

## STATINS ARE MORE EFFECTIVE THAN ASPIRIN IN SECONDARY STROKE PREVENTION: YES

J. David Spence

Stroke Prevention & Atherosclerosis Research Centre, University of Western Ontario, London, Canada

It is a myth that cholesterol is not a risk factor for stroke; this is a relic from the days when hypertension dominated stroke risk to such an extent that the importance of cholesterol was masked. In a community where hypertensive strokes were reduced by improved blood pressure control<sup>1</sup>, we showed<sup>2</sup> that cholesterol is clearly a risk factor for stroke.

The magnitude of risk reduction with cholesterol lowering can best be seen in patients with carotid stenosis. Although in the SPARCL trial<sup>3</sup> the intention-to-treat analysis showed only a 16% reduction of stroke risk, many patients randomized to placebo received statins, so the intention-to-treat analysis underestimated the benefit of atorvastatin. The increase in intracerebral hemorrhage (ICH) in SPARCL among patients randomized to atorvastatin was not due to atorvastatin, since patients with ICH did not have lower levels of LDL; it was most likely due to patients stopping all their medications (including their antihypertensive drugs) when they stopped their study medication because of adverse effects. Statins probably do not cause either ICH<sup>4</sup> or liver problems<sup>5</sup>.

Among patients in SPARCL with large artery disease<sup>6</sup>, atorvastatin reduced stroke by 33%, even in the intention-to-treat analysis. We found<sup>7</sup> that in patients with asymptomatic carotid stenosis, intensive medical therapy based on maximizing the dose of statin, the two-year risk of stroke was reduced from 8.8% to 1%, and the 2-year risk of myocardial infarction was reduced from 7.6% to 1%. This is a much bigger effect than the 25% reduction of stroke with Aspirin. Other antiplatelet agents are only marginally better than aspirin, so instead of focusing on which antiplatelet agent to use, we should be focusing on reducing risk. Furthermore, the appropriate treatment for secondary stroke prevention depends on the underlying cause; just as not all patients with stroke require statins (for example, young people with normal arteries whose stroke is due to paradoxical embolism or dissection), not all patients should receive antiplatelet agents (for example, those with cardioembolic stroke, who should be anticoagulated). With the aging of the population and better blood pressure control, fewer strokes are lacunar strokes from small vessel disease, and a higher proportion are from large artery disease (which will benefit greatly from statins) or cardioembolic (which requires anticoagulation, not antiplatelet agents). Aspirin is therefore becoming less important in stroke prevention, and statins more important.

### References

- (1) Spence JD. Antihypertensive drugs and prevention of atherosclerotic stroke. *Stroke*. 1986;17:808-10.
- (2) Hachinski V, Graffagnino C, Beaudry M, Bernier G, Buck C, Donner A et al. Lipids and stroke: a paradox resolved. *Arch Neurol*. 1996;53:303-8.
- (3) The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Investigators. High-Dose Atorvastatin after Stroke or Transient Ischemic Attack. *New England Journal of Medicine*. 2006;355:549-59.
- (4) Hackam DG, Woodward M, Newby LK, Bhatt DL, Shao M, Smith EE et al. Statins and intracerebral hemorrhage: collaborative systematic review and meta-analysis. *Circulation*. 2011;124:2233-42.
- (5) Bader T. The myth of statin-induced hepatotoxicity. *Am J Gastroenterol*. 2010;105:978-80.
- (6) Sillisen H, Amarenco P, Hennerici MG, Callahan A, Goldstein LB, Zivin J et al. Atorvastatin Reduces the Risk of Cardiovascular Events in Patients With Carotid Atherosclerosis: A Secondary Analysis of the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial. *Stroke*. 2008;39:3297-302.
- (7) Spence JD, Coates V, Li H, Tamayo A, Munoz C, Hackam DG et al. Effects of intensive medical therapy on microemboli and cardiovascular risk in asymptomatic carotid stenosis. *Arch Neurol*. 2010;67:180-6.