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Interventions in the Management of Serum Lipids for Preventing Stroke Recurrence

Bradley N. Manktelow, PhD; John F. Potter, DM, FRCP

Studies have shown interventions that reduce total and low-density lipoprotein cholesterol levels also decrease subsequent coronary heart disease (CHD) and stroke events in those with a history of CHD. However, it is uncertain whether pharmacological alteration of lipid levels in those with a history of cerebrovascular disease can prevent recurrence of either stroke or subsequent cardiovascular events.

Objectives

This systematic review investigated the effect of drug therapy to alter serum lipids in preventing subsequent cardiovascular disease and stroke recurrence in patients with a history of stroke or transient ischemia attacks (TIA).

Search Strategy

We searched the Cochrane Stroke Group Trials Register, the Cochrane Central Register of Controlled Trials, MEDLINE, and EMBASE. We also contacted pharmaceutical companies known to produce a lipid-lowering agent for information on relevant publications or unpublished work. Randomized trials of participants aged 18 years and over with a history of stroke or TIA were included.

The two review authors independently selected the trials, assessed their quality, and extracted the data. All analyses were carried out using Review Manage 5.0. Differences in outcome between the treatment groups were quantified using the Peto odds ratios (OR), with 95% confidence intervals (CI), from a fixed effects model.

Main Results

Eight trials involving approximately 10 000 participants fit the entry criteria. The active interventions were pravastatin, atorvastatin, or simvastatin in 5 trials, clofibrate in 2, and conjugated estrogen. In those with a previous history of stroke or TIA there was no evidence of a difference overall in stroke recurrence with therapy (OR 0.92, 95% CI 0.81 to

1.04), but statin-based therapy had a marginal benefit in reducing subsequent cerebrovascular events (OR 0.88, 95% CI 0.77 to 1.00; Figure). However, analysis by type of subsequent stroke (two studies) showed evidence for a protective effect of statins for ischemic stroke (OR 0.78, 95% CI 0.67 to 0.92) but evidence for an increased risk of hemorrhagic stroke (OR 1.72, 95% CI 1.20 to 2.46). There was no evidence that statin or other therapy reduced all-cause mortality or sudden death (OR 1.00, 95% CI 0.83 to 1.20). There was evidence, though, of a reduction in subsequent serious vascular events (OR 0.74, 95% CI 0.67 to 0.82) in the 3 statin trials.

Conclusions

The evidence suggests that statins, but not other lipid lowering therapy, in patients with a history of ischemic stroke or TIA significantly reduces subsequent major coronary events but only marginally reduces the risk of stroke recurrence. There is no clear evidence of beneficial effect from statins in those with previous hemorrhagic stroke, and it is unclear when after ischemic stroke statins should be started. In view of this and the evidence of the benefit of statin therapy in those with a history of CHD, patients with ischemic stroke or TIA, with or without a history of established CHD, should receive statin therapy.

Implications for Clinical Practice and Future Research

There is good evidence for a beneficial effect of statin therapy in those under the age of 80 years with a previous non-disabling ischemic stroke or TIA, but not hemorrhagic stroke, who have baseline total cholesterol levels >3.5 mmols/L in terms of reducing subsequent serious vascular events. The data also suggested a marginal benefit of statins in reducing future cerebrovascular events, but not overall mortality. In view of this evidence it is recommended that all ischemic stroke or TIA patients aged at least up to 80

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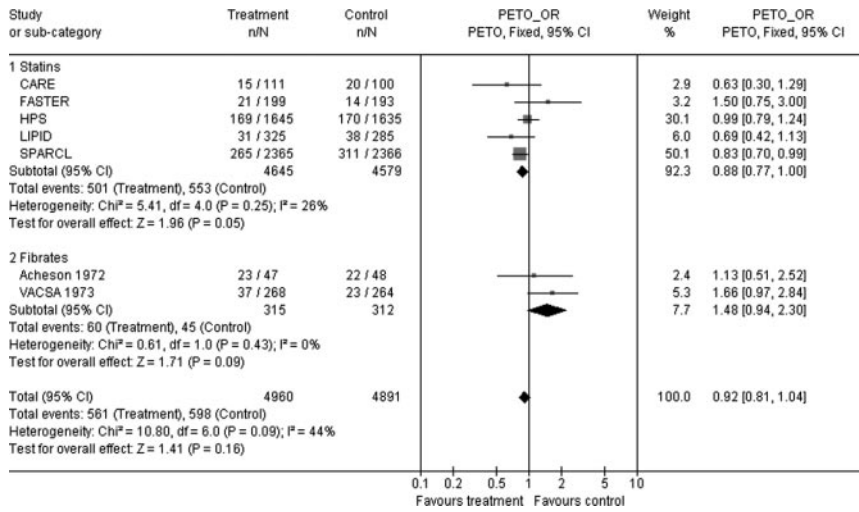


Figure. Effect of drug therapy to alter serum lipids on subsequent cerebrovascular events in those with a history of stroke or TIA, by drug type.

years should receive statin therapy as part of a secondary prevention program.

Further work is needed to answer important unresolved questions such as (1) what is the potential role of statins for those patients with a previous cerebral hemorrhage, (2) when after the cerebrovascular event therapy to alter lipid levels should be started, (3) at what baseline lipid levels treatment should be commenced, (4) what level of reduction should be aimed for, and (5) whether the very elderly (those aged over 80 years) stroke patient benefits to the same extent as a younger counterpart.

Full details and all graphical plots are available in the full version of this review published in the Cochrane Library.¹

Disclosures

None.

Reference

1. Manktelow BN, Potter JF. Interventions in the management of serum lipids for preventing stroke recurrence. *Cochrane Database Syst Rev.* 2009;3:CD002091.

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