A review of clinical trials comparing HMG-CoA reductase inhibitors

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Authors' objectives
To critically assess the efficacy and safety of the currently available 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors.

Searching
MEDLINE was searched (the search dates were unclear). One of the authors had personal knowledge of completed studies.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were included.

Specific interventions included in the review
Lovastatin, pravastatin, simvastatin and fluvastatin.

Participants included in the review
Patients with primary hypercholesterolaemia (n=3,410 for assessment of efficacy and n=86 for polysomnography studies).

Outcomes assessed in the review
The main outcome was efficacy, which was assessed using the reduction in the plasma concentrations of low-density lipoprotein (LDL) cholesterol. Where possible, safety and tolerability were also assessed by levels of liver and muscle enzymes, and by polysomnography studies.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The included trials had to be double-blind and include more than 25 patients per treatment group. The authors do not state how the papers were assessed for validity, or how many of the authors performed the validity assessment.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were combined by a narrative review.

How were differences between studies investigated?
Differences between the studies were investigated by grouping according to the specific drugs compared.

Results of the review
Ten RCTs comparing the efficacy of HMG-CoA reductase inhibitors, and 5 RCTs comparing the effects of HMG-CoA reductase inhibitors on sleep, were included.

Log-linear dose response curves were constructed for all four drugs studied. Two trials comparing lovastatin with pravastatin found them to be approximately equipotent on a mg-for-mg basis, e.g. for a 20 mg/day dose, the mean changes in LDL cholesterol were 28 and 8% for lovastatin, and 28 and 25% for pravastatin.

Two trials comparing simvastatin with lovastatin found simvastatin to be at least twice as effective per mg of drug; e.g. for doses of 10 and 20 mg/day simvastatin, and 20 and 40 mg/day lovastatin, the mean changes in LDL cholesterol were 28 and 35% for simvastatin, compared with 25 and 31% for lovastatin.

Four trials comparing simvastatin with pravastatin found simvastatin had a greater effect on lowering LDL cholesterol; e.g. 10 mg/day simvastatin reduced cholesterol concentrations by 28%, whereas 20 mg/day pravastatin only reduced cholesterol levels by 25%.

Two trials compared lovastatin (20 mg/day) with fluvastatin (20 mg/day). LDL cholesterol was reduced by 26.9% with lovastatin and by 18% with fluvastatin.

The side-effects of all four drugs were similar; earlier reports suggesting a higher incidence of sleep disorders in patients treated with lovastatin and simvastatin, compared with pravastatin, were not supported by recent clinical trials.

Authors' conclusions
The currently available HMG-CoA reductase inhibitors differed in their relative hypolipidaemic effects: lovastatin and pravastatin were approximately equipotent; simvastatin was more potent than pravastatin and lovastatin; and lovastatin was about twice as potent as fluvastatin. As a class of drugs, HMG-CoA reductase inhibitors constitute the most effective agents available to maximally reduce elevated concentrations of LDL cholesterol. In addition, they have a low incidence of side-effects, which promotes excellent patient compliance in long-term use.

CRD commentary
The authors were contacted by CRD for details of the search strategy used, as it was not documented in the review article; no information on either the dates or the search terms used was provided. It was unclear whether all the relevant studies were located and included in the review process. Ten studies used to assess the efficacy of HMG-CoA reductase inhibitors were summarised in tabular format, but it was unclear which studies were used to assess the safety of these same drugs.

Funding
Funded in part by Merck and Co. Inc.

Bibliographic details

PubMedID
7923304

Indexing Status
Subject indexing assigned by NLM

MeSH
Anticholesteremic Agents /adverse effects /therapeutic use; Clinical Trials as Topic; Humans; Hydroxymethylglutaryl-CoA Reductase Inhibitors; Hypercholesterolemia /blood /drug therapy /psychology
AccessionNumber
11994000339

Date bibliographic record published
29/01/1995

Date abstract record published
29/01/1995

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.