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


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 [HPS]).

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 blood total cholesterol concentrations >3.5 mmol/l (135 mg/dl) and a medical history of cerebrovascular disease, coronary disease, other occlusive arterial disease, diabetes, or were men >65 years with treated hypertension. Exclusion criteria: clear indication or non-indication 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 ciclosporin, 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)* (intention to treat analysis).


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%).

CONCLUSION

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

A modified version of this abstract appears in ACP Journal Club.

Commentary

Limited research has been available to support a link between elevated cholesterol concentrations and risk of ischaemic stroke. The study by Collins et al provides nurses with definitive evidence that supports the use of statins to reduce stroke in high risk populations. Reduced risk of stroke was reported within just 2 years of simvastatin use. The resultant reduction in low density lipoprotein (LDL) cholesterol concentrations of 1.0 mmol/l was associated with a 21% risk reduction in stroke. These reductions were reported in patients with and without elevated LDL cholesterol concentrations at baseline and with overall medication adherence rates of 85%.

High risk patients are often confused when they are prescribed statins by consultants if their cholesterol concentrations are known to be within normal range and if they have remained untreated by family physicians. When patients are not confident about the need for a prescribed medication or are concerned about side effects, there is a risk of non-adherence.

Based on the results of Collins et al, nurses can be confident in reinforcing the need for adherence to preventive statin therapy regimens for patients at high risk of stroke. Health teaching about the need for routine monitoring for increased liver and muscle enzymes that occur in a small percentage of patients receiving statin therapy may reduce concerns about side effects and further promote adherence.

Sandra Ireland, RN, MSc
Neuroscience Ambulatory Care Clinic
Hamilton Health Sciences
Hamilton, Ontario, Canada

Simvastatin vs placebo in patients at high risk of vascular disease*

<table>
<thead>
<tr>
<th>Outcomes at 5 years</th>
<th>Simvastatin</th>
<th>Placebo</th>
<th>RRR (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 reported in article.
†Non-fatal myocardial infarction or coronary death, stroke, or revascularisation procedure.