test.
Results of the review
Seven RCTs (8,902 participants) were included: six on LMWH (8,053 participants) and one on fondaparinux (849 participants). No studies on unfractionated heparin were included.

Results for fixed-effect and random-effects models were similar; those for fixed-effect were reported. The p value for heterogeneity was above 0.10 in all analyses.

Treatment with LMWH or fondaparinux reduced the risk of asymptomatic DVT (RR 0.49, 95% CI 0.38 to 0.64, NNT 33; five studies) and of symptomatic pulmonary embolism (RR 0.52, 95% CI 0.29 to 0.91, NNT 241; seven studies). The risk of symptomatic DVT was also reduced, but did not reach statistical significance (RR 0.52, 95% CI 0.25 to 1.08, NNT 271; five studies). There was a trend towards a higher risk of major bleeding, but this was not statistically significant (RR 1.39, 95% CI 0.77 to 2.51, NNH 598; seven studies). There was no difference in all-cause mortality (RR 0.95, 95% CI 0.79 to 1.14; seven studies).

Authors’ conclusions
Anticoagulation prophylaxis prevented approximately half venous thromboembolism events (DVT or pulmonary embolism) in acutely ill medical patients.

CRD commentary
The inclusion criteria related to study design, treatment and outcomes were clearly stated, although those related to participants were somewhat broad. The sources searched were adequate. Search terms were not reported and there was no mention of whether a language restriction was applied or not. It was not possible to comment on whether this could have affected the identification of studies. The methods of the review (study selection, data extraction) were appropriate for reducing the introduction of bias or error into the review. There was no mention of how the quality of included studies was assessed. Statistical methods used to pool data were appropriate and heterogeneity was assessed. Information about included participants was limited and this could affect the generalisability of the review. The authors commented that their conclusions were similar to those of another review on this topic (see Other Publications of Related Interest). Although some of the methods of the review were not well described, the conclusions are likely to be reasonable.

Implications of the review for practice and research
Practice: The authors stated that clinicians needed to identify patients with a sufficiently high risk of symptomatic venous thromboembolism to warrant LMWH prophylaxis.

Research: The authors stated that more studies were needed to enable clinicians to make a better risk assessment regarding venous thromboembolism.

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