Reviewer's report

Title: Effects of an open-label pilot study with high-dose EPA/DHA concentrates on plasma phospholipids and behavior in children with attention deficit hyperactivity disorder.

Version: 1 Date: 19 April 2007

Reviewer: Julian Bailes

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General
The one-arm pilot study by Sorgi et al examines dietary supplementation with high dose Omega-3 oils in nine children with attention deficit hyperactivity disorder (ADHD). Two primary outcome criteria were evaluated, changes in fatty acid levels and ADHD behavioral criteria. Fatty acid levels were determined at baseline, four weeks and 8 weeks following initiation of supplementation, with calculated ratio of arachadonic acid (AA) and eicosapentaenoic acid (EPA) as the primary endpoint. Supplementation dosages were altered at four weeks if the calculated ratio was less than 1.5; five of the nine participants required dosage reductions. ADHD behavioral criteria were evaluated by a psychiatrist who was blinded to AA:EPA ratios and to supplementation compliance. The ADHD Symptom Checklist SC-4, the four primary components, and Clinical Global Impression Scale (CGIS) were used to quantify behavioral changes.

The diagnosis and treatment of ADHD is of major concern to clinicians, educators, and parents. This small study reviews the mixed results of previous attempts with Omega-3 supplementation, and evaluates high dose supplementation as an alteration of this treatment paradigm. The study finds that supplementation results in a statistically significant reduction in the ADHD SC-4 component scores at 8 weeks. Additionally, a significant correlation is found between the decrease in AA:EPA ratio and the CGIS score. These results warrant a large prospective randomized placebo controlled trial of Omega-3 supplementation as an adjunctive therapy in the treatment of ADHD.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. The use of the term significant should be limited to statements with statistical significance and p value < 0.05. Page 7, line 18

2. The first paragraph of the results section details the method used to adjust supplementation quantities based on AA:EPA ratio. This should be moved to the methods section. Also, it is unclear if the method of dosage changes was established prior to initiation of the study.

3. No data is presented regarding the number of participants with an AA:EPA ratio less than 1.5 at the 8 week point.

4. The selection of target AA:EPA ratio > 1.5 was selected to avoid adverse events, what are the most common specific adverse events that are correlated with an AA:EPA ratio less than 1.5?

5. Compliance with treatment is described as greater than 100% increase in EPA and DHA levels. However Figure 1 would suggest that 3 of 9 participants were not compliant as demonstrated by AA/EPA ratio. Was criteria for determining compliance established prior to initiation of the study; if so this should be addressed in the methods section.

6. Percentages of mean AA:EPA ratio (Page 7, line 9) decline and relative increase of the mean from 4 to 8 weeks (Page 7, line 12) are presented. The validity of the accuracy of these percentages are difficult to determine as the values have high SD (presumably due to inclusion of noncompliant participants). Further, the percent change in the median values may be more reprehensive of actual changes in the compliant
7. Table 3 presents data suggesting continued improvement in 3 of 4 ADHD SC-4 scores from 4 to 8 weeks and improvement in CSI score from 4 to 8 weeks despite the majority of participants having a decrease in the supplementation dosages.

8. Correlation between AA:EPA ratio and CGIS is presented. Was correlation analysis performed between AA:EPA ratio and the ADHD SC-4 scores?

Discretionary Revisions (which the author can choose to ignore)

**What next?:** Accept after minor essential revisions

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.