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Effects of Omega-3 Fatty Acids on Cognitive Function with Aging, Dementia, and Neurological Diseases

Summary

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Introduction

This report was requested by the Agency for Healthcare Research and Quality (AHRQ), the National Institutes of Health (NIH) Office of Dietary Supplements, and several NIH Institutes. It is one of several reports focusing on the role of omega-3 fatty acids (FA) in the prevention or treatment of various diseases. Three Evidence-based Practice Centers (EPCs) produced this series of reports: the Southern California EPC ([SCEPC], based at RAND), the Tufts-New England Medical Center EPC, and the University of Ottawa EPC. This particular report focuses on the effects of omega-3 FA on cognitive function with aging, dementia, and neurological diseases.

Over the past 40 years, an increasing number of physiological functions have been attributed to omega-3 FA, including movement of calcium and other substances into and out of cells; relaxation and contraction of muscles; regulation of clotting and of secretion of substances that include digestive enzymes and hormones; and control of fertility, cell division, and growth. In addition, omega-3 FA may play an important role in brain development and function.[1] Docosahexaneoic acid (DHA; 22:6n-3) is the precursor to a newly-described metabolite called 10,17S-docosatriene, which is part of a family of compounds called resolvins.[2,3] They are released in the brain in response to an ischemic insult and counteract the pro-inflammatory actions of infiltrating leukocytes by blocking interleukin 1-beta-induced NF-kappaB activation and cyclooxygenase-2 expression. DHA also plays a role in retinal rod outer segments by influencing membrane fluidity so as to optimize G protein coupled signaling.[4,5]

The major dietary sources of omega-3 FA in the U.S. population are fish, fish oil, vegetable oils (principally canola and soybean), walnuts, wheat germ, and some dietary supplements.

Methods

Study Questions

We convened a technical expert panel (TEP) composed of distinguished basic scientists and clinicians with established expertise in omega-3 FA, human nutrition, dietary assessment methods, and neurology. The TEP advised us on refining the preliminary questions posed to us by AHRQ, determining the proper inclusion/exclusion criteria for the study and the populations of interest, establishing the proper outcomes measures, and conducting the appropriate analyses.

Based on the original questions that we received from AHRQ and input from our TEP, we addressed the following questions in this study:

1. What is the evidence that omega-3 FA play a role in maintaining cognitive function in normal aging?
2. What is the evidence that omega-3 FA affect the incidence of dementia including Alzheimer's disease?
3. What is the evidence that omega-3 FA are effective in the treatment of dementia including Alzheimer's disease?

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4. What is the evidence that omega-3 FA affect the incidence of neurological diseases?
5. What is the evidence that omega-3 FA prevent the progression of multiple sclerosis?

Search Strategy

The following databases were searched: MEDLINE® (1966-2003), PreMEDLINE® (December, 2003), EMBASE (1980-2003), Cochrane Central Register of Controlled Trials (4th Quarter, 2003), CAB HEALTH® (1973-2003), Dissertation Abstracts (1861-2003). All of these databases were searched using the OVID interface, except CAB HEALTH, which was searched through SilverPlatter. Any duplicate records were identified and removed within each search question using Reference Manager® software. The citations obtained from these literature searches were sent to the SCEPC via e-mail. We also reviewed the reference lists of all applicable articles and contacted our technical expert panel as well as industry experts recommended by the Office of Dietary Supplements to identify and obtain unpublished data.

Selection Criteria

Two reviewers independently reviewed each article considered for inclusion in the study. Human controlled clinical trials (randomized and non-randomized), prospective cohort studies, case-control studies, and case series were included; case reports were excluded. For inclusion, studies also had to describe a difference between omega-3 FA content in study arms for all study designs except case series and describe the effect of omega-3 FA on any of the following outcomes: cognitive function with normal aging, incidence of dementia, treatment of dementia, incidence of neurological disease, or progression of multiple sclerosis. The reviewers resolved any disagreements by consensus. Language was not a barrier to inclusion.

Data Extraction and Analysis

For each article included in the study, two reviewers independently extracted data about the trial design; the outcomes of interest; the quality of the trial; the number and characteristics of the patients; details on the intervention, such as the dose, frequency, and duration; the types of outcome measures; adverse events; and the elapsed time between the intervention and outcome measurements. Any disagreements between the reviewers were resolved through consensus. For each article, we then evaluated the quality of the design and execution of trials using a system developed by Jadad; determined a combined applicability grade based on applicability to the U.S. population and health state; performed a meta-analysis of those studies that sufficiently assessed interventions, populations, and outcomes to justify pooling; and performed a qualitative analysis of the remaining studies.

