Thromboprophylaxis in patients with acute spinal injuries: an evidence-based analysis

Ploumis A, Ponnappan RK, Maltenfort MG, Patel RX, Bessey JT, Albert TJ, Harrop JS, Fisher CG, Bono CM, Vaccaro AR

CRD summary
The review concluded that low molecular weight heparin was more effective than unfractionated heparin for prevention of deep vein thrombosis and had fewer bleeding complications in patients with spinal cord injury. Limited assessment and reporting of study quality coupled with pooling of statistically variable data mean the authors’ conclusions should be interpreted with caution.

Authors' objectives
To determine the optimum thromboprophylaxis regimen for patients with acute spinal injuries with or without spinal cord injury.

Searching
MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and Cochrane Database of Systematic Reviews were searched to April 2008 for peer-reviewed studies in any language; search terms were reported. Conference proceedings and systematic reviews were searched from 2005 to April 2008. References lists of retrieved articles were searched.

Study selection
Clinical studies of pharmacological and/or mechanical measures in adults to prevent venous thromboembolism up to three months after spinal trauma (with or without spinal cord injury) or postoperatively were eligible for inclusion. Treatment had to be for at least two weeks and use objective diagnostic tests for deep-vein thrombosis, pulmonary embolism and bleeding (tests were listed). Eligible outcomes included prevalence of deep vein thrombosis, pulmonary embolism and treatment-related adverse events.

Studies that compared unfractionated heparin with low molecular weight heparin had to be randomised controlled trials (RCTs) with adequate compliance, at least six weeks of treatment and at least six weeks follow-up. Heparin studies had to report the method of thromboprophylaxis, surgical treatment beyond 72 hours after injury and use of concomitant mechanical prophylaxis.

Treatments in the included studies varied and covered the areas: mechanical prophylaxis; vitamin K antagonists; non-vitamin K antagonists; mechanical plus pharmacological prophylaxis; and no prophylaxis. Most studies were of patients with spinal cord injury; some were of mixed populations (with and without spinal cord injury).

Three reviewers selected studies for inclusion. No further details about methods were reported.

Assessment of study quality
Only heparin RCTs were quality assessed, according to Cochrane Reviewers' Handbook guidelines of selection bias, performance bias, attrition bias, and detection bias to produce scores that reflected the number of quality items fulfilled (maximum score of 11).

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Two groups of reviewers extracted data independently in order to calculate odds ratios (OR) and 95% confidence intervals (CI). Disagreements were resolved by consensus.

Methods of synthesis
Studies were pooled using a fixed-effect model, or a random-effects model when significant heterogeneity was found. Heterogeneity was assessed using the $X^2$ statistic.
Results of the review
Twenty-one studies (n=2,236) were included in the review: nine RCTs (n=653); five retrospective studies (n=1,059); four cohort studies (n=421); and two case series (n=103). Four of the heparin RCTs satisfied six positive internal validity criteria and one passed seven criteria.

Vitamin K antagonists versus non-vitamin K antagonists in patients with acute spinal cord injury (four non-randomised studies): Lower events rates following treatment with vitamin K antagonists were found for pulmonary embolism (OR 0.10, 95% CI 0.01 to 0.63; four studies) but not for deep-vein thrombosis or bleeding (both three studies).

Unfractionated heparin versus low molecular weight heparin in patients with acute spinal cord injury (five RCTs): Patients who received unfractionated heparin had significantly higher rates of deep-vein thrombosis (OR 2.6, 95% CI 1.2 to 5.6) and bleeding (OR 7.5, 95% CI 1.0 to 58.4). Statistically significant heterogeneity was seen in both analyses.

One study compared mechanical methods alone with combined mechanical and pharmacological methods and yielded no significant differences between treatments.

Timing and duration of treatment (two studies): When treatment was given within the first two weeks after injury there were significantly fewer episodes of deep vein thrombosis than when treatment was delayed (OR 0.2, 95% CI 0.1 to 0.4; two studies).

Authors' conclusions
Low molecular weight heparin was more effective than unfractionated heparin for prevention of deep vein thrombosis and had fewer bleeding complications in patients with spinal cord injury. Use of vitamin K antagonists appeared to be effective for prevention of pulmonary embolism.

CRD commentary
The review addressed a clear question supported by appropriate inclusion criteria. Several electronic databases were searched. The authors also searched conference proceedings but the restriction to studies published in peer-reviewed journals meant that some relevant studies may have been missed. Use of methods to reduce the risk of reviewer errors and bias was inconsistently reported; although data extraction was performed independently and in duplicate, details of study selection and quality assessment methods were unclear. Study quality was assessed only for trials of heparin and no study-level details about criteria were provided, which made it difficult to assess the strength of the evidence. It appeared that suitable method were used to pool data and assess heterogeneity, but results of heterogeneity assessments were reported only for some analyses. It appeared that two types of pooled analysis were conducted and the difference between them was not clearly described, which made the synthesis difficult to follow (and few forest plots were presented).

In light of the limited assessment and reporting of study quality and the heterogeneity between studies, the authors' conclusions should be interpreted with caution.

Implications of the review for practice and research
Practice: The authors stated several recommendations related to interventions. Mechanical prophylaxis alone was safe and effective for patients who had spinal trauma with or without spinal cord injury. Oral anticoagulants were effective for prevention of pulmonary embolism in patients with acute spinal cord injury. Low molecular weight heparin was more effective (and resulted in fewer bleeding complications) than unfractionated heparin for prevention of deep vein thrombosis in patients with acute spinal cord injury (but both agents were equivalent with regard to prevention of pulmonary embolism).

Research: The authors stated that additional research was needed in relation to bleeding and other heparin-related complications.

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