Fish oil supplementation improves docosahexaenoic acid status of malnourished infants

Ella N Smit, Esther A Oelen, Ejaz Seerat, E Rudy Boersma, Frits A J Muskiet

Abstract

Aim—To investigate whether the low docosahexaenoic acid (DHA) status of malnourished, mostly breast fed, Pakistani children can be improved by fish oil (FO) supplementation.

Methods—Ten malnourished children (aged 8–30 months) received 500 mg FO daily for nine weeks. The supplement contained 62.8 mol% (314 mg) long chain polyunsaturated fatty acids of the ω3 series (LCPUFAω3) and 22.5 mol% (112 mg) DHA. Seven FO unsupplemented children served as controls. Red blood cell (RBC) fatty acids were analysed at baseline and at the study end.

Results—FO supplementation augmented mean (SD) RBC DHA from 2.27 (0.81) to 3.35 (0.76) mol%, without significantly affecting the concentrations of other polyunsaturated fatty acids (LCPUFAω6). Unsupplemented children showed no RBC fatty acid changes. One FO supplemented child with very low initial RBC arachidonic acid showed a remarkable increase from 4.04 to 13.84 mol%, whereas another with high RBC arachidonic acid showed a decrease from 15.64 to 10.46 mol%.

Conclusion—FO supplementation improves the DHA status of malnourished children. The supplement is apparently well absorbed and not exclusively used as a source of energy.

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Keywords: erythrocyte; fish oil; long chain polyunsaturated fatty acids; malnutrition

Essential fatty acids (EFAs) constitute a group of fatty acids that cannot be synthesised de novo. Long chain polyunsaturated fatty acids (LCPUFAs; containing at least 20 carbon atoms and at least three double bonds in the methylene interrupted configuration) derive either from the diet or from desaturation–chain elongation of the two parent EFAs linoleic (18:2ω6; LA) and ω3-linolenic (18:3ω3; ALA) acids. LCPUFAs are structural components of cell membrane phospholipids and precursors of eicosanoids. They play important roles in the development of the central nervous system, including the retina. Postnatal docosahexaenoic acid (22:6ω3; DHA) status is, for example, related to visual acuity and neurodevelopment, whereas arachidonic acid (20:4ω6; AA) has been associated with pre- and postnatal growth.

In a previous study we found very low erythrocyte (RBC) DHA concentrations in malnourished, mostly breast fed 4–56 month old Pakistani children. A low breast milk LCPUFAω3 content was identified as the major cause of their poor DHA status. Apart from low intake, poor PUFA status of malnourished children may also derive from malabsorption, impaired desaturation and elongation, peroxidation of PUFA, and the use of PUFA as an energy source via β oxidation. Many studies have shown that fish oil (FO) supplementation increases DHA content of many blood compartments, including RBC and plasma lipid fractions. It is, however, unknown whether this also applies to malnourished children, as they may have poor fat absorption, or use the supplement as an energy source. In the present study we supplemented 10 malnourished Pakistani children with 500 mg FO daily for nine weeks and investigated whether it improved their DHA status, as derived from their RBC fatty acid composition. Seven unsupplemented counterparts served as controls.

Subjects and methods

SUBJECTS, SUPPLEMENT, AND STUDY DESIGN

Seventeen infants were recruited from the Nutrition Rehabilitation Center of the Pediatric Department, Federal Government Services Hospital, Islamabad (Pakistan). Anthropometric, demographic, socioeconomic, and clinical data were documented. They were classified according to local growth charts, provided by the WHO. Grades 2 and 3 malnutrition were defined as weight for age below the mean minus two standard deviations (SDs) and three SDs, respectively, using the data from the United States National Center for Health Statistics (NCHS) as a reference. The study conformed to local ethical standards and the Helsinki declaration of 1975 as revised in 1989.

