Antiplatelet medications in hemodialysis patients: a systematic review of bleeding rates

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CRD summary
This review concluded that the bleeding risk appeared to increase for haemodialysis patients with combination antiplatelet therapy. Antiplatelet therapy appeared to be effective in preventing shunt and central venous catheter thrombosis, but not for preventing thrombosis of arteriovenous grafts. Despite some potential concerns with the review methodology, the authors’ conclusions are likely to be reliable based on the evidence presented.

Authors' objectives
To determine the risk of bleeding in haemodialysis patients with antiplatelet therapy, and to assess the efficacy of antiplatelet agents in reducing access thrombosis.

Searching
The following databases were searched from inception to 2008: MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials (CENTRAL). Google Scholar was also searched. Reference lists of eligible studies were also screened. Unpublished abstracts were excluded.

Study selection
Randomised controlled trials (RCTs), cohort studies, and case series that evaluated bleeding risk with antiplatelet agents in at least 10 haemodialysis patients with end stage renal disease, with at least three-month follow-up, were eligible for inclusion. The primary review outcome was the incidence of bleeding. The secondary outcome was the incidence of thrombosis.

The included studies evaluated different types of antiplatelet agents (including aspirin, clopidogrel, dipyridamole, sulfipyrazone and ticlopidine). The majority of studies (over 60%) assessed a single antiplatelet agent; the rest assessed a combination of antiplatelet agents. The definition of bleeding was not reported in the majority of included studies, and was inadequately described in some studies. The study authors’ definitions of bleeding events were used in the review. The control arm in most RCTs was a placebo. The included studies were published between 1975 and 2008.

Two reviewers independently assessed studies for inclusion, with any disagreement resolved by consensus or a third reviewer.

Assessment of study quality
The quality of RCTs was assessed using the Jadad scale, a 5-point scale evaluating blinding, randomisation and withdrawal. The quality of observational studies was assessed using the Newcastle-Ottawa scale, a 9-point scale evaluating selection of study groups, comparability of study groups, and assessment of outcomes.

Two reviewers independently performed the validity assessment, with any disagreement resolved by consensus or a third reviewer.

Data extraction
Data were extracted on the number of patients experiencing an event. Where appropriate, relative risks (RRs) and hazard ratios (HRs), with 95% confidence intervals (CIs), were also extracted. Study authors were contacted for missing data.

Two reviewers independently extracted the data, with any disagreement resolved by consensus or a third reviewer.

Methods of synthesis
The studies were combined in a narrative synthesis, supported by accompanying data tables.
Results of the review

Sixteen studies (including nine RCTs, four prospective cohort studies and three retrospective cohort studies) were included in the review (n= 40,676 patients). The sample size ranged from 16 to 28,320. The majority of included studies were of moderate to good quality. Six RCTs had a Jadad score of at least 3 (ranging from 1 to 5). Five cohort studies had a Newcastle-Ottawa score of at least 6 (ranging from 5 to 7). The median follow-up was eight months (ranging from three months to six years).

Antiplatelet agents and bleeding risk

Of the seven studies which used aspirin as a single antiplatelet agent, three reported an increased risk of bleeding. None of the four studies that used sulfipyrazone, ticlopidine and clopidogrel as single antiplatelet agents reported an increase in the risk of bleeding.

Of the three studies which used a combination of antiplatelet agents, two studies (aspirin plus clopidogrel, aspirin plus sulfipyrazone) reported an increased risk of bleeding. One study that used antiplatelet agent in combination with warfarin reported no increase in the risk of bleeding.

Antiplatelet agents and access thrombosis risk

Antiplatelet therapy was associated with a reduced risk of thrombosis in arteriovenous shunts (four studies) and central venous catheters (three studies). The results for arteriovenous grafts were mixed; two of three studies and one of two treatment arms in an additional study reported a reduced risk of thrombosis.

Authors’ conclusions

The bleeding risk appeared to increase for haemodialysis patients with combination antiplatelet therapy, but the results were mixed for those with a single antiplatelet agent. Antiplatelet therapy appeared to be effective in preventing shunt and central venous catheter thrombosis, but not for preventing thrombosis of arteriovenous grafts.

CRD commentary

The inclusion criteria of the review were clear. A number of relevant databases were searched. Efforts were made to find published studies but not unpublished studies, introducing the potential for publication bias. The authors did not state whether any language restrictions were applied in the search, which made it difficult to assess the risk of language bias. Sufficient attempts have been taken to minimise errors and biases in the review process.

Relevant criteria were used to assess the study quality. Given the high level of clinical heterogeneity between the studies, a narrative synthesis was appropriately adopted.

Based on the evidence presented, the authors' conclusions are likely to be reliable, despite some potential methodological concerns outlined above.

Implications of the review for practice and research

Practice: The authors stated that the increased risk of bleeding for the combination antiplatelet therapy in haemodialysis patients should be taken into account when initiating this therapeutic strategy.

Research: The authors stated that further RCTs with a rigorous design are required to address the risk and benefit of antiplatelet therapy in haemodialysis patients.

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