Comparative evaluation of the safety and efficacy of HMG-CoA reductase inhibitor monotherapy in the treatment of primary hypercholesterolemia

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Authors' objectives
To evaluate the comparative efficacy and safety of hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase inhibitor monotherapy in the treatment of primary hypercholesterolemia.

Searching
MEDLINE was searched to identify English-language clinical studies, abstracts and review articles. Bibliographies of identified articles were examined and the Food and Drug Administration were contacted for unpublished data.

Study selection
Study designs of evaluations included in the review
Placebo-controlled and comparative trials of HMG-CoA reductase monotherapy were included.

Specific interventions included in the review
Fluvastatin, lovastatin, pravastatin and simvastatin.

Participants included in the review
Patients with primary hypercholesterolemia were included.

Outcomes assessed in the review
Changes in total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglycerides levels, and adverse events were assessed.

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 authors do not report the method used to assess validity, or how the validity assessment was performed. Details of the study design were recorded.

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 placebo-controlled, single-agent, clinical trials and the comparative clinical trials are assessed separately in a narrative overview. The trials are grouped according to the HMG-CoA reductase inhibitors studied.

How were differences between studies investigated?
No statistical test of heterogeneity is presented.

Results of the review
There were 12 comparative clinical trials (n=3,261) and 8 placebo-controlled single-agent clinical trials.

Data from both placebo-controlled trials and comparative trials indicate that on a milligram-per-milligram basis, simvastatin is twice as potent as lovastatin and pravastatin. The hypcholesterolemic effects of fluvastatin appear to be approximately 30% less than that of lovastatin. In post-transplant patients receiving cyclosporine, safety has been documented for low doses of lovastatin and simvastatin, but when a higher dosage of an HMG-CoA reductase inhibitor is warranted, pravastatin should be considered the drug of choice because of a lower incidence of myopathy.

The most common adverse effects associated with HMG-CoA reductase inhibitors include increases in hepatic transaminases, increases in creatine kinase and myopathy. Gastrointestinal disturbances, headache, sleep and other central nervous system disturbances have also been reported.

**Cost information**

Cost comparisons between HMG-CoA reductase inhibitors:

First figure listed is the Drug and dosage(mg/d)

The second figure (in brackets) is the monthly drug cost per percent reduction in low-density lipoprotein cholesterol(US$)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage (mg/d)</th>
<th>Monthly Drug Cost per Percent Reduction in LDL Cholesterol (US$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluvastatin</td>
<td>20</td>
<td>1.45</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>1.49</td>
</tr>
<tr>
<td>Lovastatin</td>
<td>10 (NA)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>20 (3.29)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>40 (4.17)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>80 (5.77)</td>
<td></td>
</tr>
<tr>
<td>Pravastatin</td>
<td>10 (2.30)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>20 (1.70)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>40 (2.71)</td>
<td></td>
</tr>
<tr>
<td>Simvastatin</td>
<td>5 (2.23)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10(1.71)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>20(3.10)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>40(2.58)</td>
<td></td>
</tr>
</tbody>
</table>

Several economic evaluations of cholesterol-lowering agents have been published. The most favourable cost-effectiveness ratios for HMG-CoA reductase inhibitors have been demonstrated for patient groups at highest risk for
Authors' conclusions
The literature supports the comparable safety and tolerability of all four currently available HMG-CoA reductase inhibitors. Therefore, the choice of an HMG-CoA reductase inhibitor should depend on the extent of cholesterol lowering needed to meet the recommended treatment goal established by the National Cholesterol Education Program.

CRD commentary
The review presents good detail of the primary studies included in the review and a clear summary of the results. However, the review lacks much methodological detail. The search strategy is not well defined, giving no information on search terms used or years covered. Only English-language studies are included, which may introduce bias into the review. The review could also have been enhanced by a more thorough validity assessment of the primary studies, details on how relevant trials were chosen for inclusion in the review and how data extraction was undertaken.

Implications of the review for practice and research
The authors state that direct comparative studies are needed to confirm the relative, long-term cost-effectiveness of the various HMG-CoA reductase inhibitors in the treatment of primary hypercholesterolemia.

Bibliographic details

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8520093

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Subject indexing assigned by NLM

MeSH
Anticholesteremic Agents /adverse effects /pharmacology /therapeutic use; Cataract /chemically induced; Clinical Trials as Topic; Economics, Pharmaceutical; Enzyme Inhibitors /adverse effects /pharmacology /therapeutic use; Fatty Acids, Monounsaturated /adverse effects /pharmacology /therapeutic use; Humans; Hydroxymethylglutaryl-CoA Reductase Inhibitors; Hypercholesterolemia /drug therapy; Indoles /adverse effects /pharmacology /therapeutic use; Lovastatin /adverse effects /analog & derivatives /pharmacology /therapeutic use; Pravastatin /adverse effects /pharmacology /therapeutic use; Simvastatin

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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.