Safety and efficacy of prolonged use of unfractionated heparin after percutaneous coronary intervention


CRD summary
This review concluded that routine use of unfractionated heparin after uncomplicated percutaneous coronary intervention may have resulted in increased bleeding complications with no reduction in ischaemic complications. Further research was needed. Most of the data came from studies undertaken before use of stents/glycoprotein IIb/IIIa inhibitors was routine. The conclusions, which included the need for further research, appear reasonable.

Authors’ objectives
To assess the safety and efficacy of prolonged infusion of unfractionated heparin after percutaneous coronary intervention (PCI).

Searching
MEDLINE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched to June 2008. Search terms were reported. No language restrictions were applied. Reference lists of identified articles, meeting proceedings and three registers of ongoing trials were checked.

Study selection
Randomised controlled trials (RCTs) that assessed use of 12 to 24 hours unfractionated heparin infusion after PCI were eligible for inclusion. Participants in eligible trials had to receive prior aspirin and unfractionated heparin during the procedure. The outcomes of interest were the incidence of in-hospital ischaemic complications (composite of all cause death, myocardial infarction and revascularisation) and incidence of bleeding complications (need for blood transfusion, major haematoma or decrease in haemoglobin concentration greater than 3g/dL.

Most of the included studies did not use glycoprotein IIb/IIIa inhibitors (used in 1% of non-heparin group in one study) or stents (in one study 88% to 95% and in another 34%). Unfractionated heparin dosing regimens were not reported. The comparator was placebo. Other drugs used included thienopyridine, nitrates, calcium channel blockers, diltiazem, nitroglycerin, nifedipine and dipyridamole. Sheath removal occurred both before and after infusion. There were no significant differences in participant demographics between treatment and control groups (details not reported).

Two reviewers independently selected studies for inclusion. Disagreements were resolved by consensus.

Assessment of study quality
Quality was assessed on items such as treatment allocation, concealment of allocation, blinding, adequacy of analysis and use of intention-to-treat analysis.

Two reviewers independently assessed the quality of included studies.

Data extraction
Data were extracted in order to calculate risk ratio (RR) and 95% confidence intervals (CI).

The authors did not state how many of them extracted data.

Methods of synthesis
Pooled risk ratios and 95% CI were calculated using a fixed-effect method. Heterogeneity was assessed using Cochran’s Q statistic and $I^2$.

Results of the review
Seven RCTs (2,412 participants) were included. One RCT was published in 2008 and the others between 1989 and 1999.
Compared to placebo, risk of bleeding complications was higher with unfractionated heparin (RR 2.24, 95% CI 1.68 to 3.48, $I^2=20.8\%$). Risk of ischaemic events was similar in both groups ($I^2=0\%$).

Authors' conclusions
Routine use of unfractionated heparin after uncomplicated PCI may have resulted in increased bleeding complications without a reduction in ischaemic complications.

CRD commentary
The aims of the review were clearly stated in terms of the inclusion criteria. The search covered several sources, was not restricted by language and included unpublished studies, which was likely to have reduced any possible effect of language or publication bias. The methods of study selection and quality assessment aimed at reducing reviewer error or bias; methods for data extraction were unclear. Study quality was assessed, but the results were not reported and so it was difficult to comment on the validity of included data. All data came from double-blind RCTs. The methods of synthesis appeared appropriate. Heterogeneity was assessed. Little information was presented about the included participants, severity of disease and any concomitant disease and this may have affected the generalisability of the results. The use of combined outcomes composed of events of different severity may not clearly identify any possible differences in the individual outcomes. The authors commented that most of the studies were conducted before use of stents and glycoprotein IIb/IIIa inhibitors became routine.

The authors conclusions, which included the need for further research, appear reasonable.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that large RCTs were required to assess the use of unfractionated heparin after uncomplicated PCI in relation to the practice of use of drug-eluting stents, thienopyridines and glycoprotein IIb/IIIa inhibitors.

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