

Growth and Development in Preterm Infants Fed Long-Chain Polyunsaturated Fatty Acids: A Prospective, Randomized Controlled Trial

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Objectives. A randomized, masked, controlled trial was conducted to assess effects of supplementing premature infant formulas with oils containing the long-chain polyunsaturated fatty acids, arachidonic acid (AA; 20:4n6), and docosahexaenoic acid (DHA; 22:6n3) on growth, visual acuity, and multiple indices of development.

Methods. Infants ($N = 470$) with birth weights 750 to 1800 g were assigned within 72 hours of the first enteral feeding to 1 of 3 formula groups with or without long-chain polyunsaturated fatty acids: 1) control ($N = 144$), 2) AA+DHA from fish/fungal oil ($N = 140$), and 3) AA+DHA from egg-derived triglyceride (egg-TG)/fish oil ($N = 143$). Infants were fed human milk and/or Similac Special Care with or without 0.42% AA and 0.26% DHA to term corrected age (CA), then fed human milk or NeoSure with or without 0.42% AA and 0.16% DHA to 12 months' CA. Infants fed exclusively human milk to term CA (EHM-T; $N = 43$) served as a reference.

Results. Visual acuity measured by acuity cards at 2, 4, and 6 months' CA was not different among groups. Visual acuity measured by swept-parameter visual-evoked potentials in a subgroup from 3 sites (45 control, 50 AA+DHA [fish/fungal]; 39 AA+DHA [egg-TG/fish]; and 23 EHM-T) was better in both the AA+DHA (fish/fungal; least square [LS] means [cycle/degree] \pm standard error [SE; octaves] 11.4 ± 0.1) and AA+DHA (egg-TG/fish; 12.5 ± 0.1) than control (8.4 ± 0.1) and closer to that of the EHM-T group (16.0 ± 0.2) at 6 months' CA. Visual acuity improved from 4 to 6 months' CA in all but the control group. Scores on the Fagan test of novelty preference were greater in AA+DHA (egg-TG/fish; LS means \pm SE, 59.4 ± 7.7) than AA+DHA (fish/fungal; 57.0 ± 7.5) and control (57.5 ± 7.4) at 6 months' CA, but not at 9 months' CA. There were no differences in the Bayley Mental Development Index at 12 months' CA. However, the Bayley motor development index was

higher for AA+DHA (fish/fungal; LS means \pm SE, 90.6 ± 4.4) than control (81.8 ± 4.3) for infants ≤ 1250 g. When Spanish-speaking infants and twins were excluded from the analyses, the MacArthur Communicative Development Inventory revealed that control infants (LS means \pm SE, 94.1 ± 2.9) had lower vocabulary comprehension at 14 months' CA than AA+DHA (fish/fungal) infants (100.6 ± 2.9) or AA+DHA (egg-TG/fish) infants (102.2 ± 2.8). There were no consistent differences in weight, length, head circumference, or anthropometric gains.

Conclusion. These results showed a benefit of supplementing formulas for premature infants with AA and DHA from either a fish/fungal or an egg-TG/fish source from the time of first enteral feeding to 12 months' CA. *Key words:* *premature infants, docosahexaenoic acid, arachidonic acid, long-chain polyunsaturated fatty acids, infant formulas.*