LETTERS

Letters to the Editor

Higher dose statins after stroke

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We write with concern regarding the article on drugs in secondary stroke prevention, as it appears to recommend not only statins post-stroke, but high-dose statins.[1]

We checked the references cited including the Cochrane review. This showed that overall, statins confer a relatively marginal 12% relative risk reduction in cerebrovascular events, but no mortality benefit.[2]

Safety data were not discussed, but are particularly relevant in a vulnerable age group. Importantly, there appears to be no specific evidence to support high doses of statins. Clinical guidelines should consider all of the evidence available. In the Heart Protection Study, simvastatin 40 mg daily, which has equivalent efficacy for reducing low-density lipoprotein to 5 mg atorvastatin, reduced ischaemic stroke by about one-quarter, in patients with coronary disease.[3]

A higher statin dose does not appear to reduce stroke further. In the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial, atorvastatin 80 mg daily after a recent stroke reduced stroke by only about one-sixth. It was associated with increased cerebral haemorrhage and more non-cardiovascular deaths.[4] Atorvastatin 80 mg in the Treating to New Targets (TNT) study reduced stroke by almost one-quarter but with a 25% increase in non-cardiovascular deaths.[5]

The number of patients who needed to be treated for one year to prevent one stroke or transient ischaemic attack in SPARCL was 115.[4] The number needed to harm was less than 20 in the large clinical studies. This is an underestimate because patients with any history of adverse effects from statins were excluded. Neither total nor cardiovascular mortality were significantly reduced by higher doses, but more adverse effects were observed.

In recommending statins post-stroke, clinicians need to weigh up clinical trial data and then consider the risks of harm and benefit for the individual patient before deciding whether to prescribe a drug and at what dose.

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Chris Tremonti and Mark Thieben, the authors of the article, comment:

The Stroke Foundation guideline recommends 'All patients with ischaemic stroke or transient ischaemic attack with possible atherosclerotic contribution and reasonable life expectancy should be prescribed a high-potency statin, regardless of baseline lipid levels.'

The risk of haemorrhagic stroke with high-dose statin therapy has been a vexed question in stroke research. In the SPARCL trial[1] the risks were confounded by the low rate of haemorrhagic stroke (55 with high-dose statin and 33 with placebo). This contrasts with 218 ischaemic strokes with statins and 274 with placebo.

A subsequent meta-analysis[2] initially suggested an increased risk of haemorrhagic stroke, however post hoc influence analysis found this was impacted by the largest trial included, which was SPARCL. When SPARCL was excluded from the analysis there

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was no increased risk of haemorrhagic stroke with high-dose statin therapy. This meta-analysis again showed the greatest benefit was from a higher dose statin.

The TNT study was specifically for patients with stable coronary disease.[3] We therefore feel a recent trial is more relevant as it is studying cholesterol management after stroke or transient ischaemic attack.[4]

Given the low incidence of haemorrhagic stroke in SPARCL,[1] the results of the meta-analysis,[2] and the recommendations of the Stroke Foundation, we feel confident recommending careful management of cholesterol after a transient ischaemic attack or stroke. Our practice is to reduce low-density lipoprotein below 1.8 mmol/L.

For patients with large artery disease, for example high-grade carotid stenosis, we recommend high-intensity statins, such as rosuvastatin 20–40 mg or atorvastatin 40–80 mg. The patient's blood pressure should be controlled before starting high-dose statins. In patients without significant large artery disease, our practice has been to use moderate intensity statins such as rosuvastatin 5–10 mg or atorvastatin 10–20 mg.

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Beyond romosozumab

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I am writing in relation to the new drug comment about romosozumab (Evenity),[1] published in *Australian Prescriber*. There is no mention that when treatment with romosozumab is completed transition to an antiresorptive therapy is required to preserve bone mass, as recommended in the Australian approved product information. This states, 'After completing Evenity therapy, transition to an antiresorptive osteoporosis therapy is required to preserve bone mass.' I bring this to the attention of your readers in the interest of the quality use of medicines.

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Conflicts of interest: Jeffrey Hassall is employed by Amgen Australia and has stock/stock options in Amgen Inc.

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