Results

We screened 5,865 article titles. From these article titles, we chose to review 502 full-text articles, of which 497 were retrievable. Of these full-text articles, 62 met our selection criteria and were chosen for data extraction. After data extraction, 12 articles met our inclusion criteria for our study questions.

Evidence that omega-3 FA play a role in maintaining cognitive function in normal aging. Only one study that met inclusion criteria assessed the role of omega-3 FA in maintaining cognitive function. Fish consumption was only weakly associated with a reduced risk of cognitive impairment and had no association with cognitive decline; omega-3 FA consumption was not associated with either outcome.

Evidence that omega-3 FA affect the incidence of dementia including Alzheimer's disease. Three studies evaluated the effect of omega-3 FA on the incidence of dementia. All three of the studies assessed the incidence of dementia relative to fish consumption; one also assessed risk relative to total omega-3 fatty consumption, and relative to each alpha-linolenic acid (ALA; 18:3n-3); eicosapentaenoic acid (EPA; 20:5n-3), and DHA consumption. Fish was associated with a significant reduction in the incidence of non-Alzheimer's dementia in only one of the studies. Fish consumption was associated with a reduced risk of Alzheimer's dementia in all three of the studies but this association was significant in only one study. Total omega-3 FA consumption and consumption of DHA (but not ALA or EPA) were associated with a significant reduction in the incidence of Alzheimer's.

Evidence that omega-3 FA are effective in the treatment of dementia including Alzheimer's disease. Only one study assessed the effects of omega-3 FA for the treatment of dementia. DHA resulted in a small improvement in scores on a dementia rating scale.

Evidence that omega-3 FA affect the incidence of neurological diseases. Four studies addressed the association of omega-3 FA consumption with risk or incidence of particular neurological diseases other than dementia. Two studies that assessed the association between omega-3 FA intake and the incidence of multiple sclerosis found no significant effects, although one study found a reduced risk with fish consumption among women. The one study that assessed the association between omega-3 FA consumption and the risk for

Parkinson's disease found no significant association for fish, ALA, EPA, or DHA. The one study that assessed the association between maternal omega-3 FA consumption and the risk of giving birth to a child with cerebral palsy found that consumption of fish once a week throughout pregnancy was associated with a lower risk.

Evidence that omega-3 FA prevent the progression of multiple sclerosis. Three studies reported on the effects of omega-3 FA intake on the progression of multiple sclerosis. In one study, treatment with an omega-3 FA supplement, MaxEPA, had no effect on disability or relapse rates. However, two other studies reported a significant reduction in disability and one reported improvement on an index of disease progression.

Thus, the quantity and strength of evidence for effects of omega-3 FA on outcomes in the conditions assessed varied greatly.

Discussion

We offer the following observations and recommendations regarding future research on the effects of omega-3 FA on the neurological conditions reviewed:

- Additional research on the effects of omega-3 FA needs to be performed on all of the conditions reviewed in this report before recommendations regarding the use of omega-3 FA can be made for these conditions.
- Of particular importance, properly designed randomized clinical trials that are sufficiently powered and of an adequate length (e.g., 3 to 5 years of followup) need to be conducted for dementia, especially Alzheimer's disease, and for multiple sclerosis.
- Studies that assess the effects of omega-3 FA should be designed to evaluate the effect of source, dose, treatment duration, and the sustainment of effect after discontinuation of omega-3 FA consumption.
- Trials of omega-3 FA should include a baseline assessment of dietary omega-3 and omega-6 FA intake.
- In controlled trials that assess the effects of omega-3 FA, analysis should include and report explicit testing of the effects of the omega-3 FA relative to the control substance.
- All studies that assess the effects of omega-3 FA should use standard validated instruments to assess clinical outcomes.
- Observational studies should report data about type of fish consumed and method of preparation.

Availability of the Full Report

The full evidence report from which this summary was taken was prepared for the Agency for Healthcare Research and Quality (AHRQ) by the Southern California Evidence-based Practice Center under Contract No. 290-02-0003. It is expected to be available in February 2005. At that time, printed copies may be obtained free of charge from the AHRQ Publications Clearinghouse by calling 800-358-9295. Requesters should ask for Evidence Report/Technology Assessment No. 114, *Effects of Omega-3 Fatty Acids on Cognitive Function with Aging, Dementia, and Neurological Diseases*. In addition, Internet users will be able to access the report and this summary online through AHRQ's Web site at www.ahrq.gov.

Suggested Citation

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