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Lipid and Stroke

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The occurrence of stroke increases with age, particularly affecting the older elderly, a population also at higher risk for coronary heart disease (CHD). Epidemiologic and observational studies have not shown a clear association between cholesterol levels and all causes of stroke. Nonetheless, large, long-term statin trials in patients with established or at high risk of coronary heart disease have shown that statins decrease stroke incidence.

We performed a systematic review and meta-analysis of all statin trials which have now included over 90,000 patients, to determine the effect of statins and LDL-C reduction on stroke prevention¹⁾. The relative risk reduction for stroke was 21% (OR 0.79 [0.73–0.85]) with no heterogeneity between trials. Fatal strokes were reduced, but not significantly, by 9% (OR 0.91 [0.76–1.10]). There was no increase in haemorrhagic strokes (OR 0.90 [0.65–1.22]). The extent of statin's effect was closely associated with LDL-C reduction. LDL reduction explained 34 to 80% of the observed benefit, leaving also room for other, pleiotropic, effects. Each 10% reduction in LDL-C was estimated to reduce the risk of all strokes by 13.2% (95%CI, 4.8–20.6) and carotid intima-media thickness (IMT) by 0.73% per year (95%CI = 0.27–1.19). By comparison, the number of strokes prevented per 1,000 patients treated for 5 years in patients with coronary heart disease is 6.4 for statins versus 17.3 for antiplatelet agents. Our meta-analysis shows that statins may reduce the incidence of all strokes without any increase in hemorrhagic strokes, and this effect is mainly driven by the extent of between-group LDL-C reduction.

Statin have not yet been shown to reduce stroke risk in the typical general population without known coronary heart disease, nor have they been shown to prevent recurrent stroke in patients with prior stroke. Potential reasons for the effects of statins on stroke and the non-cholesterol-lowering mechanisms that may be involved will be discussed. Additional studies in patients representative of the typical stroke population are needed.

Statin have a good overall safety profile with no increased incidence of hemorrhagic stroke and cancer. They have positive effects in primary prevention of cardiovascular disease in high risk young as well as elderly populations. Statins reduced stroke incidence in high risk populations—mainly CHD, diabetics in Heart Protection Study (HPS) and Collaborative Atorvastatin Diabetes Study (CARDS) trial and hypertensives in Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) trial—even with a normal baseline blood cholesterol level, which argues for a global cardiovascular risk-based treatment strategy^{2)~4)}. In patients with prior strokes, statins reduce the incidence of coronary events as shown by the HPS trial, but it is not yet proven that statins actually reduce the incidence of recurrent strokes in secondary prevention³⁾.

Based on the evidence, there are no longer discussions that for all stroke patients with a past history of myocardial infarction clinicians should consider adding a statin, even when serum cholesterol level is in the 'normal' range. In patients with ischemic stroke with no past history of coronary event, who constitutes 80% of the stroke population, no clear recommendation can be made. The Stroke Prevention by

Aggressive Reduction in Cholesterol Levels (SPARCL) study is a unique large randomized, placebo-controlled trials which is on-going and will definitely answer this question with aggressive cholesterol lowering with atorvastatin 80 mg/day in patients with stroke and no past-history of cerebrovascular diseases⁹⁾. Results will be available in early 2006.

References

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