Review: Low-molecular-weight heparin may be as effective and safe as vitamin-K antagonists in symptomatic venous thromboembolism

van der Heijden JF, Hutten BA, Büller HR, Prins MH. **Vitamin K antagonists or low-molecular-weight heparin for the long term treatment of symptomatic venous thromboembolism.** Cochrane Database Syst Rev. 2000;(4):CD002001 (latest version 28 Mar 2000).

QUESTION

In patients with symptomatic venous thromboembolism, is long-term treatment with low-molecular-weight heparin (LMWH) as effective and safe as that with vitamin-K antagonists?

DATA SOURCES

Studies were identified by searching MEDLINE, EMBASE/Excerpta Medica, and *Current Contents*; hand searching relevant journals; personally communicating with colleagues; and contacting pharmaceutical companies.

STUDY SELECTION

Studies were selected if they were randomized controlled trials evaluating the effectiveness of long-term treatment with LMWH or vitamin-K antagonists in patients with symptomatic venous thromboembolism (diagnosed using an accepted objective test).

DATA EXTRACTION

Data were extracted on patient characteristics; type and duration of therapy; and the incidence and timing of recurrent venous thromboembolism, major bleeding complications, and mortality.

MAIN RESULTS

5 studies involving 850 patients (all with deep venous thrombosis) met the selection criteria. Treatment groups did not differ for recurrent symptomatic venous thromboembolism, major bleeding, or mortality at 3 or 12 months (only 4 studies involving 774 patients) of follow-up (Table). These results did not change when only the studies of a higher methodologic quality were combined.

CONCLUSION

In patients with symptomatic venous thromboembolism, long-term treatment with low-molecular-weight heparin is possibly as effective and safe as long-term treatment with vitamin-K antagonists.

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Low-molecular-weight heparin (LMWH) vs vitamin-K antagonists (VKA) at 3 and 12 months of follow-up in patients with symptomatic venous thromboembolism (VTE)*

Outcomes	Weighted event rates		RRR (95% CI)	NNT (CI)
	LMWH	VKA		
Recurrent VTE				
3 months	5.7%	7.7%	26% (–22 to 55)	Not significant
12 months	9.8%	10.6%	7% (–40 to 39)	Not significant
Major bleeding				
3 months	1.1%	1.8%	35% (–87 to 78)	Not significant
12 months	1.3%	2.1%	35% (–87 to 78)	Not significant
			RRI (CI)	NNH (CI)
Mortality				
3 months	2.6%	2.3%	12% (–51 to 156)	Not significant
12 months	5.9%	4.7%	28% (–30 to 131)	Not significant

*Abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article.

COMMENTARY

The well-done systematic review by van der Heijden and colleagues addresses the question of whether LMWHs may be substituted for vitamin-K antagonists in the second phase of VTE treatment. All 5 of the reviewed studies treated patients initially with a conventional unfractionated heparin or LMWH regimen for 7 to 10 days and then randomly allocated patients to either conventional vitamin-K antagonist therapy (monitored using the international normalized ratio) or to 1 of 4 different LMWHs. For almost all patients studied, the duration of "long-term" anticoagulation was 3 months, with LMWH given daily, usually at fixed doses lower than those given for the initial treatment of VTE (e.g., enoxaparin, 40 mg, or dalteparin, 5000 units subcutaneously). No statistically significant differences in 3 important outcomes were found.

At this time, however, vitamin-K antagonists rather than LMWHs should continue to be used. Because all LMWHs are not necessarily equivalent, more studies of each LMWH are needed to make sure that important outcome differences have not been missed. Because many patients should receive anticoagulation for 6 or more months (1), studies of longer treatment durations are needed, especially considering the potential complications of thrombocytopenia and osteoporosis with heparin (2). Furthermore, the current cost of LMWH is far more than that of vitamin-K antagonists, even taking into account the expense of laboratory testing.

Some patients, such as those unable to have laboratory testing because of geographic barriers, may not be able to take vitamin-K antagonists safely. In selected patients, LMWH treatment for 3 months may be a reasonable alternative.

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