
Efficacy of cilostazol in reducing restenosis in patients undergoing contemporary stent based PCI: a meta-analysis of randomised controlled trials

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CRD summary

This review concluded that cilostazol in addition to conventional dual antiplatelet therapy was associated with a reduction in angiographic restenosis in patients who underwent stent-based percutaneous coronary intervention. The authors' conclusions reflected the evidence presented. However, without further details on study quality and given the other methodological concerns, it is difficult to judge the reliability of these conclusions.

Authors' objectives

To assess the efficacy of cilostazol on restenosis in patients who underwent contemporary stent-based percutaneous coronary intervention.

Searching

MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Knowledge, Current Contents and International Pharmaceutical Abstracts were searched from 1996 to November 2008. Search terms were reported. Conference proceedings of American Heart Association, American College of Cardiology and European Society of Cardiology were searched from 2005 to 2008. Relevant publications and internet-based sources of information were screened.

Study selection

Randomised controlled trials (RCTs) that compared triple antiplatelet therapy (cilostazol, aspirin and thienopyridine) with conventional dual therapy (aspirin and thienopyridine) in patients who underwent contemporary stent-based percutaneous coronary intervention were eligible for inclusion. The primary review outcomes were binary angiographic restenosis and in-segment late loss. Additional outcomes were mortality, target lesion revascularisation, bleeding and skin rash.

Included studies used either drug-eluting or bare metal stents; drug-eluting stents were more common. Where reported, mean age of included patients ranged from 57 to 67.6 years and the proportion of males ranged from 44% to 77%. The proportion of people with diabetes in included studies ranged from 22% to 100%.

The authors stated neither how papers were selected for the review nor how many reviewers performed study selection.

Assessment of study quality

Study quality was assessed using these criteria: concealment of allocation; intention-to-treat analysis; and blinded assessment of outcomes.

The authors did not state how many reviewers performed the validity assessment.

Data extraction

For dichotomous outcomes, event rates were extracted to enable the calculation of odds ratios (ORs) and 95% confidence intervals (CIs). For continuous outcomes, mean and standard error were extracted to enable calculation of mean differences and 95% CIs.

Two reviewers independently performed data extraction. Any disagreements were resolved by consensus.

Methods of synthesis

The studies were combined in a meta-analysis. A random-effects model was used if there was significant heterogeneity.

Otherwise, a fixed-effects model was employed. Pooled odds ratios or weighted mean differences (WMDs), with 95% CIs, were calculated. Statistical heterogeneity was assessed using the Cochrane Q test. Sensitivity analysis was performed to assess the impact of each individual study on the pooled estimate. Publication bias was visualised using a funnel plot and assessed by the rank order correlation, fail-safe N and Eggers test. Subgroup analyses were conducted on different types of stents (drug-eluting versus bare metal).

Results of the review

Ten RCTs (n=2,809) were included in meta-analyses. Average follow-up in included trials ranged from six to nine months. Study quality was not reported.

Compared with dual therapy, triple therapy with cilostazol was significantly associated with a reduction in binary angiographic restenosis (OR 0.52, 95% CI 0.41 to 0.66; 10 RCTs), in-segment late loss (WMD -0.15mm, 95% CI -0.20 to -0.11; 10 RCTs) and target lesion revascularisation (OR 0.38, 95% CI 0.25 to 0.58; seven RCTs). Triple therapy showed an increased risk of skin rash (OR 3.67, 95% CI 1.86 to 7.24; three RCTs).

There were no significant differences in reinfarction, subacute stent thrombosis, major bleeding and mortality between the two groups.

Sensitivity analyses did not materially affect the results. No evidence of publication bias was observed. No evidence of statistical heterogeneity was found. Subgroup analyses on different types of stents were reported.

Authors' conclusions

Cilostazol in addition to dual antiplatelet therapy was associated with a reduction in angiographic restenosis in patients who underwent stent-based percutaneous coronary intervention.

CRD commentary

This review's inclusion criteria were clear. A number of relevant databases were searched. Efforts were made to find both published and unpublished studies, which minimised potential for publication bias. Publication bias was assessed and little evidence of it was found. The authors did not state whether language restrictions were applied in the search, which made it difficult to assess the risk of language bias. Steps were taken to minimise bias by having more than one reviewer undertake data extraction. It was unclear whether the processes of study selection and validity assessment were performed in duplicate. Relevant criteria were used to assess study quality, but the results were not presented. Statistical heterogeneity was assessed and appropriate statistical methods were used to pool results. The authors' conclusions reflected the evidence presented. However, without further details on study quality and given the other methodological concerns, it is difficult to judge the reliability of these conclusions.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors stated that large and definitive RCTs were required to assess the benefit of cilostazol in patients with a high risk of restenosis.

Funding

Not stated.

Bibliographic details

Tamhane U, Meier P, Chetcuti S, Chen KY, Rha SW, Grossman MP, Gurm H. Efficacy of cilostazol in reducing restenosis in patients undergoing contemporary stent based PCI: a meta-analysis of randomised controlled trials. *EuroIntervention* 2009; 5(3): 384-393

PubMedID

19736165

Indexing Status

Subject indexing assigned by NLM

MeSH

Aged; Angioplasty, Balloon, Coronary /adverse effects /instrumentation; Aspirin /therapeutic use; Coronary Angiography; Coronary Restenosis /etiology /prevention & control /radiography; Coronary Stenosis /therapy; Drug Therapy, Combination; Drug-Eluting Stents; Exanthema /chemically induced; Female; Hemorrhage /chemically induced; Humans; Male; Metals; Middle Aged; Odds Ratio; Platelet Aggregation Inhibitors /adverse effects /therapeutic use; Prosthesis Design; Publication Bias; Pyridines /therapeutic use; Randomized Controlled Trials as Topic; Risk Assessment; Stents; Tetrazoles /adverse effects /therapeutic use; Thrombosis /etiology; Treatment Outcome

AccessionNumber

12009109108

Date bibliographic record published

03/02/2010

Date abstract record published

07/04/2010

Record Status

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