The children were randomly assigned to receive one 500 mg capsule of FO (Pikasol, Hadsund, Norway) daily for approximately nine weeks (n = 10), or no oil (controls; n = 7). As the capsules proved too big to swallow, they were pierced and the oil was given by spoon. As stated by the manufacturer, each capsule contained 1.5 IU vitamin E. Table 1 provides details of the fatty acid composition, as established by us. The daily intakes corresponded with 190 mg eicosapentaenoic acid (EPA), 112 mg DHA, and 10 mg AA. EDTA anticoagulated blood (2.5 ml at most) was taken in an undefined metabolic state at base-
Fish oil supplementation during malnutrition

Table 1  Fatty acid composition of the fish oil capsules

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<tbody>
<tr>
<td>18:3ω3</td>
<td>1.0</td>
<td>6.1</td>
<td>2.0</td>
<td>37.0</td>
<td>3.8</td>
</tr>
<tr>
<td>18:3ω6</td>
<td>1.4</td>
<td>0.4</td>
<td>0.3</td>
<td>0.2</td>
<td>0.5</td>
</tr>
<tr>
<td>20:4ω3</td>
<td>1.6</td>
<td>1.0</td>
<td>0.1</td>
<td>5.9</td>
<td>9.3</td>
</tr>
<tr>
<td>20:5ω3</td>
<td>73.1</td>
<td>5.1</td>
<td>6.5</td>
<td>9.3</td>
<td>66.1</td>
</tr>
<tr>
<td>22:5ω3</td>
<td>0.14 (0.03) 0.14 (0.05) 0.17 (0.08) 0.26 (0.10)</td>
<td>0.57 (0.09) 0.57 (0.11) 0.60 (0.12) 0.60 (0.14)</td>
<td>3.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2  Characteristics of the malnourished children

<table>
<thead>
<tr>
<th>Age (mth)</th>
<th>Controls (n = 7)</th>
<th>Fish oil (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>8.0 (4.0–10.3)</td>
<td>5.9 (4.3–8.3)</td>
</tr>
<tr>
<td>Grade 2/3grade 3</td>
<td>4/3</td>
<td>3/7</td>
</tr>
<tr>
<td>HD (μV)</td>
<td>104 (73–122)</td>
<td>80 (60–100)</td>
</tr>
<tr>
<td>BRC (%)</td>
<td>4.37 (3.91–5.05)</td>
<td>4.20 (3.02–5.01)</td>
</tr>
<tr>
<td>Infections*</td>
<td>5/7</td>
<td>8/10</td>
</tr>
<tr>
<td>Breast fed</td>
<td>4/7</td>
<td>4/9</td>
</tr>
</tbody>
</table>

Data presented as mean (SD) and are expressed as mol% (mol/100 mol). For abbreviations see Table 1. Controls received nutritional rehabilitation for 9.7 weeks (range 8–16); the fish oil group was supplemented with 500 mg fish oil (see Table 1) daily for 9.1 weeks (range 7–12).

Table 3  Erythrocyte fatty acids of fish oil supplemented children and controls

<table>
<thead>
<tr>
<th>Fatty acids</th>
<th>Controls (n = 7)</th>
<th>Fish oil (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18:3ω3</td>
<td>0.16 (0.05) 0.15 (0.05)</td>
<td>0.18 (0.12) 0.22 (0.14)</td>
</tr>
<tr>
<td>20:4ω3</td>
<td>0.26 (0.08) 0.28 (0.17)</td>
<td>0.31 (0.33) 0.32 (0.42)</td>
</tr>
<tr>
<td>22:5ω3</td>
<td>1.62 (0.35) 1.52 (0.47)</td>
<td>1.51 (0.75) 2.08 (0.92)</td>
</tr>
<tr>
<td>22:6ω3</td>
<td>2.11 (0.49) 2.07 (0.71)</td>
<td>2.57 (0.81) 3.35 (0.76)</td>
</tr>
</tbody>
</table>

Data represent a selection of fatty acids, expressed in mol% that daily administration of 500 mg FO, containing 62.8 mol% LCPUFA (polyunsaturated fatty acids, expressed in mol% of the reference average weight for age (NCHS) their median weights improved from 53.5% (range 47–68%) to 60% (46–69%) in the FO group and from 63% (57–68%) to 68% (60–70%) in the control group.

Table 3 presents the characteristics of the study group. The mean FO supplementation period was 9.7 weeks (range 8–16). Eight infants in the FO supplementation group and all controls had gained weight at the study end. When expressed as percentage of the reference average weight for age (NCHS) their median weights improved from 53.5% (range 47–68%) to 60% (46–69%) in the FO group and from 63% (57–68%) to 68% (60–70%) in the control group.

