

Statins May Cut AD Risk, Even in ApoE4 Carriers

BY MICHELE G. SULLIVAN

Statins appear to cut the risk of developing Alzheimer's disease by up to 56%, even in those with the high-risk apolipoprotein E4 allele.

The link between statin use and risk reduction was consistent for lipophilic and hydrophilic agents, but absent in nonstatin cholesterol-lowering drugs, wrote Dr. M.D.M. Haag and colleagues (J. Neurol. Neurosurg. Psychiatry 2009; 80:13-7).

They used data from the Rotterdam Study, a prospective population-based cohort study of age-related disorders that included 7,000 Dutch citizens who were free of dementia at baseline (1990-1993). Follow-up exams were conducted through 2004. Average follow-up was 9 years, with nearly 63,000 person-years of follow-up.

At baseline, the subjects' mean age was 69 years; 26% were known to be pos-

itive for the apolipoprotein E4 allele (ApoE4). During the follow-up period, dementias were diagnosed in 739 participants, including 582 with Alzheimer's disease, 81 with vascular dementia, and 76 with other types of dementia.

There were 30,241 filled prescriptions for cholesterol-lowering drugs during the study; 92% were for statins and 8% for nonstatins. Most of the prescribed statins were lipophilic (72%). Simvastatin was

the most common (59%), followed by atorvastatin and pravastatin (both 13%).

Overall, the use of any statin was associated with a significantly decreased risk of Alzheimer's, compared with nonuse (hazard ratio, 0.57 after adjustment). Nonstatin agents were not significantly different from never-use (HR, 1.05).

Lipophilic and hydrophilic statins were equally effective in reducing the risk (HR, 0.54 each). The protective effect was

seen regardless of the duration of statin use (HR, 0.44 for 2.9 years or less, 0.78 for more than 2.9 years) and remained consistent even when analysis was restricted to those 65 or older at baseline.

ApoE4 allele status did not appear to have a confounding effect on the association between statins and Alzheimer's.

The study was funded by Dutch government and university grants. The authors reported no financial conflicts. ■

Cerebral Injury In Dementia Is Tied to Diabetes

Two distinct patterns of cerebral injury were associated with dementia in autopsy studies, depending on whether or not the subject had diabetes.

In subjects without diabetes, dementia was associated with a greater load of amyloid- β peptide and greater free radical damage. In those with diabetes, dementia was associated with more microvascular infarcts and greater activation of neuroinflammation, said Dr. Joshua A. Sonnen of the department of pathology, University of Washington, Seattle, and his associates (Arch. Neurol. 2009;66:315-22).

These findings suggest that the pathogenesis of dementia differs between patients with diabetes and those without it.

The researchers examined autopsy data from subjects in an ongoing community-based study of brain aging and incident dementia. The subjects included 196 elderly men and women divided into four groups: those who had no diabetes and no dementia (92 cases), those who had diabetes but no dementia (33 cases), those who did not have diabetes but did have dementia (45 cases), and those who had both diabetes and dementia (26 cases).

Subjects with both diabetes and dementia died with a lower burden of amyloid- β peptide in brain parenchyma and cerebral blood vessels, compared with those who had dementia but no diabetes. They also showed significantly more deep microvascular injuries, suggesting "the basal-penetrating vessels may be especially vulnerable to damage from diabetes," the researchers reported.

These subjects also had higher levels of neuroinflammation than did their nondiabetic counterparts, which may be related to their higher numbers of microvascular injuries, the authors wrote.

—Mary Ann Moon

Adverse events in major depressive disorder (MDD): The most commonly observed adverse events associated with the use of paroxetine hydrochloride extended-release tablets were: abnormal ejaculation, abnormal vision, constipation, decreased libido, diarrhea, dizziness, female genital disorders, nausea, somnolence, sweating, trauma, tremor, and yawning. Adverse events in a study of elderly patients with MDD were: abnormal ejaculation, constipation, decreased appetite, dry mouth, impotence, infection, libido decreased, sweating, and tremor.

Contraindications: Concomitant use in patients taking monoamine oxidase inhibitors (MAOIs), thioridazine or pimozide is contraindicated. Paroxetine hydrochloride extended-release tablets are also contraindicated in patients with a hypersensitivity to paroxetine or to any of the inactive ingredients in paroxetine hydrochloride extended-release tablets.

Suicidality and Antidepressant Drugs: Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of paroxetine or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Paroxetine is not approved for use in pediatric patients. (See WARNINGS: Clinical Worsening and Suicide Risk, PRECAUTIONS: Information for Patients and PRECAUTIONS: Pediatric Use.)

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