Do statins delay onset or slow progression of Alzheimer's dementia?

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EVIDENCE-BASED ANSWER

Statins (coenzyme-A reductase inhibitors) should not be used with the single intent to delay the onset or slow the progression of dementia. Large randomized control trials (RCTs) found that the administration of a statin had no significant effect on preventing or slowing all-cause cognitive decline (strength of recommendation [SOR]: **A**, based on large RCTs with narrow confidence interval).[1,2] Specifically, there is insufficient evidence that statins delay the onset or slow the progression of Alzheimer's dementia (SOR: **B**, based on systematic review with heterogeneity).[3]

While 3 epidemiologic studies[4–6] have found a decreased incidence of dementia among those taking statins, these studies have significant methodological shortcomings and do not show a causal relationship (SOR: **C**, based on poor-quality studies).

CLINICAL COMMENTARY

We are obligated to protect patients from potential risks of unnecessary medications

Alzheimer's disease is a difficult and emotionally charged topic. Many patients who have watched a family member suffer from Alzheimer's disease would go to great lengths to delay or prevent developing Alzheimer's disease themselves. As a result of direct drug marketing to consumers, plus increased lay media coverage of health issues, our patients are now better informed than ever and make more direct requests for certain medications by name.

Imagine talking with a well-read patient who has learned from a newspaper article or morning news show about 1 of the 3 epidemiological studies that show decreased incidence of dementia among statin users. The patient now stands before you, requesting a prescription for a statin. Though this patient is otherwise healthy and has a desirable cholesterol level, you will still find it difficult to explain to the patient why you will not write the prescription. As physicians, we are obligated to protect our patients from the potential risks of unnecessary medications. We are also obligated to protect our healthcare system from escalation of already high healthcare costs. Evidence from rigorous clinical trials is the tool that can help us provide this protection.

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Evidence summary

Approximately 4 million people in the United States suffer with Alzheimer's disease. The prevalence rises with age and is approximately 47% among those aged 85 years and older.[7]

Amyloid plaques are thought to be responsible for clinical changes associated with Alzheimer's dementia. Research has indicated that amyloid precursors may be more prevalent in a cholesterol-rich environment. This led to the theory that treating hypercholesterolemia may decrease the prevalence of Alzheimer's disease.[8]

The PROSPER trial, which was designed to test the effect of pravastatin (Pravachol) on coronary heart disease and stroke, randomized 5804 study participants into 1 group assigned to take pravastatin and another group assigned to take

placebo. An additional study endpoint was pravastatin's effect on cognitive function as measured by 4 different tests, including the Mini-Mental Status Exam (MMSE). Overall cognitive function declined at the same rate in treatment and placebo groups. There was no significant difference between the 2 groups over 3 years using 4 different methods of assessment. In particular, the MMSE scores differed by only 0.06 points (95% confidence interval [CI], 0.04–0.16; *P*=.26).

The largest RCT of a statin agent, the Heart Protection Study, enrolled more than 20,000 people and randomized them to simvastatin (Zocor) or placebo. After a median of 5 years of follow-up, there was no difference in cognitive scores or the rate of diagnosis of dementia between the 2 groups.[2]

A systematic review concluded that no good evidence recommended statins for reducing the risk of Alzheimer's dementia.[3] Notably, the review did find a body of inconclusive evidence that lowering serum cholesterol may retard disease pathogenesis. An observational study of 56,790 charts included in the computer databases of 3 hospitals found that the prevalence of probable Alzheimer's dementia in the cohort taking statins was 60% to 73% (*P*<.001) lower than in the total patient population or in patients taking antihypertensive or cardiovascular medications.[4]

Also included in the review was a nested case-control study of 1364 patients that found an adjusted relative risk for dementia of 0.29 (95% CI, 0.013–0.063; *P*=.002) among those taking statins.[5] This study did not distinguish between Alzheimer's dementia and other forms of dementia. These studies do not demonstrate a causal relationship between statins and Alzheimer's dementia.

The best way to determine if there is a true effect of statins on Alzheimer's dementia is to conduct a clinical trial. Two ongoing clinical trials are designed specifically to determine if the use of statins delay the onset or slow the progression of Alzheimer's dementia.[9,10] To date, these trials have not published interim findings.

Recommendations from others

No organization has issued recommendations for the use of statins to delay the onset or slow the progression of Alzheimer's dementia.

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FAST TRACK

While 3 studies have found lower incidence of dementia in those taking statins, these studies have significant methodological shortcomings