Treatment of hypertriglyceridermia with omega-3 fatty acids: a systematic review

Lewis A, Lookinland S, Beckstrand RL, Tiedeman ME

CRD summary
This review concluded that the limitations of the available trials made it difficult to draw firm conclusions about the efficacy of long-chain omega-3 fatty acids, in the treatment of hypertriglyceridermia, in otherwise healthy people. The review had some limitations, but the authors' cautious conclusions reflect the evidence presented and seem appropriate.

Authors' objectives
To assess the effectiveness of omega-3 fatty acid supplements, for the treatment of mild-to-moderate hypertriglyceridermia.

Searching
Eight databases, including EMBASE, PubMed, CINAHL and The Cochrane Library, were searched for studies published in English, from 1994 to February 2003. Search terms were reported. Reference lists of included studies were searched, and their authors were contacted to identify additional studies.

Study selection
Eligible studies evaluated the effects of the long-chain omega-3 fatty acids, eicosapentaenoic acid or docosahexaenoic acid, at doses of 3g per day or more, for people with total triglyceride levels of over 150mg/dL, or total cholesterol of over 200mg/dL, or both. It appears that inclusion was limited to randomised controlled trials (RCTs). Trials were excluded if participants had secondary hypertriglyceridermia, coronary heart disease, diabetes, or various other conditions.

The included trials evaluated omega-3 fatty acid doses ranging from 3.4 to 4g per day. Most trials were placebo controlled, and most participants (83%) were male. In most cases the type of hyperlipidaemia was not reported. One trial was completed in the UK.

The authors did not state how many reviewers selected studies for inclusion.

Assessment of study quality
Trial quality was assessed by two independent reviewers, using the Boyack and Lookinland Methodological Quality Index, which comprised 26 questions on study design, methods and analysis. Disagreements were resolved by consensus. The results were expressed as percentages, with higher values reflecting higher quality.

Data extraction
The data on changes in lipid levels were extracted and expressed as percentages. It was unclear whether these were differences between groups or changes from baseline in the intervention groups. Lipid levels in millimoles per litre were converted to mg/dL by dividing by 0.0259 for cholesterol and 0.0113 for triglycerides.

The authors did not state how many reviewers extracted data for the review.

Methods of synthesis
A narrative synthesis was presented. Average changes in triglycerides, total cholesterol, and other lipids, across studies, were calculated.

Results of the review
Ten RCTs with 606 participants were included. The average quality score was 36% (range 26 to 54). Follow-up ranged from four to 16 weeks. Limitations included a lack of a power calculation, no intention-to-treat analysis, no report of blinded outcome assessment, and no control for dietary omega-3 fatty acid intake.

Nine of the 10 trials reported a significant decrease in triglycerides with eicosapentaenoic or docosahexaenoic acid (average 29%; range 16 to 45). Three trials reported significant decreases in total cholesterol (average 9.3%), but the
other seven reported no significant effects.

The results for high-density lipoprotein, low-density lipoprotein, and very low-density lipoprotein were reported. There were some discrepancies between figures reported in the text and those in the abstract.

**Authors' conclusions**
The limitations of the available trials made it difficult to draw firm conclusions about the efficacy of long-chain omega-3 fatty acids, in the treatment of hypertriglyceridaemia.

**CRD commentary**
The review question and inclusion criteria were broadly clear. The search covered a range of relevant sources. The restriction to reports in English meant that some relevant studies could have been omitted. It was unclear whether study selection was done in duplicate, to minimise the risk of error and bias.

Trial quality was assessed in detail, and the results were used in the synthesis; quality was generally low. A narrative synthesis was presented. The synthesis methods were not reported and it was unclear why the authors did not attempt a meta-analysis.

Overall the review had some limitations, but the authors' cautious conclusions reflect the limited evidence and seem appropriate. It should be noted that the findings referred to otherwise healthy people and not to those with conditions like heart disease or diabetes.

**Implications of the review for practice and research**
**Practice:** The authors stated that omega-3 fatty acids were not recommended, in place of lipid-lowering medications, to treat secondary hypertriglyceridaemia. This implication did not follow directly from the review, which did not examine lipid-lowering medication.

**Research:** The authors stated that large RCTs, stratified by type of hyperlipidaemia, were required. They recommended trials of women and patients from ethnic minorities, with high triglyceride levels.

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