Preterm Human Milk Macronutrient and Energy Composition

A Systematic Review and Meta-Analysis

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KEYWORDS

• Human milk • Breastfeeding • Macronutrients • Preterm

KEY POINTS

- The current systematic review allows the clinician to calculate in a more evidence-based manner the macronutrient and energy intakes of a preterm infant fed his own mother's milk.
- The numbers we provide here for all macronutrients and energy contents are reliable, since they are based on a very large sample of studies which all used the same methodology of pooled 24 hours human milk collection.
- Theoretical calculations on energy and macronutrient intake of preterm infant must be made according to a lactation time specific manner. This is particularly crucial for protein content which is essentially half's itself within 10–12 weeks.

INTRODUCTION

Human milk (HM) is a living and highly dynamic biological fluid that is nutrient specific to adapt to the needs of the growing human infant.[1] Its composition is notoriously variable and depends on several factors, only some of which are currently known.[2–9] For instance, there is striking mother-to-mother variability, which may be caused by differences in dietary habits but might also be related to other environmental or genetic variables.[2] These differences may explain the day-to-day[3] and day-to-night[4,5] variations in HM macronutrient content. Moreover, HM composition also varies as lactation progresses over time[6] or as maternal age increases[7,8] but seems to be unaffected by

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breast size or breast asymmetry.[9] In 1978, it was reported for the first time that gestational age at delivery affects the composition of HM, and it was even argued that preterm HM, with its higher protein content, is more adapted to the nutritional needs of the preterm infant, as if there were physiologic mechanisms that may allow for this to happen.[10] In spite of the differences between term HM and preterm HM, it is now clear that even its own mother's milk alone cannot provide sufficient nutrition to the preterm infant, hence, the need for fortification. In recent years, there have been attempts to tailor the amount of fortification of HM based on bedside analysis of expressed HM, rather than by using calculations based on the known, theoretic content of the milk used. Unfortunately, this strategy requires expensive technology (near-infrared spectroscopy)[11] and is yet to show its superiority in terms of growth outcomes.

This systematic review of the macronutrient and energy composition of preterm HM will help enable the practicing neonatologist make informed and more precise nutritional decisions with regard to feeding the preterm infant.

MATERIALS AND METHODS

This systematic review was conducted in August 2016. Only studies reporting biochemical composition of human preterm milk (<37 weeks' gestational age) were included. One author searched MEDLINE, EMBASE, and Google Scholar using the key words: *preterm*, *prematurity*, *human milk*, *breast milk*, *macronutrients*, *fat*, *lipid*, *protein*, *carbohydrates*, *lactose*, *energy*, and *calories*. The references in studies identified as potentially relevant were also examined. Three authors screened titles and abstracts of all records identified by the search and coded records as "order" or "exclude." All records coded as order were assessed and the final decision was made about which records were ordered as full-text articles. The full texts were read to assess suitability for inclusion based on prespecified inclusion and exclusion criteria. Then the data were extracted independently using a data collection form to aid extraction of information on design, methods, and participants from each included study. Disagreements were discussed until a consensus was reached. If data from a given article were insufficient, the report was excluded from analysis. For the purpose of the meta-analysis, only articles that provided macronutrients and/or energy analysis from a pooled milk sample of a total 24 hours collection were retained, as suggested by Ballard and Morrow.[12] All studies reporting outcomes exclusively on term infants were excluded, but studies that reported preterm and term HM data (and excluded the term *data* from the same papers) were retained.

Analysis

Meta-analyses were conducted in all the studies that reported 1 or more of the following: total energy (kilocalories per deciliter), true protein (grams per deciliter), fat (grams per deciliter) and lactose (grams per deciliter). To help compare our analysis with the previous meta-analysis of Gidrewicz and Fenton[13] we also group the data into the following lactation days: 1 to 3 days (ie, colostrum), 4 to 7 days, week 2, week 3 to 4, week 5 to 6, week 7 to 9, and week 10 to 12. We noted for each study whether analyses were conducted using chemical methods (for protein, lactose, and fat) or near infrared spectroscopy (NIRS) and those calculating energy content using theoretic considerations versus those that used bomb calorimetry. The Minitab Statistical Package, version 16 (Minitab; State College, PA) was used for analyses. Meta-analyses were calculated and expressed as weighted averages with pooled standard deviations. Variation over time of macronutrients and energy was also studied using linear regression. Results are expressed as mean $\pm$ standard deviation, and a *P*-value of less than .05 was deemed significant.