Extending enoxaparin 1 month after hospital discharge reduced thromboembolism after elective hip surgery

Bergqvist D, Benoni G, Björgell O, et al. **Low-molecular-weight heparin (enoxaparin) as prophylaxis against venous thromboembolism after total hip replacement.** N Engl J Med. 1996 Sep 5;335:696-700.

Objective

To compare the effectiveness of 1 month of anticoagulant therapy with enoxaparin with enoxaparin given only during hospitalization in patients having elective total hip replacement.

Design

Randomized, double-blind, placebo-controlled trial with maximum 23-day follow-up after discharge from the hospital.

Setting

Hospital in Sweden.

Patients

262 patients who were aged > 39 years (median age 70 y, 57% women) and weighed > 60 kg having elective hip arthroplasty. Exclusion criteria were renal insufficiency; hypersensitivity to contrast medium, heparin, or low-molecular-weight heparin (LMWH); risk for hemorrhage; endocarditis; severe liver disease; untreated hypertension; venous thromboembolism in the past 3 months; receipt of heparin, LMWH, oral anticoagulants, or nonsteroidal anti-inflammatory drugs within 5 days of surgery; ipsilateral hip surgery in the past 6 months; or pregnancy or lactation. 89% of patients were included in the analysis.

Intervention

While in the hospital, patients received enoxaparin, 40 mg injected subcutaneously once daily. At the end of hospitalization, 131 patients were assigned to continue receiving enoxaparin, 40 mg/d, and 131 were assigned to placebo. Outpatient prophylaxis was scheduled to last 21 days or until the time of phlebography.

Main outcome measures

Deep venous thrombosis (DVT), distal and proximal thrombosis, pulmonary embolism, hemorrhage, and death.

Main results

21 patients (18%) receiving enoxaparin developed DVT or pulmonary embolism compared with 45 patients (39%) receiving placebo ($P < 0.001$). {This absolute risk reduction (ARR) of 21% means that 5 patients would need to be treated (NNT) with enoxaparin (compared with placeb for 1 month to prevent 1 additior patient from developing DVT or pu monary embolism, 95% CI 3 to 1 the relative risk reduction (RRR) w 54%, CI 28% to 71%.}* 8 patier (7%) receiving enoxaparin develop proximal DVT compared with 28 p tients (24%) receiving placebo (P 0.001) {ARR 17%; NNT 6, CI 4 12; RRR 72%, CI 42% to 86% Hematomas occurred at the injecti site in 6 patients in the enoxapar group and in 1 patient in the placel group. No patients in either treatme group died or had major complic tions.

Conclusion

One month of enoxaparin, compar with enoxaparin alone during hosp talization, led to fewer venous throi boembolic complications in patier having elective hip replacement.

Sources of funding: Swedish Medical Resear Council; Swedish Heart and Lung Found tion; Rhône-Poulenc Rorer.

For article reprint: Dr. D. Bergqvist, Ac demic Hospital, Department of Surge S-751 85 Uppsala, Sweden. FAX 46-1 508-127.

*Numbers calculated from data in article.

Abstract and Commentary also published *ACP Journal Club.* 1997;126:11.

Commentary

The study by Bergqvist and colleagues is the latest in a number of recent randomized trials (1–3) that assess the risk for thromboembolism after hospital discharge and the efficacy of continued prophylaxis with LMWH. Like the previous trials, this study confirmed both the substantial incidence of thrombosis in patients with arthroplasty despite receiving prophylaxis with LMWH until hospital discharge and the reduction in venous thrombosis overall with prolonged prophylaxis. Unlike the recent study by Planes and colleagues (1), however, this study showed a substantial reduction in the incidence of proximal DVT. This difference in results may be because of differences in study design. For instance, Planes and colleagues only randomized patients with normal venography at discharge, and the study had a longer period of in-hospital prophylaxis (13 to 15 d).

The findings by Bergqvist and colleagues raise several clinical issues: Are thrombi found after hospital discharge clinically significant? Does the high incidence of thrombosis despite 4 weeks of prophylaxis suggest that even longer periods of prophylaxis are required? Although this study showed a reduction in the incidence of proximal thrombosis, the placebo group had a higher incidence of proximal DVT (24%) than did the placebo group in the study by Planes and colleagues (8%). However, the treatment groups had similar rates. Does this reflect efficacy of prophylaxis after hospital discharge or failure of the shorter period of hospital prophylaxis? The latter possibility has ramifications because of the curre trend toward shorter hospital stays.

Until these issues are addressed, the o timal duration and method of prophyla for patients with arthroplasty after surge remains to be determined. However, wh combined with those of previous studi the results of this trial support a potent benefit for prophylaxis after hospital d charge, especially when patients are d charged shortly after surgery.

Richard M. Jay, M
Sunnybrook Health Science Cen
Toronto, Ontario, Cana

References

1. **Planes A, Vochelle N, Darmon J** et
Lancet. 1996;348:224-8.
2. **Dahl OE, Andreassen G, Muller C** et
Thromb Haemost. 1995;73:1094.
3. **Lassen MR, Borris LC.** Thromb Haemo
1995;73:1104.