Effects of omega-3 fatty acids on eye health

CRD summary
This review evaluated the effects of omega-3 fatty acids on eye health. The authors concluded that there was insufficient evidence to draw firm conclusions and further research is required. This was a well-conducted review and the authors’ cautious conclusions reflect the limited evidence from a small number of largely observational studies.

Authors' objectives
To evaluate the effects of omega-3 fatty acids on eye health.

Searching
MEDLINE, PREMEDLINE, EMBASE, the Cochrane Library, CAB Health and Dissertation Abstracts were searched from inception to 2003 or 2004; search terms were reported. No language restrictions were applied and both published and unpublished studies were eligible for inclusion. In addition, the reference lists of all included studies and systematic reviews were screened and the files of experts in the field were searched.

Study selection
Study designs of evaluations included in the review
No restrictions were applied to study design. The included studies were randomised controlled trials (RCTs), controlled and non-controlled before-and-after studies, prospective cohort studies, retrospective studies, case control studies and cross-sectional studies.

Specific interventions included in the review
Studies that evaluated omega-3 fatty acids for primary or secondary prevention were eligible for inclusion. Eligible interventions could be of any dose, from any source and delivered in any form. Some of the included studies evaluated specific doses of some form of omega-3 fatty acid; others measured omega-3 intake using food questionnaires (over varying time periods) and took fish, shellfish, or specified vegetable intake (defined variously) as a proxy measure of omega-3 fatty acid intake.

Participants included in the review
Studies of populations or sub-populations of any age and with any of the following eye conditions were eligible for inclusion: degenerative diseases of the retina (macular degeneration and retinitis pigmentosa); vascular diseases of the retina (retinal vein and retinal artery occlusions); vascular diseases of the retina in people with diabetes; and cataracts. The review graded studies according to their applicability to the population of otherwise healthy North Americans (or similar) from level I for the highest applicability to level III for the lowest applicability.

Outcomes assessed in the review
Studies that evaluated at least one relevant clinical outcome were eligible for inclusion. The included studies assessed the following outcomes: prevention and the slowing of progression of various stages of age-related macular degeneration (ARMD) using self-report, photography, review of medical records, fundoscopy examination and angiography, macular photography and single-eye fundus photography; slowing of the progression of retinitis pigmentosa; slowing of the progression of proliferative retinopathy and clinically significant macular oedema in patients with diabetic retinopathy; prevention and slowing of the rate of progression of age-related cataracts; and adverse effects.

How were decisions on the relevance of primary studies made?
Two reviewers selected the studies and resolved any disagreements through consensus, with the aid of a third reviewer if required.
Assessment of study quality
Two reviewers assessed validity using specified criteria for each study design (e.g. Jadad scale for RCTs, Newcastle Ottawa for case control studies); the criteria were reported in full. Study quality was then classified from A for the highest quality to C for the lowest quality.

Data extraction
Two reviewers independently extracted the data onto an electronic form. A third reviewer verified the data. For some individual studies, relative risks (RRs) with 95% confidence intervals (CIs) or levels of statistical significance were presented for some outcomes.

Methods of synthesis
How were the studies combined?
The studies were grouped by type of eye disease and combined in a narrative, with greater weight given to evidence from prospective and controlled studies. Each study was described in the text and additional descriptive information was tabulated.

How were differences between studies investigated?
Differences between the studies were discussed with respect to population, exposure, cointerventions, confounders, outcomes, study quality, applicability and results.

Results of the review
Sixteen studies (n=91,426) were included: 2 RCTs (n=79), 1 controlled before-and-after study (n=20), 4 non-controlled before-and-after studies (n=69), 2 prospective cohort studies (n=72,750), 1 retrospective study (n=2,152), 2 case-control studies (n=874) and 4 cross-sectional studies (n=15,482).

Prevention of ARMD (6 observational studies).
One prospective cohort study (n=72,489) reported no significant association between the intake of individual omega-3 fatty acids, white-meat fish or dark-meat fish and ARMD. It found that eating tinned tuna (RR 0.61, 95% CI: 0.45, 0.83) or all fish (RR 0.65, 95% CI: 0.46, 0.91) and eating any type of fish more than four times a week (RR 0.65; 95% CI: 0.46, 0.91) compared with eating fish three or fewer times per week were associated with a significantly reduced risk of ARMD using multivariate analysis. One cross-sectional study (n=3,654) reported eating fish one to three times per month was associated with a significantly reduced risk of late ARMD compared with eating fish less than once a month, in an adjusted analysis. The study found no significant association between fish intake and a reduced risk of early ARMD.

