

Statins and cognitive impairment

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Clinical question

Do statins affect cognitive decline or dementia?

Bottom line

Evidence indicates statins do not prevent, treat, or cause cognitive impairment or dementia. The US Food and Drug Administration warning is based on case reports that might reflect idiosyncratic, short-term, “fuzzy” thinking. Decisions to prescribe statins should not be altered.

Evidence

- A systematic review of 57 studies (19 RCTs, 26 cohort studies, 6 case-control studies, and 6 cross-sectional studies)¹ showed the following:
 - 1 RCT (20 536 patients) showed no effect on incidence of dementia or cognitive impairment.
 - Observational studies reported that statins reduced the incidence. In 10 cohort studies of 4360 137 patients, the relative risk was 0.87 (95% CI 0.82 to 0.92). Results are unreliable owing to biases (eg, people at lower risk are more likely to use statins).
 - In 18 RCTs (8305 patients) with healthy patients, those with high cholesterol, or those with dementia, overall, 87.7% showed no effect on performance on cognitive function tests, 4.5% improved with statins, and 7.7% improved with placebo. In the largest study (5804 patients), the mean age was 75 years and patients did not have dementia. Patients were followed for 3 years and showed no difference in Mini-Mental State Examination scores.
 - For cognitive adverse events, there was no difference between taking statins and taking clopidogrel or losartan.
- No effect of statins preventing dementia was seen in a systematic review of 2 RCTs (26 340 patients).² Limitations included cognitive function being a secondary outcome.
- No effect was found in a systematic review of 3 RCTs of statins for treatment of dementia (748 patients with a mean age of 79 years, with probable or possible Alzheimer disease, followed for 6 months or longer).³
 - Trends favour statins preventing cognitive decline. In 1 study, Mini-Mental State Examination scores between those taking statins and those taking placebo were not statistically different (mean difference -1.53 [95% CI -3.28 to 0.21]). However, the results were highly inconsistent.
- Two systematic reviews found similar results.^{4,5}

Context

- In 2012, based mostly on case reports,¹ the US Food and Drug Administration warned that statins might cause cognitive impairment, memory loss, forgetfulness, or confusion.⁶

The adverse reaction might be better described as “fuzzy” or unfocused thinking.⁶ It appears to be idiosyncratic and rare, and resolves when the medication is stopped.⁶⁻⁸

- Lipophilic statins might be more likely to cross the blood-brain barrier and have more central nervous system effects.^{6,7} This is not based on reliable clinical evidence.

Implementation

Statin nonadherence is common. In 1 small sample, 75% did not fill new statin prescriptions within 12 weeks, and half of noncompliers feared side effects.⁹ Safety concerns might be missed in RCTs because subjects are healthier, patients with adverse events might be excluded, and adverse events might be superficially explored.¹⁰ Myalgia occurs in 7.5% of placebo and statin RCT patients,¹⁰ but in 10.5% of cohort study patients.¹¹ Therefore, 10% to 11% of patients might have myalgia but 7.5% of those cases might be unrelated to statins. RxFiles offers a good guide to reintroducing statin therapy in myalgia patients with no or minimal creatine kinase elevation.¹² Patients should be reassured that there are no identified risks of cognitive impairment.

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