

A Fatty Acid Found in Fish Linked to Lower Dementia Risk

BOSTON, Nov. 15 -- Patients with higher plasma levels of docosahexaenoic acid (DHA), a fatty acid found in fish, had a significant 47% reduction in the risk of all-cause dementia and a 39% reduced risk of Alzheimer's, researchers here reported.

In a subset analysis, the researchers found a link between fish intake, an important source of DHA, and a reduction in dementia, Ernst Schaefer, M.D., of Tufts here, and colleagues, reported in the November issue of *Archives of Neurology*.

Plasma phosphatidylcholine docosahexaenoic acid (PC DHA) is a ω -3 fatty acids, and must be obtained either by synthesis from dietary alpha-linolenic acid in the liver, or directly by consuming food rich in DHA, such as fish or fish oil, or DHA supplements, they wrote.

In a 9.1-year study of 899 men and women free of dementia at baseline (median age of 76.0), 99 new cases of dementia (including 71 cases of Alzheimer's disease) occurred during follow-up, the researchers reported.

After adjustment for age, sex, apolipoprotein E ϵ 4 allele, plasma homocysteine concentration, and education level, those in the upper quartile of baseline plasma DHA levels, compared with those in the lower three quartiles, had a relative risk of 0.53 for developing all cause dementia (95% confidence interval, 0.29-0.97; $P=0.04$).

The relative risk of developing Alzheimer disease was 0.61 (CI, 0.31-1.18; $P=0.14$), they reported.

In a subset of 488 nonrandomly selected participants, those in the upper quartile of plasma DHA levels had a mean DHA intake of 0.18 g/d and a mean fish intake of three servings per week ($P<0.001$).

Mean plasma DHA levels were equal to 3.5% of total fatty acids in men, 3.7% in women, and 3.6% for the whole population. The top quartile had values of greater than 4.2%, the researchers. No other plasma phosphatidylcholine fatty acid was independently linked to the risk of dementia.

In this study, the correlation between plasma DHA content and fish intake was significant, indicating that fish intake is an important source of dietary DHA, the researchers said. Furthermore, they added, subjects with plasma DHA levels in the highest quartile were those with the greatest fish consumption.

Moreover, they said, the major fatty acids in fish are DHA and eicosopentaenoic acid, but there was no relationship between the latter fatty acid and dementia. This finding is consistent with earlier studies showing low DHA content in the brain of individuals with Alzheimer's, they wrote.

The strengths of this study, the researchers noted, are its prospective design, its long follow-up, the size of the sample, and the analysis of dietary data along with the assessment of dementia and plasma phospholipid fatty-acid content.

Its limitations are that plasma DHA levels were measured only once, that dietary data were available for only a subset of individuals, and that there were only 99 new incident cases of dementia and few cases of Alzheimer's disease.

"In the future, it will be important to determine whether combined dietary supplementation with DHA can decrease further mental deterioration in patients with established dementia," Dr. Schaefer's team concluded.

The researchers wrote that in addition to government grants, co-author Vanina Bongard, M.D., Ph.D., of Tufts, held a grant from Martek Biosciences Corp. of Columbia, Md., and from Pfizer, France.

In an editorial in the same issue, Martha Morris, Sc.D., of Rush in Chicago wrote that the Schaefer trial provides the first evidence that direct measurement of DHA in plasma is related to lower Alzheimer's risk.

She wrote that on the basis of available epidemiological evidence, the amount of DHA required for a protective benefit would be one fish meal a week, 0.18g/d of DHA, (based on one 3-oz serving of cooked Atlantic salmon, for example).

On the basis of these data, trials that included participants who already consumed fish frequently may have failed to observe a DHA effect because the placebo group would be already at the level of the protective effect. Therefore, she said, future trials should be designed to either eliminate current fish consumers, or to be adequately powered to stratify fish by consumption.

Addressing the concern about the harmful effects of mercury-contaminated fish, Dr. Morris noted an apparent decrease in fish consumption in the U.S.

Most risk analyses, she said, are based on extrapolations from high-dose mercury toxicity levels and the mercury content of selected fish samples. These hypothetical calculations may be misleading, she said. "The harmful effects from fish consumption have not been borne out in epidemiologic studies, which consistently find positive health effects on mortality, cardiovascular risk factors and now dementia," she wrote.

The only way to resolve the risk-benefit question, Dr. Morris said, is to examine these risks directly in humans relative to the beneficial effects of the ω -3 fatty acids consumed.

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