Can Statins Reduce Risk of Dementia?

Jick H, Zornberg G, Jick SS, et al. Statins and the risk of dementia. Lancet 2000;356:1627–31.

Study Overview

Objective. To determine the potential effects of hydroxymethylglutaryl-coenzyme reductase inhibitors and other lipid-lowering agents (LLAs) on dementia.

Design. Nested case-control analysis. This was an observational study.

Setting and participants. Information about patients was gathered from 368 practices that contribute to the UK-based General Practice Research Database. All patients selected were aged 50 years and older. Three study groups were identified: group I consisted of patients aged 50 to 89 years who had received at least 1 prescription for a statin (atorvastatin, cerivastatin, fluvastatin, pravastatin, or simvastatin) or another LLA (bezafibrate, ciprofibrate, clofibrate, fenofibrate, gemfibrozil, colestipol, cholestyramine, acipimox, or niacin / nicotinic acid) at any time (n = 24,480); group II included patients with a computer-recorded ICD code diagnosis of hyperlipidemia who were not taking LLAs (n = 11,421); and group III consisted of a random sample of patients aged 50 to 89 years who did not have a diagnosis of hyperlipidemia and had not received LLAs at any time (n = 25,000). Patients with significant neurologic problems (eg, Parkinson's disease, motor neuron disease, chronic psychosis) or severe chronic illness (eg, chronic renal disease, epilepsy, stroke) were excluded from analysis.

Patients were followed from 1 January 1992 and 1 January 1998, and all patients who developed a first-time diagnosis of dementia or Alzheimer's disease (AD) during this time were identified. The date of first diagnosis was defined as the index date. Using the base population, up to 4 controls (ie, patients without a diagnosis of dementia) from the study population were matched to each subject with dementia for age (± 1 year), sex, practice, index date, and years of previous recorded history in the database.

Main outcome measure. The association between risk of dementia according to type of drug exposure (statins or other LLAs) and untreated hyperlipidemia, as assessed by a matched analysis (conditional logistic regression).

Main results. 284 eligible patients with a first-time diagnosis of dementia and 1080 matched controls were identified. Among controls, 746 (69%) did not have hyperlipidemia and were not treated with LLAs, 142 (13%) had hyperlipidemia but received no LLA therapy, 114 (11%) had received statins, 74 (7%) had received nonstatin LLAs, and 4 (0.4%) received both a statin and another LLA. When adjusted for age, sex, history of coronary artery disease, hypertension, coronary bypass surgery and cerebral ischemia, smoking, and body mass index, relative risk estimates of dementia were 0.72 (95% confidence interval [CI], 0.45 to 1.14) in patients with untreated hyperlipidemia (P = 0.16), 0.29 (95% CI, 0.13 to 0.63) in current statin users (P = 0.002), and 0.96 (95% CI, 0.47 to 1.97) in current users of other LLAs (P = 0.91). Past users of other LLAs had an estimated relative risk of 1.31 (95% CI, 0.66 to 2.61; P = 0.44).

Conclusion

Patients 50 years and older who were receiving statin treatment had a lower risk of developing dementia compared with patients receiving other LLAs or those who had untreated hyperlipidemia. The data did not distinguish between AD and other forms of dementia.

Commentary

This article by Jick and colleagues highlights a new potential benefit from the statin class of drugs: reduced risk of developing AD. Other recent studies have found that statins have effects beyond cholesterol reduction. One study showed that these agents may decrease osteoporosis risk in elderly women [1]. Another study by Wolozin et al [2] showed that among subjects taking pravastatin or lovastatin, the prevalence of probable AD was 60% to 73% lower than in the total study population or compared with subjects receiving medications to treat hypertension or cardiovascular disease. This was also an observational study, and the authors were careful to mention that their results showed only an association and did not suggest causative mechanisms between these agents and lowered disease prevalence.

Although Jick et al's research confirmed these earlier findings, this confirmation should be viewed with caution. First, the study is retrospective, and thus investigators did not have control over their data. Results were separated to demonstrate the effects of individual statins; however, because of the small size of groups, no difference was detected between

specific drugs. The authors suggest that statins affect dementia through a different mechanism than the one that lowers cholesterol, but that other mechanism remains unclear. In addition, specific information on lipid control was not provided. Patients taking a statin may have had better control of their hyperlipidemia than patients taking other LLAs. Compliance to treatment also could not be assessed. Overall, this study should be seen as hypothesis generating. The idea that statins can help to prevent AD is interesting and merits further exploration. A prospective cohort study using the same database could probably be conducted and might provide more definitive results. Also, more basic research is needed to elucidate the mechanism by which statins may protect against AD.

Applications for Clinical Practice

Although the results are promising, recommending statin therapy for patients with AD based on this study would be premature. Further research is needed to clearly demonstrate the association between statin therapy and AD risk.

References

1. Chan KA, Andrade SE, Boles M, et al. Inhibitors of hydroxymethylglutaryl-coenzyme A reductase and risk of fracture among older women. Lancet 2000;355:2185–8.
2. Wolozin B, Kellman W, Ruosseau P, et al. Decreased prevalence of Alzheimer's disease associated with 3-hydroxy-3-methyglutaryl coenzyme A reductase inhibitors. Arch Neurol 2000;57:1439–43.