

Review: Extended out-of-hospital prophylaxis with heparin prevents deep venous thrombosis in elective hip arthroplasty

Hull RD, Pineo GF, Stein PD, et al. Extended out-of-hospital low-molecular-weight heparin prophylaxis against deep venous thrombosis in patients after elective hip arthroplasty: a systematic review. *Ann Intern Med.* 2001 Nov 20;135:858-69.

QUESTION

In patients who have received total hip replacement, is extended out-of-hospital prophylaxis with low-molecular-weight heparin (LMWH) more effective than placebo for reducing venous thromboembolism (VTE)?

DATA SOURCES

Studies were identified by searching MEDLINE (1976 to May 2001) and the Cochrane Library, reviewing lists of conference abstracts and bibliographies of relevant articles, and contacting investigators and pharmaceutical companies for unpublished studies.

STUDY SELECTION

Studies in any language were selected if they were randomized controlled trials (RCTs) comparing extended out-of-hospital prophylaxis consisting of LMWH with placebo, patients had had elective hip arthroplasty, the presence or absence of all episodes of deep venous thrombosis (DVT) and proximal venous thrombosis were objectively documented by using bilateral ascending contrast venography, and objective methods were used to assess bleeding complications.

DATA EXTRACTION

Data were extracted on sample size, key components of the intervention, study quality, length of hospital stay, time interval from surgery to venography, and outcomes. Main outcomes included all episodes of DVT, proximal venous thrombosis, symptomatic DVT and pulmonary embolism, and major bleeding complications.

MAIN RESULTS

6 RCTs (1953 patients) met the selection criteria. LMWH preparations assessed were enoxaparin (Aventis Pharmaceuticals, Inc., Bridgewater, NJ, USA) (3 RCTs) and dalteparin (Pharmacia Corp., Peapack, NJ, USA) (3 RCTs). The rates of all episodes of

DVT, proximal DVT, and symptomatic VTE were lower in the LMWH group than in the placebo group (all *P* values < 0.05) (Table). Major bleeding occurred in 1 of 826 patients in the placebo group.

CONCLUSION

In patients who have received total hip replacement, extended out-of-hospital prophylaxis with low-molecular-weight heparin is more effective than placebo for reducing venous thromboembolism.

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Low-molecular-weight heparin (LMWH) vs placebo for extended out-of-hospital prophylaxis of thromboembolism after total hip replacement*

Outcomes at 18 to 29 d	Weighted event rates		RRR (95% CI)	NNT (CI)
	LMWH	Placebo		
All deep venous thrombosis	12%	23%	59% (46 to 68)	10 (8 to 14)
Proximal deep venous thrombosis	6%	11%	69% (53 to 80)	18 (13 to 30)
Symptomatic venous thromboembolism	2%	4%	64% (33 to 80)	51 (31 to 154)

*Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article using fixed-effects models.

COMMENTARY

LMWH is an effective form of thromboprophylaxis after elective hip arthroplasty, but the optimal duration of therapy is controversial. It has been shown that the risk for VTE extends beyond the usual 7- to 10-day period of prophylaxis (1).

The review by Hull and colleagues is the third meta-analysis (2, 3) of RCTs examining the risks and benefits of extending the duration of therapy with LMWH to 4 to 6 weeks. The review has explicit and comprehensive search strategies and adheres to strict methodologic guidelines. Unlike the previous meta-analyses, it focuses exclusively on elective hip arthroplasty and only includes RCTs in which mandatory venography was done at the end of the study period. Therefore, it is more likely to show the efficacy of extended prophylaxis in reducing the incidence of asymptomatic DVT diagnosed by venography. Extended prophylaxis seems to be safe, because no reported cases of major bleeding occurred in the treatment group. Conclusions about reducing the incidence of symptomatic VTE are less clear-cut because assurance was not given in 5 of 6 RCTs included in the review that clinical assessment was blinded to venographic outcome.

What conclusions can be drawn? Extended prophylaxis after total hip replacement reduces the incidence of asymptomatic DVT and probably also that of symptomatic VTE. The cost-effectiveness of extended prophylaxis is unknown, and evaluating its effect on fatal pulmonary embolism would require much larger studies. Reluctance to incorporate extended thromboprophylaxis into routine clinical practice

in all patients receiving total hip replacement is largely caused by the inconvenience and logistic difficulties associated with extended therapy. We agree with the authors' conclusions that "extended out-of-hospital prophylaxis with LMWH should be considered in patients undergoing elective hip replacement" and that "further research is warranted to determine whether thromboprophylaxis should be extended to all patients undergoing surgery or to selected high-risk patients only." We believe that further research on extended prophylaxis should include evaluating oral agents (both anticoagulants and oral antiplatelet drugs) that do not require laboratory monitoring.

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References

- White RH, Romano PS, Zhou H, Rodrigo J, Bargar W. Incidence and time course of thromboembolic outcomes following total hip or knee arthroplasty. *Arch Intern Med.* 1998;158:1525-31.
- Cohen AT, Bailey CS, Alikham R, Cooper DJ. Extended thromboprophylaxis with low molecular weight heparin reduces symptomatic venous thromboembolism following lower limb arthroplasty—a meta-analysis. *Thromb Haemost.* 2001;85:940-1.
- Eikelboom JW, Quinlan DJ, Douketis JD. Extended-duration prophylaxis against venous thromboembolism after hip or knee replacement: a meta-analysis of the randomised trials. *Lancet.* 2001;358:9-15.