

Statins Linked to Reduced Dementia

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AMSTERDAM — Two new studies may have somewhat allayed concerns about cognitive dysfunction being a possible adverse effect of statins.

The studies, both from Taiwan and reported at this week's European Society of Cardiology (ESC) Congress 2013, both suggest that statin drugs may instead be linked to lower rates of dementia in older people.

The first study of 58,000 patients showed a dose-related inverse relationship between statin use and new-onset nonvascular dementia. The second report, in 5221 patients with atrial fibrillation, found a lower incidence of dementia in patients taking statins compared with those not taking statins.

Commenting on these findings for *Medscape Medical News*, Professor Jose Gonzalez-Juanatey, University Hospital, Santiago de Compostela, Spain, said, "These new data suggest that high-potency statins may reduce the incidence of dementia in patients with atrial fibrillation and in elderly patients. Nevertheless, before we can know for sure that statins may prevent dementia, a clinical trial confirming these findings is mandatory."

Also asked to comment, Seth S. Martin, MD, Johns Hopkins Hospital, Baltimore, Maryland, who is conducting a systematic review of the literature on statins and cognition/dementia, said these current results fit in well with existing studies.

"While the study of Dr. Lin and colleagues could not control for all possible confounders, the dose response seen in the study is intriguing and supports a causal relationship. The work strengthens existing literature that is compatible with a protective effect of statins on dementia. Overall, statins appear to be good for the brain."

Previous Randomized Trials Negative

Spokesperson at an ESC press conference on the latest new statin studies, Dr. Terje R. Pedersen, Oslo University Hospital, Norway, pointed out that although it is plausible that statins might have a favorable effect on dementia caused by atherosclerosis of cerebral arteries, 2 randomized trials — PROSPER (Prospective Study of Pravastatin in the Elderly at Risk) with pravastatin in the elderly and the LEADe (Lipitor's Effect on Alzheimer's Dementia) study with atorvastatin in patients with early Alzheimer's disease — have not shown any benefit of statins on risk for dementia.

Another spokesman at the press conference, Professor Heinz Drexel, VIVIT-Institut Feldkirch, Austria, explained that data so far on dementia and statins have been conflicting, with some studies suggesting an increased risk, others showing a reduced risk, and other showing no effect. Commenting for *Medscape Medical News*, he said the larger Taiwanese study presented at the ESC meeting was particularly encouraging. "This is very impressive data. Yes, it is an observational study in just one population, and so needs confirmation, but there was a large effect which was dose-dependent, and the mechanism appears not to be antiatherosclerosis as they excluded vascular dementia."

Professor Drexel said he thought the balance of opinion on statins and dementia was starting to change toward a feeling of benefit. Noting that the previous randomized trials on this issue have been relatively

small, he added: "The debate will continue until we have a largescale radomized trial, but this new data from Taiwan is certainly good news."

Dr. Tin-Tse Lin, National Taiwan University Hospital, Hsin-Chu, who presented the first study, pointed out that recent reports of statin-associated cognitive impairment have led the US Food and Drug Administration (FDA) to list statin-induced cognitive changes, especially for the older population, in its safety communications.

"Previous studies had considered statin therapy to exert a beneficial effect on dementia," Dr. Lin said. "But few large-scale studies have focused on the impact of statins on new-onset, nonvascular dementia in the geriatric population. To the best of our knowledge, this is the first large-scale, nationwide study to examine the effect of different statins on new onset nonvascular dementia in an elderly population."

Dose-Dependent Inverse Relationship

For the study, Lin and colleagues examined whether statin use was associated with new diagnoses of dementia in a random sample of 1 million people covered by Taiwan's National Health Insurance.

From this they identified 57,669 individuals older than age 65 years who had no history of dementia in 1997 and 1998. Of these, 15,200 were taking statins. Propensity scoring was used to match these patients with controls not taking statins. Patients receiving statins were divided into tertiles according to dose.

The researchers identified 5516 new diagnoses of dementia (excluding vascular dementia) during the 4.5 years of follow-up. Results showed an inverse relationship between statin use and dementia, with the risk for dementia decreasing with increasing statin dose. This trend remained in different age, sex, and cardiovascular risk subgroups.

Table. Risk for Dementia With Various Statins by Dosage Tertiles

Statin	Lowest-Dose Tertile (Hazard Ratio)	Mid-Dose Tertile (Hazard Ratio)	Highest-Dose Tertile (Hazard Ratio)	P Value for Trend
Atorvastatin	0.680	0.543	0.305	<.001
Rosuvastatin	0.365	0.134	0.129	.011
Fluvastatin	0.971	0.578	0.255	.058
Simvastatin	0.747	0.664	0.510	.064
Pravastatin	0.662	0.933	0.491	.422
Lovastatin	1.382	0.930	1.626	.116
All statins	0.923	0.806	0.311	<.001

"The adjusted risks for dementia were significantly inversely associated with increased total or daily equivalent statin dosage," Dr. Lin said. "Patients who received the highest doses of statins had a 3-fold decrease in the risk of developing dementia. High-potency statins such as atorvastatin and rosuvastatin showed a significant inverse association with developing dementia in a dose-response manner. Higher doses of high-potency statins gave the strongest protective effects against dementia."

All the statins except lovastatin were associated with a decreased risk for new-onset dementia when taken at higher daily doses. Dr. Lin suggested lovastatin may have shown different results because it has less cholesterol-lowering effect than other statins.

Statins Halved Dementia Risk in AF Patients

The second study, by a group led by Min-Tsun Liao, also from National Taiwan University Hospital, Hsin-Chu, included 5221 patients with atrial fibrillation, which is known to be a predisposing factor for dementia. Of these, 1652 were taking statins.

During a 6-year follow-up, 2.1% of the patients taking statins developed dementia compared with 3.5% of the nonstatin group, a statistically significant difference ($P = .002$).

Cox regression analysis showed an odds ratio of 0.565 for statin use and the risk for new-onset dementia. Other factors that were associated with a reduced risk for dementia included male sex and lower CHADS2 score. History of myocardial infarction, peripheral artery disease, coronary artery disease, chronic kidney disease, and valvular heart disease were not associated with new-onset dementia.

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