THE INFLUENCE OF MODERATE AND HIGH FORMULA DOCOSAHEXAENOIC ACID ON TERM BABOON NEONATE TISSUE COMPOSITION AND CLINICAL PARAMETERS

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Long-chain polyunsaturated fatty acids (LCPUFA) are indispensable for normal infant growth and development. Docosahexaenoic acid (DHA, 22:6n-3) and arachidonic acid (ARA, 20:4n-6) are LCPUFA that play a critical role in central nervous system development. During the brain growth spurt, rapid accumulation of LCPUFA occurs in the brain and retina. Currently, insufficient evidence exists to determine optimal levels of dietary LCPUFA required during the perinatal period.

In the context of a safety and efficacy study of dietary LCPUFA in baboon neonates, we examined the influence of medium and high levels of formula DHA levels on tissue fatty acid composition and hematological and clinical chemistry measures. Infant formulas were fed from birth to 12 weeks of age: Control (C, no DHA/ARA); 1× LCPUFA (L, 0.32%DHA/0.64%ARA); 3× LCPUFA (L3, 0.96%DHA/0.64%ARA).

At 12 weeks, tissue DHA levels were more sensitive to dietary manipulations than ARA. While DHA in the cerebral cortex increased with higher concentrations of DHA, no differences between L and L3 were detected in the basal ganglia and limbic system. These findings indicate that current levels of LCPUFA in infant formula are not sufficient to optimize DHA levels in the developing cortex.

RBC, hematocrit, hemoglobin, and red blood cell distribution width (RDW) were significantly elevated by formula DHA and ARA. All erythrocyte values were

within accepted normal ranges for infant baboons and no differences were detectable at 12 weeks. These data provide the first indication that dietary LCPUFA may influence hematopoiesis during the first weeks of life and mitigate the precipitous decline in red cell values associated with neonatal anemia.

All clinical chemistry parameters were normal up to 12 weeks of age. Many of the trends observed were similar to those documented in human infant development. No negative effects on growth measures, hematological or clinical assessments were observed between formula groups. These results suggest that levels of DHA higher than presently included in US infant formulas enhance cerebral cortex DHA and may provide additional benefits by improving erythropoiesis. They also provide a basis for interpretation of parallel human infant studies currently underway.

BIOGRAPHICAL SKETCH

Andrea T. Hsieh was born on October 21, 1978 in Elmhurst, Illinois. She was the oldest of four children and spent her childhood and adolescent years in the sprawling suburbs of Chicago. She attended the University of Illinois Urbana-Champaign and received a Bachelors of Science in Biochemistry. In 2000, she moved to Ithaca, NY and joined the Division of Nutritional Sciences at Cornell University.

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ALA, α-linolenic acid (18:3n-3)

ARA, arachidonic acid (20:4n-6)

C, Control formula: DHA (0%w/w), ARA (0%w/w)

CBC, complete blood count

CNS, central nervous system

DHA, docosahexaenoic acid (22:6n-3)

DHGLA, dihomo-γ-linolenic acid (20:3n-6)

DPA, docosapentaenoic acid (22:5n-3, 22:5n-6)

EDTA, ethylenediaminetetraacetic acid

EFA, essential fatty acid

EPA, eicosapentaenoic acid (20:5n-3)

EPO, erythropoietin

ERG, electroretinography

FA, fatty acid

FAME, fatty acid methyl ester

GC, gas chromatography

GI, gastrointestinal tract

GLA γ-linolenic acid (18:3n-6)

IUGR, intrauterine growth restriction

L, LCPUFA intermediate formula: DHA (0.32%), ARA (0.64%)

L3, LCPUFA high formula: DHA (0.96%), ARA (0.64%)

LA, linoleic acid (18:2n-6)

LCPUFA, (≥20 carbons) long-chain polyunsaturated fatty acids

MCV, mean cell volume

MCH, mean cell hemoglobin

MCHC, mean cell hemoglobin concentrations

MDI, Mental Development Index

MPV, mean platelet volumes

MS, mass spectrometry

MUFA, monounsaturated fatty acids

NEC, necrotizing enterocolitis

NHP, non-human primate

PDI, Psychomotor Development Index

RBC, red blood cells

RDW, red blood cell distribution width

SID, Bayley Scales of Infant Development

SFA, saturated fatty acids

VEP, visual evoked potential

VLBW, very low-birth weight

WBC, white blood cell

w/w, weight ratio of FA to total FA