Review: low molecular weight heparin reduces risk of venous thromboembolism in adults with leg immobilisation

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QUESTION
In adults with leg immobilisation, does low molecular weight heparin (LMWH) prevent venous thromboembolism (VTE)?

REVIEW SCOPE
In adults with leg immobilisation, does low molecular weight heparin (LMWH) prevent venous thromboembolism (VTE)?

REVIEW METHODS
Included studies compared LMWH with placebo or no thromboprophylaxis in adults with a leg injury requiring immobilisation in a plaster cast or brace in an ambulatory setting. Outcomes were symptomatic or asymptomatic VTE (deep venous thrombosis [DVT] or pulmonary embolism) and bleeding events.

METHODS
The search identified 2350 records. After duplicates were removed, 1756 were screened for eligibility. Eighteen studies comprising 1490 patients met the inclusion criteria. Six RCTs (n = 1490, mean age 34–49 years, 46–79% men) met the selection criteria. DVT was diagnosed by venography or by compression ultrasonography and/or duplex scanning confirmed by phlebography or venography. Four trials reported adequate concealment of allocation, five placebo-controlled trials were double-blinded, and the outcome assessor was blinded in one trial.

MAIN RESULTS
LMWH reduced risk of VTE (symptomatic or identified by screening) and asymptomatic VTE (table). Treatment effect was similar in patients with below-knee casts, in operated or non-operated patients, in patients with fractures or soft-tissue injuries, and in patients with distal or proximal segment DVT. Pulmonary embolism was reported in 2 patients (0.4%), both receiving placebo. Major bleeding events were rare, and groups did not differ for minor bleeding events.

CONCLUSION
In adults with leg immobilisation, thromboprophylaxis with low molecular weight heparin reduces risk of venous thromboembolism by about half, with low risk of bleeding events.

Low molecular weight heparin (LMWH) vs placebo or no thromboprophylaxis (control) to prevent venous thromboembolism (VTE) in adults with leg immobilisation*

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Number of trials (n)</th>
<th>Weighted event rates</th>
<th>At cast removal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LMWH</td>
<td>Control</td>
<td>RRR (95% CI)</td>
</tr>
<tr>
<td>Any VTE</td>
<td>6 (1490)</td>
<td>10%</td>
<td>18%</td>
</tr>
<tr>
<td>Symptomatic VTE</td>
<td>4 (1303)</td>
<td>0.4%</td>
<td>2.5%</td>
</tr>
</tbody>
</table>

*Abbreviations defined in glossary. Weighted event rates, RRR, NNT, and CI calculated from data in article using a random-effects (any VTE) or fixed-effect (symptomatic VTE) model.

COMMENTARY
The most serious short-term consequence of VTE is death. Long-term consequences, including post-thrombotic syndrome, venous stasis, and venous ulceration, often result in chronic health problems. Thus, prevention of VTE is an important component of care for at-risk patients. The review by Testroote et al focused on trials comparing LMWH with placebo or no prophylaxis in one at-risk group—ambulatory adults with leg injury requiring immobilisation in a cast or brace. The trials included in the meta-analysis were well done, with similar findings and sampling that allows generalisation of results.

The review found that LMWH reduces risk of DVT in low-risk patients. There was a low risk of bleeding complications. However, only 6 trials, with approximately 1500 patients, were found to meet the inclusion criteria for the review. This may not have been a large enough sample to detect the rare serious adverse events that can result from LMWH. Although the evidence of risk reduction is strong, these medications can result in serious side effects and one must carefully weigh the risks and benefits. The patient’s perspective must also be considered because daily injections may not be acceptable to many patients. Practical considerations include insurance coverage and teaching patients or caregivers how to inject the drug. Other options for thromboprophylaxis not included in this review, especially oral agents, may be more acceptable. LMWH is clearly an option to be considered and possibly offered on an individual basis after thorough discussion with patients of risks and benefits and consideration of additional risk factors.

The meta-analysis by Testroote et al is of interest to physicians, nurse practitioners, physician assistants, and nurses in various settings. Patients with lower leg injuries present and receive follow-up care in many settings: emergency departments, trauma centres, home care, primary care offices, and clinics. All healthcare providers should be prepared to discuss with patients options to reduce risk of VTE because these encounters often occur in urgent and time-limited settings.

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