

With this example under its nose of research and audit fitting so neatly together the Northern region has decided to link its regional research and audit activities. As Professor Peckham conceded, there is still no link at national level, but the main message emerging from the meeting in

Newcastle was that audit and research, although not the same thing, have much to contribute to each other and must be linked at every level. Regions take note.

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Low molecular weight heparin

Probably better than conventional heparin in orthopaedic practice but not in general surgical practice

Heparin has been in routine use for over 50 years, but the problems with conventional heparin are that it has to be given two or three times a day when used subcutaneously and that it sometimes causes bleeding.¹ Low molecular weight heparins have been developed in an attempt to overcome these problems: they persist longer in the body,^{2,3} have better availability,⁴ and have less effect on clotting times.^{5,6} But are these new heparins better in practice than the much cheaper traditional heparin?

A meta-analysis on p 913 by Leizorovicz and others suggests that low molecular weight heparins are better than placebo at preventing deep vein thrombosis in orthopaedic and general surgical practice and better than dextran in orthopaedic practice.⁷ The superiority over placebo was expected, but the superiority over dextran is important because dextran has to be given by intravenous infusion and potentially has more serious side effects than low molecular weight heparin—it may, for example, cause volume overload and acute hypersensitivity reactions.⁸ Leizorovicz and others also conclude that low molecular weight heparins are better than conventional heparin in orthopaedic and general surgical practice. These findings contrast with the conclusions of Nurmohamed and others in another meta-analysis recently published in the *Lancet*: they found that low molecular weight heparins, although superior in orthopaedic practice, are not better in general surgical practice.⁹

Leizorovicz and others base their conclusions on 39 trials, including several reported only as abstracts. Although 25 of the trials were in general surgery, the risk of deep vein thrombosis was not significantly lower with low molecular weight heparins than with conventional heparin. The analysis of the 14 orthopaedic trials similarly did not show a significant benefit, but when all 39 trials were analysed together there was a significant benefit for low molecular weight heparins.

Nurmohamed and others began with 23 studies and also concluded that low molecular weight heparins were better than conventional heparin in preventing both deep vein thrombosis and pulmonary embolism in general surgical and orthopaedic practice. The authors then conducted an analysis of only those studies that satisfied more than six predetermined criteria of methodological strength and found different results: the superiority of low molecular weight heparins disappeared in the eight studies from general surgical practice and remained only for preventing deep vein thrombosis (but not pulmonary embolism) in the five studies from orthopaedic practice.

The criteria of methodological strength adopted by Nurmohamed and others are ones that many support. They include the need for the publication to be a full, peer reviewed paper; clearly specified inclusion and exclusion criteria; adequate description of the clinical characteristics of the study group; description of bleeding complications; accurate diagnosis of deep vein thrombosis, which means using

phlebography in the orthopaedic studies; blinded assessment at the end point; and adequate description of patients who did not complete the study. The application of these strict criteria may mean that more confidence can be put in the results of Nurmohamed and others.

Nurmohamed and others had, even before considering the 23 studies in their paper, excluded eight studies in which the doses of heparins used were higher than those currently recommended and 12 in which an inadequate screening method was used to detect deep vein thrombosis. Yet six of the studies with high doses of heparin and seven of those with inadequate screening methods were included in the analysis by Leizorovicz and others. The difference in results may thus be partly explained by different inclusion criteria.

Neither overview (meta-analysis) showed any difference in the incidence of major bleeding between the two groups, which suggests that factors other than clotting time are important in determining the risk of bleeding.

The conclusion for now is that in orthopaedic practice—where thrombosis occurs in about one in five patients compared with one in 20 patients in general surgical practice—low molecular weight heparins are probably more effective than conventional heparin in preventing thromboembolic complications. They are certainly more convenient, as adjusted subcutaneous doses may be necessary to obtain optimal prophylaxis whereas low molecular weight heparins can be given in fixed dose once daily. However, in general surgical practice there is no clear evidence that low molecular weight heparins are superior and the convenience of their administration must be weighed against their much greater cost.

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