Fish oil therapy for IgA nephropathy: efficacy and interstudy variability

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Authors' objectives
To assess the efficacy of fish oil therapy for immunoglobulin A (IgA) nephropathy.

Searching
MEDLINE was searched from 1966 to 1995 and the references from published articles were examined.

Study selection
Study designs of evaluations included in the review
Controlled studies of which three were randomised (two double-blind), one was not, and patient allocation could not be determined in the other. The duration of the treatment ranged from 0.5 to 1.7 years.

Specific interventions included in the review
Omega 3 fatty acids (fish oils).

Participants included in the review
Patients with IgA nephropathy, with serum creatinine levels between 1.1 and 2.8 mg/dL, were included.

Outcomes assessed in the review
The reciprocal of serum creatinine concentration, and the clearance rate of creatinine and the Cr-EDTA (chromium-ethylenediaminotetracetic acid) marker, were assessed.

How were decisions on the relevance of primary studies made?
The author does not state how the papers were selected for review, or how many of the reviewers performed the selection.

Assessment of study quality
The studies were weighted by the length of follow-up and the number of measurements of renal function. The author does not state how the papers were assessed for validity, or how many of the authors performed the validity assessment.

Data extraction
The study outcomes were converted into effect sizes. An academic nephrologist (blinded to the question) was asked to rank the most reliable outcomes for IgA nephropathy. In studies where the renal function was measured by more than one method, the effect size was calculated using the single method ranked most reliable.

Methods of synthesis
How were the studies combined?
The effect sizes were combined by a random-effects model. The effect size weights were calculated as the inverse of each study's variance, adjusted for length of follow-up and the number of measurements of renal function.

How were differences between studies investigated?
Heterogeneity of treatment effects was measured using the Q statistic. Unexplained variance between studies was calculated as Q minus (k minus 1), where k was the number of studies. Correlations between the effect size and the following were calculated: the duration of treatment; the dose of eicosapentanoic acid and docosahexanoic acid; the inverse of the mean, initial serum creatinine concentration; and the natural logarithm of the mean, initial, daily urinary protein excretion. These were calculated using weighted regression under an assumption of mixed effects. The
statistical significance of outlier results was tested by contrasting individual study results with the mean of all other studies.

**Results of the review**
Five studies (202 patients) were included.

Two of the 5 studies had positive results for treatment with fish oil therapy, whilst 3 had negative results.

Forty-four per cent of the between-study variance could be attributed to differences in the follow-up times and, less significantly, the number of renal function measurements.

Combining the results, and accounting for the between-study variance by weighting the studies, gave a mean effect of +0.25 (standard deviation 0.23), indicating that treatment was superior to control. The combined results were, however, not statistically significant, although the calculated probability of at least a minor beneficial effect was 75%.

The mixed-effects regression suggested that fish oil therapy may be more effective among individuals with more proteinuria.

**Authors' conclusions**
The published literature did not prove that fish oil therapy is effective for IgA nephropathy.

**CRD commentary**
This review highlights the little research that has been undertaken in this area, and which is generally of a poor quality. The statistical methods employed in the review were extensive and well described, but the poor quality of the primary studies limited their use.

The literature search for the studies was vague, there was no indication as to whether the search was restricted by language, and the search terms were not given. Limiting the search to a single database may have missed relevant articles; this is potentially an important methodological weakness since it would require only a few additional studies to overturn the results of this review (only five studies were included, each with a relatively small sample size).

The variance between the studies in this review occurred as a result of the open inclusion criteria. However, more stringent criteria would have seriously restricted the number of studies included. The reason for between-study variance was fully explored.

**Implications of the review for practice and research**
The author states: ‘An additional placebo controlled trial is warranted. A sample size calculation indicated that such a trial should be larger than those to date or should attempt to increase the treatment effect, perhaps by treating for more than 2 years or enrolling more severely proteinuric individuals’.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.