ELSEVIER

Nutrition 24 (2008) 451–457

NUTRITION™

www.elsevier.com/locate/nut

Applied nutritional investigation

Carbohydrate intake is the main determinant of growth in infants born <33 weeks' gestation when protein intake is adequate

Carmel T. Collins, Ph.D.[a,b,e], Robert A. Gibson, Ph.D.[a,c], Jacqueline Miller, B.Sc., Dipl.Nutr.Diet.[a,b], Andrew J. McPhee, M.B.B.S.[f], Kristyn Willson, B.Sc.[d], Lisa G. Smithers, Ph.D[a,b], and Maria Makrides, Ph.D.[a,b,*]

[a] *Child Health Research Institute, Women's and Children's Hospital, North Adelaide and Flinders Medical Centre, Bedford Park, South Australia, Australia*

[b] *Discipline of Paediatrics, The University of Adelaide, Adelaide, South Australia, Australia*

[c] *Discipline of Functional Food Science, The University of Adelaide, Adelaide, South Australia, Australia*

[d] *Discipline of Public Health, The University of Adelaide, Adelaide, South Australia, Australia*

[e] *School of Nursing and Midwifery, University of South Australia, Adelaide, South Australia, Australia*

[f] *Neonatal Medicine, Women's and Children's Hospital, North Adelaide, South Australia, Australia*

Manuscript received March 2, 2007; accepted January 24, 2008.

Abstract

Objective: We investigated the relative contribution of macronutrients to postnatal growth in preterm infants born <33 wk of gestation.

Methods: An audit of daily parenteral and enteral intakes of protein, carbohydrate, fat, energy, and growth (daily weight, weekly length, and head circumference) from birth to discharge home in 138 infants at <33 wk of gestation admitted to an Australian tertiary hospital was done. A mixed-model analysis of variance with random effects (slope and intercept) for subject and controlling for time, sex, gestational age, and total energy was used to determine the relative contribution of macronutrients to growth.

Results: A higher energy intake (kilocalories per day) had a positive influence on growth. With total energy held constant, the contribution of carbohydrate to total energy had a positive relation to weight, length, and head circumference gains; protein had no relation and fat was negatively associated. For every 1% increase in energy from carbohydrate, there was a 2.3-g/d increase in weight (95% confidence interval 1.6–3.0, $P < 0.0001$), a 0.013-cm/d increase in length (95% confidence interval 0.003–0.022, $P = 0.007$), and a 0.015-cm/d increase in head circumference (95% confidence interval 0.009–0.022, $P < 0.0001$).

Conclusion: A re-examination of the macronutrient balance in the diet of preterm infants is required in relation to optimizing growth.

Keywords: Infant; premature; Infant nutrition; Growth

Introduction

The nutritional management of very preterm infants presents an ongoing challenge in determining an approach that optimizes short- and longer-term outcomes. Postnatal growth failure is a common consequence of very preterm birth [1–4] and in turn is associated with adverse neurodevelopmental outcomes [5,6]. Although the ideal postnatal rate of weight gain and body composition for very preterm infants is not known [7], current nutritional management is directed toward achieving a postnatal growth rate similar to

This work was supported by the National Health and Medical Research Council (grant 250322); the Channel 7 Children's Research Foundation of South Australia; National Health and Medical Research Council Senior Fellowships (R.A.G., M.M.); The University of Adelaide, Faculty of Health Sciences Early Career Research Fellowship (C.C.); The University of Adelaide, Divisional Ph.D. Scholarship (J.M.); and the Women's and Children's Hospital Foundation MS McLeod Ph.D. scholarship (J.M.).

* Corresponding author. Tel.: +61-8-8161-6067; fax: +61-8-8161-8228.

E-mail address: maria.makrides@cywhs.sa.gov.au (M. Makrides).

0899-9007/08/$ – see front matter
doi:10.1016/j.nut.2008.01.014

intrauterine growth [8]. This includes attempting to "catch up" the inevitable early postnatal weight loss, with a more aggressive approach to nutritional management [9,10]. Such an approach involves early introduction and advancement of parenteral amino acids and early introduction of enteral nutrition.

There is increasing evidence, on which recent consensus guidelines have been developed, to guide the protein and energy intakes necessary to achieve intrauterine rates of weight gain and protein accretion [11]. However, there is limited evidence on the relative contribution of energy from fat versus carbohydrate to growth in this population [12,13].

