

Statin-Associated Memory Loss: Analysis of 60 Case Reports and Review of the Literature

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Abstract

Objective: To review case reports of statin-associated memory loss as well as the available published evidence for and against such a link.

Methods: We searched the MedWatch drug surveillance system of the Food and Drug Administration (FDA) from November 1997-February 2002 for reports of statin-associated memory loss. We also reviewed the published literature (using MEDLINE) and prescribing information for these drugs.

Results: Of the 60 patients identified who had memory loss associated with statins, 36 received simvastatin, 23 atorvastatin, and 1 pravastatin. About 50% of the patients noted cognitive adverse effects within 2 months of therapy. Fourteen (56%) of 25 patients noted improvement when the statin was discontinued. Memory loss recurred in four patients who were rechallenged with the drug. None of the 60 reported cognitive test results. Two placebo-controlled trials found no benefits for statins on cognition or disability. One randomized controlled trial of simvastatin found no effects on cerebrospinal amyloid levels. In one small, randomized study, patients receiving statins showed a trend toward lower cognitive performance than those receiving placebo. Five observational studies found a lower risk of dementia among patients receiving statins.

Conclusion: Current literature is conflicting with regard to the effects of statins on memory loss. Experimental studies support links between cholesterol intake and amyloid synthesis; observational studies indicate that patients receiving statins have a reduced risk of dementia. However, available prospective studies show no cognitive or anti-amyloid benefits for any statin. In addition, case reports raise the possibility that statins, in rare cases, may be associated with cognitive impairment, though causality is not certain.

Introduction

The 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors, also known as statins (atorvastatin, fluvastatin, lovastatin, pravastatin, and simvastatin), are the most widely prescribed drug class for treatment of dyslipidemias because of their convincingly proven benefits. With more aggressive guidelines and an aging population, statins will be increasingly prescribed, more statins will be developed, and the trend will be toward earlier treatment and higher dosage.

The patient population receiving statins is already at risk for memory loss because of cardiac risk factors, advancing age, and amyloidosis. However, in contrast to the cardiovascular benefits, the effects of statins on cognition and neuronal function are not as well studied. Since cerebrovascular disease is known to cause memory loss, there is growing interest in examining whether statins have cognitive benefits. Experimental studies have shown that cholesterol-fed wild-type rabbits develop brain pathology similar to that of Alzheimer's disease.^[1] Transgenic mouse models of Alzheimer's disease exhibited increased amyloid plaques when mice were fed a cholesterol diet.^[1] Cell culture and in vivo animal studies have shown that reducing cholesterol can inhibit b-amyloid synthesis.^[1]

Consistent with these preclinical findings, observational studies have found that patients receiving statins have a lower risk of dementia.^[2-6] Paradoxically, published case reports^[7, 8] and an increasing number of anecdotal stories in the lay media have linked statin intake to adverse effects of memory loss or amnesia. Because cholesterol synthesis is essential for neurons to function normally, it is theoretically possible that excessive inhibition of cholesterol synthetic pathways may occasionally result in neurocognitive adverse effects. To gain further insight into links between statins and memory loss, we systematically reviewed a sample of adverse events reported to MedWatch, the drug surveillance system of the Food and Drug Administration (FDA) as well as the current literature.

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