Meta-analysis comparing bivalirudin versus heparin monotherapy on ischemic and bleeding outcomes after percutaneous coronary intervention

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CRD summary
This review concluded that in people undergoing transfemoral percutaneous coronary intervention, there were significantly fewer major bleeds with bivalirudin, than with unfractionated heparin, but the rates of major adverse cardiac events were similar. As there were some questions about the quality of the included data, the conclusions should be treated with caution.

Authors’ objectives
To assess the effects of bivalirudin, compared with unfractionated heparin, for people undergoing percutaneous coronary intervention.

Searching
PubMed, EMBASE and The Cochrane Library were searched to January 2012. Search terms were reported. No language restrictions were applied. Abstracts of international cardiology meetings, and bibliographies of selected studies were checked. Only peer-reviewed papers were eligible.

Study selection
Studies that compared bivalirudin with unfractionated heparin alone, for people undergoing percutaneous coronary intervention, were eligible for inclusion. Case reports and studies in which more than 20% of participants received glycoprotein IIb or IIIa inhibitors were excluded. The outcomes of interest were major adverse cardiac events (death, myocardial infarction, and urgent revascularisation), all-cause deaths, myocardial infarction, major bleeding and the need for transfusion.

In the included studies, the mean group age ranged from 64 to 93 years and 67% of patients were men. In some studies, the patients were undergoing elective percutaneous coronary intervention, in others they had acute coronary syndrome. Over all studies 36% of patients had diabetes. In one study all patients had chronic kidney disease; in others, where reported, between 2.5% and 26% had it. All percutaneous interventions were carried out using the femoral approach. Most participants were on clopidogrel.

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

Assessment of study quality
The authors did not state that they assessed quality.

Data extraction
Data were extracted to calculate odds ratios and 95% confidence intervals. Two reviewers independently extracted the data and disagreements were resolved by consensus. Where necessary, the authors were contacted for missing information.

Methods of synthesis
A random-effects model was used to calculate the odds ratios and 95% confidence intervals. Studies were grouped according to their design (randomised controlled trials versus observational studies) and analysed together. Heterogeneity was assessed using Cochran Q and I². Subgroup analyses investigated the inclusion of only those studies that did not use glycoprotein IIb or IIIa inhibitors.

Results of the review
Sixteen studies (32,492 participants) were included. Three were randomised controlled trials (RCTs; 5,642 participants) and 13 were observational studies (26,850 participants). Sample size ranged from 114 to 5,973 participants. Six studies had follow-up at 30 days, and 10 followed-up during the hospital stay.
Compared with unfractionated heparin, bivalirudin resulted in no statistically significant differences, in either RCTs or observational studies, in major cardiovascular events (three RCTs, I²=79%; 12 observational studies, I²=58%) and in myocardial infarction (three RCTs, I²=68%; 11 observational studies, I²=65%). There was a decrease in mortality (OR 0.58, 95% CI 0.45 to 0.75; 16 studies; I²=0), but this was not statistically significant in the RCTs alone (three trials, I²=0).

Bivalirudin was associated with a decrease in major bleeding (OR 0.55, 95% CI 0.43 to 0.72; 14 studies; I²=41%). The effect was greater in the RCTs (three trials, I²=0) than in observational studies (11 studies, I²=52%). In the subgroup analysis of studies that did not use glycoprotein IIb or IIIa inhibitors, the results were similar to the main analysis (eight studies). There was no statistically significant effect on the transfusion rates (two RCTs, I²=0; seven observational studies, I²=42%).

Authors’ conclusions
In people undergoing transfemoral percutaneous coronary intervention, there were significantly fewer major bleeds with bivalirudin, than with unfractionated heparin, but the rates of major adverse cardiac events were similar.

CRD commentary
The aims of this review were clearly stated in the inclusion criteria. Inclusion was limited to peer-reviewed articles and it is possible that studies were missed and that publication bias affected the review. The methods of study selection and data extraction aimed to avoid reviewer error and bias. Study quality was not assessed and it is difficult to comment independently on the validity of the included data. The methods of synthesis were generally appropriate, as the authors included analyses for the two study designs, but there was significant heterogeneity between-studies for some outcomes. As the authors acknowledged, the data from observational studies might have been influenced by confounding factors, such as selection bias, but to allow for this, they undertook separate analyses for the RCTs.

As there were some questions about the quality of the included data, the conclusions should be treated with caution.

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

Research: The authors stated that there was a need for a large international randomised trial comparing bivalirudin with unfractionated heparin monotherapy for people undergoing percutaneous coronary intervention. Future trials should focus on the interaction between the anticoagulant choice and the access-site choice. An investigation of the costs was also needed.

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