As part of a randomized controlled trial investigating the impact of docosahexaenoic acid supplementation on developmental outcome in infants born at <33 wk of gestation, we collected comprehensive information on nutritional intake and growth (weight, length, and head circumference) until discharge from the hospital. Our aim was to characterize the nutritional management in our unit and use the detailed nutritional intake and growth data to investigate the relative contribution of macronutrients to postnatal growth.

Materials and methods

Data source

Data were collected from the first 138 infants enrolled in the randomized controlled trial [14]. The purpose of the trial was to assess whether increasing the level of docosahexaenoic acid in milk (breast milk, through maternal supplementation with tuna oil capsules, or in preterm formula) would improve the developmental outcome at 18 mo of corrected age of infants born at <33 wk of gestation. These infants were recruited from the Neonatal Unit of the Women's and Children's Hospital, Adelaide, Australia from April 2001 to September 2003.

The docosahexaenoic acid intervention had no effect on growth. The conduct of the trial had no impact on any other aspect of the feeding approach and therefore reflected current nutritional practice in the unit. The investigators and all trial personnel remain blinded to treatment allocation.

Enteral intake, weight, length, and head circumference had been prospectively collected by trained research nurses under randomized controlled trial conditions from the time of enrollment (which occurred ≤5 d after enteral feeds commenced) until discharge from the hospital. Enteral intake and anthropometric measurements for the short time before enrollment and all parenteral intakes were collected retrospectively from the daily fluid balance charts, fluid, and drug orders.

Ethics

Ethics approval for this study was granted by the research and ethics committee of the Children, Youth and Women's Health Service (incorporating the Women's and Children's Hospital).

Typical feeding approach

The usual feeding practice for infants enrolled in this study aimed to commence fluid intake at 45–60 mL $\cdot$ kg^{-1} $\cdot$ d^{-1} and increase up to 150 to 160 mL $\cdot$ kg^{-1} $\cdot$ d^{-1} over 5 to 7 d; commence parenteral nutrition (amino acid and dextrose solution) on day of birth, with 1 g $\cdot$ kg^{-1} $\cdot$ d^{-1} of protein and increase to 3 to 3.5 g $\cdot$ kg^{-1} $\cdot$ d^{-1} over 5 to 7 d; commence intravenous lipids on day 2 at 0.5 g $\cdot$ kg^{-1} $\cdot$ d^{-1} and increase to 3 to 3.5 g $\cdot$ kg^{-1} $\cdot$ d^{-1} over 5 to 7 d; and commence enteral feeds when the infant was stable, aiming for days 2 to 3. Enteral feeds were started using unfortified expressed breast milk with fortifier added when the enteral intake reached approximately 100 mL $\cdot$ kg^{-1} $\cdot$ d^{-1}. Feeds were commenced with a 1- to 2-mL bolus every 2 h and increased by 1 mL every 12 to 24 h as tolerated; if bolus feeds were not tolerated, continuous feeds were commenced. Preterm formula (24 kcal/30 mL) was used when breast milk was not available. Medium-chain triacylglycerol (MCT) oil was commenced at 1 mL $\cdot$ kg^{-1} $\cdot$ d^{-1} in four to six divided doses if clinicians considered growth to be suboptimal.

Data collection

Nutritional intake

All enteral intakes were collected prospectively on a daily basis from the time of enrollment in the randomized controlled trial. All parenteral intakes and the enteral intake before enrollment were collected retrospectively using the fluid balance charts and the parenteral fluid and drug-order charts. Each change in intravenous fluid composition and the amount infused were recorded to enable an exact calculation of the constituents. Amounts infused were tallied using the documented hourly intake. For the purposes of this study, the macronutrient content of human milk was based on published values: 1.4 g of protein/100 mL, 3.4 g of fat/100 mL, and 6.6 g of carbohydrate/100 mL [15]. Macronutrient content of formula, human milk fortifier, and parenteral intakes were based on published manufacturers' figures. To calculate energy intake, we used the Atwater factors 4 kcal/g of protein, 4 kcal/g of carbohydrate, and 9 kcal/g of fat. Day-of-discharge intake data were excluded.

A large proportion of women chose to provide breast milk for their babies. Over the length of hospital stay, direct breast feeds therefore made up an increasing proportion of infants' intakes. At 7 d of age, four infants (3%) were having one feed at the breast; by 3 wk of age, 41 (30%) were feeding directly from the breast, with a median of two feeds per day (range 1–3). The quantity of expressed breast milk given by bottle or tube was easily documented; however, we could not ignore the amount an infant would receive from direct breast feeds. To estimate the volume of milk con-