TITLE: Low Molecular Weight Heparin for Patients Requiring Hemodialysis: Clinical Effectiveness and Cost-Effectiveness

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RESEARCH QUESTIONS:

1. What is the clinical effectiveness of the use of low molecular weight heparin in patients requiring hemodialysis?

2. What is the evidence that low molecular weight heparin and unfractionated heparin have comparative doses and adverse events in patients requiring hemodialysis?

3. What is the cost-effectiveness of low molecular weight heparin in patients requiring hemodialysis?

METHODS:

A limited literature search was conducted on key health technology assessment resources, including PubMed, the Cochrane Library (Issue 9, 2010), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI (Health Devices Gold), EuroScan, international health technology agencies, and a focused Internet search. The search was limited to English language articles published between January 1, 2000, and September 29, 2010. For the first and second question, filters were applied to limit the retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, and safety data. For the third question, filters were applied to limit the retrieval to economic studies. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.
RESULTS:

HTIS reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, and economic evaluations.

Two randomized controlled trials, and seven non-randomized studies were identified regarding clinical effectiveness, comparative effectiveness, and cost-effectiveness of low molecular weight heparin (LMWH) in patients requiring hemodialysis. No relevant health technology assessments, systematic reviews, meta-analyses, or economic evaluations were identified. Due to the large volume of relevant literature, articles published from 2000 to 2004 are located in the appendix.

OVERALL SUMMARY OF FINDINGS:

Three studies\textsuperscript{1,2,4} compared the effects of enoxaparin, a LMWH, versus unfractionated heparin (UFH) in patients undergoing chronic hemodialysis (HD). Minor bleeding was observed after the use of enoxaparin, but not with UFH.\textsuperscript{1} A statistically significant decrease in the average number of blood clots was observed in patients receiving standard heparin.\textsuperscript{4} Single bolus dose of enoxaparin was efficient and convenient for use for anticoagulation during HD.\textsuperscript{2} The authors concluded that a mean dose of 0.67 mg/kg, which is generally lower than the directed dose, can be recommended for over-dialytic regular use.\textsuperscript{2} One study\textsuperscript{1} observed the life span of the filter to be similar between both groups, while a second study\textsuperscript{4} concluded enoxaparin was easier on the dialysis equipment than UFH. For patients without a contraindication, UFH was considered to be an effective, lower cost option for systemic anticoagulation.\textsuperscript{1}

Three studies compared the effects of tinzaparin sodium (TS) versus UFH.\textsuperscript{3,6,8} Tinzaparin sodium use resulted in efficient performance of HD\textsuperscript{8} and less frequent clotting of the dialyzer and air-trap.\textsuperscript{3,6} No significant problems were observed during use of TS, and the authors considered it to be a safe and effective alternative to UFH.\textsuperscript{8}

Three studies\textsuperscript{5,7,9} observed LMWH heparins alone or compared with each other. The authors of a long-term study of LMWH reported its long-term use in HD was practical and safe.\textsuperscript{5} The authors of a study of the use of LMWH during HD for patients with arrhythmias determined LMWH could be effective for protection against arrhythmia-related cardiac events.\textsuperscript{7} The study comparing the effects of TS and bemiparin demonstrated they did not differ significantly in the occurrence of fibrin or clot formation in the extracorporeal circuit.\textsuperscript{9} Results of the same study indicated the anticoagulant profile of bemiparin was superior to that of TS.\textsuperscript{9}

In summary, five of the included studies reported the use of LMWH for HD to be safe\textsuperscript{1,5,7,8} and effective\textsuperscript{2,8}. One study reported an increase in clotting with enoxaparin over UFH.\textsuperscript{4} Observed extracorporeal circuit clot formation\textsuperscript{4,8} and filter life span\textsuperscript{1,3,4,6} were similar or improved with the use of LMWH. For patients without a contraindication, UFH was considered to be an effective and lower cost option for systemic anticoagulation.\textsuperscript{1}
REFERENCES SUMMARIZED:

Health technology assessments
No literature identified.

Systematic reviews and meta-analyses
No literature identified.

Randomized controlled trials


Non-randomized studies


Structured abstract available from: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=22009100123


Economic evaluations
No literature identified.

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APPENDIX – FURTHER INFORMATION

Systematic reviews – published from 2000 to 2004


Randomized controlled trials

Secondary outcomes


Published from 2000 to 2004


Non-randomized studies

Secondary outcomes


Published 2000 to 2004


Economic evaluations

Published 2000 to 2004


Safety reports


Cochrane protocols


Additional references


In patients on chronic dialysis, unfractionated heparin (UFH) is the most commonly used agent for anticoagulation of the hemodialysis extracorporeal circuit, for hemodialysis catheter "locking" between dialysis treatments, and for nondialysis indications such as venous thromboembolic disease, peripheral vascular disease, and acute coronary artery disease. Potentially serious complications of UFH, such as hemorrhage, osteoporosis, and thrombocytopenia, have led to consideration of other options for anticoagulation, including low molecular weight heparin (LMWH) and direct thrombin inhibitors (DTIs). **LMWH can be used for anticoagulation of the hemodialysis circuit, but whether this has significant benefit compared to UFH remains to be proven. Because of the somewhat unpredictable risk of severe bleeding complications when LMWH is used for other indications in dialysis patients, UFH rather than LMWH is preferred for treatment of thromboembolic disease in these patients.** DTIs have been used for anticoagulation in dialysis patients with heparin-induced thrombocytopenia (HIT), with argatroban being the preferred agent if heparin-free hemodialysis cannot be performed. UFH still remains the preferred anticoagulant in the vast majority of dialysis patients requiring systemic anticoagulation and for anticoagulation of the extracorporeal hemodialysis circuit.