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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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Statins and haemorrhagic stroke risk

The impact of statins in stroke risk in patients with a history of cerebrovascular disease had been recently evaluated in the SPARCL (Stroke Prevention by Aggressive Reduction in Cholesterol) trial which was published in 2006. A total of 4731 patients with a stroke or TIA within one to six months were included, other inclusion criteria included LDL levels of 2.6 to 4.9 mmol/L, and absence of coronary heart disease. Patients were randomly assigned to atorvastatin 80mg or placebo and were followed up for a median of 4.9 years with a primary end point being the first nonfatal or fatal stroke. The SPARCL trial has found that statins exert beneficial effects in reducing occurrence of overall stroke. When subtypes of strokes were analysed, statins were associated with a reduction of ischemic stroke but also a significant increase in haemorrhagic stroke risk. Similar results were observed in a subgroup of patients with a history of cerebrovascular disease in the Heart Protection Study in which the use of statins increased the occurrence of haemorrhagic stroke without an effect on overall stroke incidence. The results from the two studies are summarised in below:

Study	No. of patients with a history of cerebrovascular disease	Qualifying entry event to the study	Time to entry event	Relative Risk (95% CI) for patients on statin treatment to experience:		
				Overall stroke	Ischaemic stroke	Haemorrhagic stroke
HPS	3280	Ischaemic stroke, TIA	> 6 months (mean 4.3 yrs)	0.99 (0.81 - 1.21)	0.82 (0.63 - 1.05)	1.9 (0.92 - 3.93)
SPARCL	4731	Ischaemic stroke, TIA, haemorrhagic stroke	one to six months	0.85 (0.73 - 0.99)	0.80 (0.67 - 0.94)	1.67 (1.09 - 2.56)

The results generated from the SPARCL and HPS trial have raised concerns about a possible association between statin use in patients with a history of cerebrovascular disease and an increased occurrence of haemorrhagic strokes. A recently published progress review (Vergouwen 2008) pooled the results of both studies and confirmed the association even after accounting for potential confounding factors (such as by excluding patients with haemorrhagic stroke as entry event in SPARCL trial) through sensitivity analyses.

Some of the plausible explanations suggested in the literature for the increased occurrence of haemorrhagic stroke include enhanced fibrinolysis and inhibited blood coagulation caused by statins; a higher background risk of haemorrhage related to cerebral small vessel disease in this group of patients, and a possible interaction between statins and antiplatelet or anticoagulant agents.

To date, there is no clear consensus on the use of statin in patients with a history of haemorrhagic stroke. Different hospitals may have local guidelines they follow, in accordance with expert opinions. Identifying patients who might be at higher risk of haemorrhagic stroke and avoiding the use of statin in these patients could be very difficult, it is therefore important to assess each patient's individual overall cardiovascular risk in order to decide whether statins should be re-introduced after a cerebrovascular event.

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FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@rgh.sa.gov.au
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