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Abstract

Metabolic Hormone Levels in Infants Fed Formulas with Age-Adapted Protein Concentrations from Birth to 12 Months †

Jibran A. Wali [1,*], J. Manuel Ramos Nieves [1], Corinne A. Zufferey [1], Nicholas P. Hays [2] and Jean-Charles Picaud [3]

[1] Nestlé Research, EPFL Innovation Park, 1015 Lausanne, Switzerland; manuel.ramos@rdls.nestle.com (J.M.R.N.); corinne.ammonzufferey@rdls.nestle.com (C.A.Z.)
[2] Nestlé Product Technology Centre-Nutrition, 1800 Vevey, Switzerland; nicholaspaul.hays@nestle.com
[3] Hôpital de la Croix Rousse, Hospices Civils de Lyon, 69317 Lyon, France; jean-charles.picaud@chu-lyon.fr
* Correspondence: jibran.wali@rd.nestle.com
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Abstract: Background: Breast milk protein content changes with the phases of lactation, whereas it is relatively static in infant formula (IF). The "early protein hypothesis" posits that higher protein intake in infancy increases insulin and IGF-1 secretion, exacerbating weight gain and increasing the risk of cardiometabolic disease. In addition, the FGF-21 hormone also regulates metabolism by enhancing fat oxidation, energy expenditure, and insulin sensitivity. It is strongly induced by dietary protein restriction in adults and is inversely associated with growth rates in infancy. Here, we examined metabolic hormones in infants fed from 0 to 360 days, either standard or sequential IFs with age-adapted protein content, compared to breast-fed infants. Methods: Infants were randomized into two groups: 1. Standard Regimen-1 (n = 233): Standard IF (SIF = 1.85g protein/100kcal; 0–90 days) + Follow-up formula (FuF = 1.50g protein/100kcal; 90–360 days); 2. Age-adapted Regimen-2 (n = 227): New IF (2.50g protein/100kcal; 0–30 days) + SIF (30–90 days) + FuF (90–360 days). Breast-fed infants (n = 231) served as a reference. Plasma insulin, C-peptide, IGF-1, and FGF-21 were measured at 30, 120, and 360 days by ELISA. Results: Insulin and C-peptide concentrations remained similar in Regimen-1 and -2 across 360 days and were significantly higher (up to +64%) than in breast-fed infants. Moreover, both IF regimens showed similar IGF-1 levels that were significantly higher (up to +26%) than breast-fed infants at 120 and 360 days. At 30 days, FGF21 levels were similar in BF and Regimen-1 but significantly lower in Regimen-2 infants. At 120 days, breast-fed infants showed a striking increase in FGF-21 levels (+42 and +74% higher vs. Regimen-1 and -2, respectively). At 360 days, FGF-21 in the breast-fed group remained significantly higher than Regimen-2 but not Regimen-1. These differences in FGF-21 levels were more prominent in males. Discussion: Overall, IGF-1, insulin, and C-peptide concentrations were similar between both IF regimens and significantly higher than in the breast-fed group. In contrast, FGF-21 levels were generally higher in the latter. Interestingly, the lower protein content of SIF in the first month (Regimen-1) brought FGF-21 levels closer to those observed in breast-fed infants. This study highlights FGF-21 as a possible novel mediator underpinning the early protein hypothesis.

Keywords: infant formula; breast milk; growth; protein; hormones; IGF-1; insulin; FGF-21; early protein hypothesis

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Informed Consent Statement: Written informed consent to participate in the study was provided by the participants' parents/legal guardian.

Data Availability Statement: The datasets presented in the abstract are not readily available they will be provided with the publication of the full study results, but will be made available upon reasonable request from the corresponding author.

Conflicts of Interest: Jibran A. Wali, Manuel R. Nieves, Corinne A. Zufferey, and Nicholas P. Hays are employees of Société des Produits Nestlé S.A., the sponsor of the study.