Two case-control studies (n=21 and n=853, respectively), 1 retrospective study (n=2,152) and 1 cross-sectional study (n=7,883) reported no significant association between fish intake and early or late ARMD.

Slowing of progression of ARMD (1 RCT).
One RCT (n=35) reported a significantly shorter recovery time in patients who received photodynamic therapy plus antioxidant/polyunsaturated fatty acid compared with photodynamic therapy alone at 20 days, but not at 40 or 60 days.

Progression to advanced form of ARMD (1 prospective study).
One prospective study (n=261) reported no significant association between fish intake and advanced ARMD.

Progression of retinitis pigmentosa (1 RCT, 1 comparative before- and-after study and 2 non-comparative before-and-after studies).
One RCT (n=44) reported a non-statistically significantly lower loss of cone function and rod electroretinography (ERG) loss in patients allocated to docosahexaenoic acid (DHA) compared with placebo, but no significant difference...
between treatments in visual fields, acuity and dark adaptation. Fundal photography showed that progression was significantly less in patients allocated to DHA compared with placebo.

One controlled before-and-after study (n=20 enrolled, n=16 analysed) reported significant improvements in visual acuity in the 16 patients with follow-up data allocated to either lutein or lutein plus omega-3 fatty acids plus vitamin B plus enzymes.

One report of 2 small uncontrolled before-and-after studies (n=6 in total) reported no significant change in ERG results.

Progression of proliferative retinopathy and clinically significant macular oedema in patients with diabetic retinopathy.

One non-comparative before-and-after study (n=48) reported improvements in the number of functioning capillaries, a decrease in presumed vitreous permeability to fluorescein dye, and a reduction in the visual acuity factor in the photostress test. However, the results data were sparse and difficult to interpret.

Prevention and slowing of the rate of progression of age-related cataracts (2 cross-sectional studies). One cross-sectional study (n=2,900) reported that omega-3 plus omega-6 consumption (using broccoli/spinach consumption as a distant proxy measure) was associated with cortical but not nuclear cataract. One cross-sectional study (n=1,045) reported no significant association between omega-3 consumption, obtained from food or oils from fish or seafood, and nuclear cataract.

One non-comparative before-and-after study (n=15) reported that 9 of the 14 patients with pre-existing cataract showed improved vision, measured using Landolt's rings, associated with DHA.

Adverse effects.

One RCT (n=44) reported no withdrawals in patients due to adverse effects. Six patients allocated to placebo and 4 patients allocated to an omega-3 fatty acid-containing intervention reported short-term minor adverse effects.

**Authors' conclusions**

There was insufficient evidence to draw firm conclusions. Further research is required.

**CRD commentary**

The review addressed a clear question that was defined in terms of the intervention, participants and outcomes; the inclusion criteria for the study design were broad but this appeared appropriate given the limited evidence identified. Several relevant sources were searched and attempts were made to minimise publication and language bias. Validity was evaluated using specified criteria and the limitations of individual studies were discussed. Adequate information about the included studies was provided. Methods were used to minimise reviewer errors and bias in the study selection, validity assessment and data extraction processes. In view of the diversity amongst the studies, a narrative synthesis that took account of study quality was appropriate. This was a well-conducted review and the authors' cautious conclusion reflects the limited evidence from a small number of largely observational studies.

**Implications of the review for practice and research**

Practice: The authors stated that there was insufficient evidence to make clinical recommendations.

Research: The authors stated the need for further research into secondary prevention of advanced forms of ARMD. An adequately powered RCT is required to compare omega-3 supplementation with placebo. Specific doses of purified DHA in capsule form are required to standardise treatment, but preliminary uncontrolled trials are needed to determine the appropriate dose and type of omega-3 fatty acid and duration of intervention. Research should take account of background dietary omega-3 intake, the omega-3 to omega-6 ratio and other potential confounders.

Observational studies are required to examine the relationship between omega-3 exposure and the onset and
progression of different subtypes of retinitis pigmentosa, and to identify potential interventions to be tested in RCTs. Prospective observational studies are required to examine the relationship between omega-3 fatty acids and diabetic retinopathy using significant macular oedema as the main outcome. Prospective cohort studies are required to examine the relationship between a clearly specified omega-3 exposure and cataract development and progression from mild to severe, measured using regular assessment of the lens; studies should stratify participants by type of cataract.

Preliminary observational studies are required to examine the relationship between omega-3 fatty acids and retinal vein/artery occlusion.

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