Meta-analysis of the role of high-dose statins administered prior to percutaneous coronary intervention in reducing major adverse cardiac events in patients with coronary artery disease


CRD summary
The review found that high-dose statin therapy administered prior to percutaneous coronary intervention compared to placebo was effective for prevention of major adverse cardiac events in patients with coronary artery disease. The authors' conclusion reflected the evidence and was appropriate, but should be interpreted cautiously due to potential for missing relevant studies and risk of publication bias.

Authors' objectives
To assess the efficacy of high-dose statins administered prior to percutaneous coronary intervention (PCI) in the prevention of major adverse cardiac events in patients with coronary artery disease.

Searching
MEDLINE was searched for relevant studies published in English between 1980 and 2009; search terms were reported. Reference lists of retrieved studies and reviews were searched.

Study selection
Eligible studies were randomised placebo controlled trials (RCTs) where high-dose statin treatment (40mg/day or higher) was administered before PCI. Studies without outcome data were excluded. Eligibility criteria for outcomes were not reported.

Participants in the included studies had a mean age range of 63 to 67 years. Most participants (range 60% to 87%) were male. Participants had cardiac conditions that included stable angina, non-ST-segment elevation acute coronary syndromes, hypertension and multivessel coronary artery disease. The proportion of participants with diabetes ranged from 19% to 39%. Participants also received other medical therapy such as aspirin, ticlopidine/clopidogrel, glycoprotein inhibitors, beta-blockers and angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers. Most of the included studies used Atorvastatin (doses ranged from 40mg to 80mg plus an additional 40mg). One study used Rosuvastatin 40mg. Statin therapy was mostly initiated one day before PCI; some participants received therapy seven days before PCI. Outcomes included 30-day post-procedural major adverse cardiac events and incidence of increased creatine kinase-MB (CKMB) and troponin I.

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

Assessment of study quality
The included studies were assessed for validity with the five-point Jadad scale of randomisation, blinding, withdrawals and dropouts.

Two reviewers independently performed the validity assessment. Disagreements were resolved by consensus.

Data extraction
Data on event rates of post-procedural 30-day major adverse cardiac events and increases in CKMB and troponin I were extracted using a standardised protocol and reporting form.

Two reviewers independently performed the data extraction. Disagreements were resolved by consensus.

Methods of synthesis
Studies were pooled in meta-analyses. Summary odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using a fixed-effect model. Heterogeneity between studies was assessed by $X^2$ and $I^2$.

**Results of the review**

Five placebo controlled RCTs (n=1,789; 902 received statins and 887 received placebo) were included in the review. The included studies were considered of good quality (Jadad score 3 or more).

High-dose statin therapy was associated with significantly fewer post-procedural 30-day major adverse cardiac events (OR 0.43, 95% CI 0.31, 0.59; five studies) and lower incidence of increased CKMB (OR 0.43, 95% CI 0.33, 0.58; five studies) and troponin I (OR 0.53, 95% CI 0.43, 0.67; four studies). There was no evidence of significant heterogeneity between trials.

**Authors' conclusions**

High-dose statin therapy before PCI provided significant benefit over placebo in prevention of post PCI major adverse cardiac events.

**CRD commentary**

The review addressed a clear research question. Inclusion criteria appeared appropriate, but criteria for eligible outcomes were not reported. One electronic database was searched for studies published in English; potential for relevant trials to be missed could not be ruled out. No explicit attempts were made to find unpublished studies and so publication bias cannot be ruled out. Appropriate methods to minimise reviewer error and bias were used for study selection, validity assessment and data extraction. A valid tool was used for validity assessment and all included studies were considered of reasonable quality. The decision to pool studies was appropriate. Methods used to assess heterogeneity were appropriate. The authors acknowledged that their findings may not have been generalisable to real world clinical practice because the control group did not receive standard dose statin therapy.

The authors’ conclusion reflected the evidence base and was appropriate. But relevant studies were potentially missed and publication bias was possible, so the conclusion should be interpreted cautiously.

**Implications of the review for practice and research**

**Practice:** The authors stated that high-dose statins should be used routinely before PCI in patients with coronary artery disease.

**Research:** The authors stated that further research was required to define the optimal dose, timing of initiation of therapy and duration of therapy.

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