The controls did not exhibit RBC fatty acid differences between enrolment and study end.

The blood samples were immediately cooled in melting ice. Haematological indices were measured within 24 hours by means of a Sysmex counter. The remaining volume was centrifuged at 800 g for 10 minutes in a cooled centrifuge. The plasma and buffy coat were removed and the RBCs were washed three times with isotonic saline. The RBCs were finally resuspended to a haematocrit of about 50% and counted again. For the analysis of RBC fatty acids, 200 μl of this suspension was transferred to a 15 ml Teflon stoppered tube, containing 1 mg butylated hydroxytoluene (antioxidant) and 50 μg maragarcic acid (17:0; internal quantification standard). The preserved RBC samples were stored at –20°C and transported to the Netherlands in dry ice. Fatty acid measurements were performed using our previously reported methods—capillary gas chromatography with flame ionisation detection.
show that the FO supplement is apparently well absorbed in malnourished children and that the LCPUFAo3 are not exclusively used as a source of energy under these conditions.

This is to our knowledge the first report to show the effects of LCPUFA supplementation on the RBC fatty acid composition of malnourished children. Koletzko et al. monitored the plasma fatty acid composition of eight recovering malnourished children during treatment with a high energy and high protein diet (including maize porridge, milk, eggs, beans, fish, meat, and vegetable oils). They found a slight improvement of the essential fatty acid status after 14 days treatment without additional LCPUFA supplements.

The most remarkable changes in the RBC fatty acid composition were recorded in a severely malnourished 21 month old, almost exclusively breast fed marasmic girl. Her weight was only 5.5 kg (47% of the reference average) at enrolment and a she had a “dry” skin. After nine weeks FO supplementation she had gained 1.8 kg (to reach 60% of the reference average). There was no clinical evidence that this weight gain was caused by water retention. Concomitantly she displayed an increase of both RBC o3 and o6 fatty acids, mainly at the expense of the sum of the saturated fatty acids (from 65.39 to 48.24 mol%). RBC DHA increased from 0.41 to 2.50 mol%. Surprisingly, a large increase was on account of RBC AA (from 4.04 to 13.84 mol%). It seems unlikely that this increase can be explained by the low AA intake from the supplement (10 mg per day). The RBC 18:2o6/20:4o6 ratio (a parameter of combined activities of Δ6-desaturase, chain elongation, and Δ5-desaturase) decreased from 1.60 to 0.71 mol/mol, while the RBC 20:3o6/20:4o6 ratio (a parameter of Δ5-desaturase activity) did not change. The data of this child suggest a low activity of Δ6-desaturase at enrolment, which subsequently improved during the intervention period. A positive effect of o3 fatty acids on LCPUFAo6 fatty acids has previously been reported by Bjerve et al. They observed an increase of plasma and RBC LCPUFAo6 in patients with o3 fatty acid deficiency following FO supplementation. It was suggested that o6 fatty acids cannot accumulate normally in cell membranes at the condition of low o3 fatty acid supply. In contrast to the above case, a 30% decrease of RBC AA was observed in a 16 month old girl with a relatively high RBC AA level at baseline (from 15.64 to 10.46 mol%). Reduction of plasma and RBC AA concentrations after FO supplementation has previously been noticed in preterm and term infants and adults. The contradictory findings in the two cases may indicate that the effect of FO supplementation on RBC AA concentrations is dependent on baseline RBC AA contents, causing increases at low initial RBC AA status, and decreases at high initial RBC AA status.

We conclude that FO supplementation of malnourished Pakistani children improves their DHA status. Replacement of the presently employed purified FO by the much cheaper cod liver oil (approximately 10% DHA) may give similar results. Another factor in favour of cod liver oil as a supplement would be its high vitamin A and D contents. Malnourished children often have low vitamin A and D status. Further investigations are needed to clarify whether AA supplementation should be recommended in addition to DHA supplementation to prevent any adverse affects on the LCPUFAo6 status that are caused by augmentation of the LCPUFAo3 status.

We would like to thank the nurses at the Nutrition Rehabilitation Center for their help in weighing and selecting the children, Mrs IA Martin is acknowledged for her technical and practical contribution and Mr M Volmer for his statistical analyses.

References


