Cholesterol lowering with simvastatin reduced stroke in patients with, or at high risk of, vascular disease


Clinical impact ratings GP/FP/Primary care ★★★★★☆☆ IM/Ambulatory care ★★★★★☆ Internal medicine ★★★★★☆ Neurology ★★★★★☆ Geriatrics ★★★★★☆☆

Q Does cholesterol lowering with simvastatin reduce the incidence of stroke in patients with, or at high risk of, vascular disease?

METHODS

Design: randomised controlled trial (Heart Protection Study).

Allocation: [concealed*]†

Blinding: blinded [patients, clinicians, and data monitoring committee]*†

Follow up period: 5 years.

Setting: [69 hospitals in the UK]*†

Patients: 20 536 patients [mean age 64 y, 75% men] who had non-fasting total cholesterol concentrations >3.5 mmol/l (135 mg/dl) and a medical history of cerebrovascular disease, coronary disease, other occlusive arterial disease, or diabetes, or were men >65 years of age treated for hypertension. Exclusion criteria: clear indication or contraindication for statin therapy; stroke, myocardial infarction, or admission for angina in the previous 6 months; chronic liver disease; severe renal disease; inflammatory muscle disease; concurrent treatment with cyclosporin, fibrates, or high dose niacin; child bearing potential; concurrent treatment with previous 6 months; chronic liver disease; severe renal disease; inflammatory muscle disease; concurrent treatment with cyclosporin, fibrates, or high dose niacin; child bearing potential; severe heart failure; or life threatening conditions.

Intervention: simvastatin, 40 mg daily (n = 10 269), or matching placebo (n = 10 267) for 5 years.

Outcomes: first major vascular events (ie, non-fatal myocardial infarction or coronary death, stroke, or revascularisation procedure). Secondary outcomes included total (non-fatal and fatal) stroke, presumed ischaemic stroke, and haemorrhagic stroke.

Patient follow up: (99.7% of patients had complete follow up over 5 years)*† (intention to treat analysis).

*See glossary.

MAIN RESULTS

At 5 years, patients in the simvastatin group had greater reductions in first occurrence of major vascular events and stroke than patients in the placebo group (table). The groups did not differ for haemorrhagic stroke (0.5% v 0.5%).

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CONCLUSION

Cholesterol lowering with simvastatin reduced stroke in patients with, or at high risk of, vascular disease.

Abstract and commentary also appear in ACP Journal Club.

Simvastatin (Sim) v placebo in patients at high risk of vascular disease*

<table>
<thead>
<tr>
<th>Outcomes at 5 years</th>
<th>Sim</th>
<th>Placebo</th>
<th>RR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1 major vascular event</td>
<td>20%</td>
<td>25%</td>
<td>24% (19 to 28)</td>
<td>17 (15 to 21)</td>
</tr>
<tr>
<td>≥1 stroke</td>
<td>4.3%</td>
<td>5.7%</td>
<td>25% (15 to 34)</td>
<td>71 (52 to 117)</td>
</tr>
<tr>
<td>≥1 ischaemic stroke</td>
<td>2.8%</td>
<td>4.0%</td>
<td>30% (19 to 40)</td>
<td>84 (63 to 133)</td>
</tr>
</tbody>
</table>

*Abbreviations defined in glossary; NNT and CI calculated from control event rate and rate ratio in article.

†Non-fatal myocardial infarction or coronary death, stroke, or revascularisation procedure.
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