

Abstract

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Docosahexaenoic acid supplementation and cognitive decline in Alzheimer disease: a randomized trial.

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CONTEXT: Docosahexaenoic acid (DHA) is the most abundant long-chain polyunsaturated fatty acid in the brain. Epidemiological studies suggest that consumption of DHA is associated with a reduced incidence of Alzheimer disease. Animal studies demonstrate that oral intake of DHA reduces Alzheimer-like brain pathology.

OBJECTIVE: To determine if supplementation with DHA slows cognitive and functional decline in individuals with Alzheimer disease.

DESIGN, SETTING, AND PATIENTS: A randomized, double-blind, placebo-controlled trial of DHA supplementation in individuals with mild to moderate Alzheimer disease (Mini-Mental State Examination scores, 14-26) was conducted between November 2007 and May 2009 at 51 US clinical research sites of the Alzheimer's Disease Cooperative Study.

INTERVENTION: Participants were randomly assigned to algal DHA at a dose of 2 g/d or to identical placebo (60% were assigned to DHA and 40% were assigned to placebo). Duration of treatment was 18 months.

MAIN OUTCOME MEASURES: Change in the cognitive subscale of the Alzheimer's Disease Assessment Scale (ADAS-cog) and change in the Clinical Dementia Rating (CDR) sum of boxes. Rate of brain atrophy was also determined by volumetric magnetic resonance imaging in a subsample of participants (n = 102).

RESULTS: A total of 402 individuals were randomized and a total of 295 participants completed the trial while taking study medication (DHA: 171; placebo: 124). Supplementation with DHA had no beneficial effect on rate of change on ADAS-cog score, which increased by a mean of 7.98 points (95% confidence interval [CI], 6.51-9.45 points) for the DHA group during 18 months vs 8.27 points (95% CI, 6.72-9.82 points) for the placebo group (linear mixed-effects model: P = .41). The CDR sum of boxes score increased by 2.87 points (95% CI, 2.44-3.30 points) for the DHA group during 18 months compared with 2.93 points (95% CI, 2.44-3.42 points) for the placebo group (linear mixed-effects model: P = .68). In the subpopulation of participants (DHA: 53; placebo: 49), the rate of brain atrophy was not affected by treatment with DHA. Individuals in the DHA group had a mean decline in total brain volume of 24.7 cm³ (95% CI, 21.4-28.0 cm³) during 18 months and a 1.32% (95% CI, 1.14%-1.50%) volume decline per year compared with 24.0 cm³ (95% CI, 20-28 cm³) for the placebo group during 18 months and a 1.29% (95% CI, 1.07%-1.51%) volume decline per year (P = .79).

CONCLUSION: Supplementation with DHA compared with placebo did not slow the rate of cognitive and functional decline in patients with mild to moderate Alzheimer disease.

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