ESPGHAN Satellite Symposium

Current formula concepts for infants and toddlers: what are the scientific facts?

Friday, 8th May 2015
07:30 to 08:30 a.m.
Room E104-E107

Chair:
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Pre-, pro- and synbiotics in infant formulas: efficacy, safety and current recommendations

There is continuous modification of the composition of infant formulas in order to improve health outcomes. With the increasing evidence of the critical role of gut microbiota in physiologic, metabolic and immunologic processes, there has been much interest in strategies to stimulate “healthy” gut microbial patterns in early life. This includes the addition of pre-, pro- and synbiotics to infant formula.
Breast milk is rich in human milk oligosaccharides (HMOs). HMOs are complex non-digestible oligosaccharides, and as such, they stimulate the growth of beneficial microorganisms such as bifidobacteria and lactobacilli in the colon. Oligosaccharides can be fermented by commensal bacteria to produce short-chain fatty acids (SCFAs) that have nutritive and anti-inflammatory effects. SCFAs can also promote gut epithelial integrity. Because of their complex and structural diversity, HMOs cannot yet be commercially produced. With human milk as a model, galactooligosaccharides and/or fructooligosaccharides have commonly been added to infant formula to try to mimic the effects of HMOs.
Breast milk can also provide small amounts of probiotic bacteria. Probiotics have been defined by the FAO/WHO as “ live microorganisms which, when administered in adequate amounts, confer a health benefit on the host”. Generally, different strains of lactobacilli and bifidobacteria have been evaluated in clinical trials targeting infants. When prebiotics and probiotics are combined, the combination is termed synbiotics.
Prebiotics in infant formula have been demonstrated to increase counts of bifidobacteria, and in some studies also lactobacilli. Specific prebiotics may also increase secretory IgA, decrease pH, influence the SCFA pattern and increase stool frequency. Data on the preventative effects of prebiotics on infections and allergic manifestations are conflicting. In the most recent Cochrane review on prebiotics in infant feeds for allergy prevention, meta-analysis of 4 studies (including 1428 infants with a family history of allergic disease) showed a reduction of eczema risk (RR 0.68, 95%CI, 0.48-0.97) but no reduction of any other allergic manifestation. The authors stressed the need for further research, including studies targeting infants with no predisposition for allergic disease, before any recommendation on the routine use of prebiotics can be given. Probiotics have been evaluated in clinical trials for a number of pediatric conditions, but the majority of these studies used probiotic supplements. To date, few studies have assessed the effects of probiotics added to infant formula on clinical outcomes, and the evidence of the effectiveness is therefore limited. There is preliminary evidence that specific probiotics added to infant formula may prevent infections and colic, and reduce the need for antibiotic treatment. There are also data to suggest that specific synbiotics in infant formula may prevent allergic manifestations but confirmatory studies are needed. In otherwise healthy children, the addition of pre-, pro- and synbiotics to formula is considered safe regarding growth and adverse effects. However, new products need to be evaluated on their own merits. As long-term data are scarce, follow-up data are also requested.

Summary

The addition of pre-, pro- and synbiotics can transiently influence gut microbiota composition and their administration to otherwise healthy infants is safe regarding growth and adverse outcomes. To date, synbiotics have not been clearly demonstrated to be superior to pre- or probiotics because the conducted studies are few. Although there is preliminary evidence that specific pre-, pro and synbiotics in infant formula can improve immunological parameters, reduce the incidence of infections and prevent the development of allergic disorders, no firm conclusions on clinical benefits can be drawn. To date, many of the conducted studies have been small, confirmatory studies using the same type of intervention are lacking and the outcome measures have varied, which makes it difficult to translate these findings into clear clinical recommendations. Using nutritional strategies to program gut microbial composition and functionality for improved health outcomes should remain a research priority. Consequently, there is need for adequately powered randomized controlled trials, with predefined and validated outcome measures. Next-generation probiotics and novel oligosaccharides that are more structurally similar to HMOs might also provide a new avenue.

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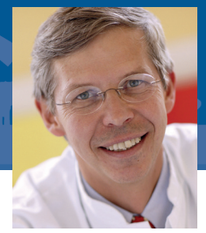

Protein for infants — quantity and quality

Both the amount and quality of protein supplied to infants is of central importance for growth, development, and organ functions and has long-term consequences for later health [1, 2]. A prolonged protein intake clearly below metabolic requirements induces growth faltering, retarded brain development and a secondary immune deficiency with increased infection risks. In contrast, a prolonged protein intake far above metabolic requirements induces increased plasma concentrations of urea and IGF-1, an enhanced renal molar load and risk of dehydration under stress, and an increased risk of high weight gain in infancy and of obesity in later life [3-6]. Therefore, the World Health Organisation and other groups of experts now recommend lower protein intakes in infancy than previously advised [7-9]. With a lower protein supply, it becomes particularly important to provide an adequate protein quality, which is highly dependent on the amounts of bioavailable indispensable amino acids. We studied the effects of a modified infant formula with optimized protein content and quality on growth and energetic efficiency in health infants born at term. To improve protein quality, alpha-lactalbumin was added, which contributes about one fourth of human milk proteins but only 0.15% of cows’ milk protein, and represents a major source of tryptophane and cysteine. In addition, tryptophane and phenylalanine and LC-PUFA were added. In a controlled, double blind randomised clinical trial we included 213 neonates which received up to the age of 120 days either a conventional infant formula (control: 1.5g protein and 67kcal per 100ml) or the modified formula (intervention: 1.3g protein and 67kcal per 100ml)[10]. Breastfed infants were followed as a non-randomized reference group. Protein intake was significantly higher in controls compared to intervention at the ages of 30, 60, 90 and 120 days, and energy intake was higher on days 90 and 120 (controls: 569±152 and 617±169 kcal/d, intervention: 509±117 and 528±123 kcal/d, P<0.01). Complementary feeding was not different. The two randomized groups did not differ in parameters reflecting safety and acceptance and in gain of weight (controls: 28.3±6.5 g/d, intervention: 30.2±6.3 g/d, MW±SD, P=0.06) and head circumference, whereas length gain was significantly higher in intervention (1.0±0.2 vs. 1.1±0.2 mm/d, P=0.02). Breast fed infants had a weight gain of 26.7±6.4 g/d and a length gain of 1.0±0.2 mm/d. Energetic efficiency (gain/100 kcal intake) was lower in the control than in the intervention group for weight gain (5.67±2.21 vs. 6.45±2.01 g/100 kcal, P=0.02) and length gain (0.20±0.08 vs. 0.23±0.08 mm/100 kcal, P=0.04).

Conclusions

The protein modified infant formula studied here is well tolerated, promotes normal growth and seems well suitable and safe for infant feeding. The observed increased energetic efficiency appears to result from the increased content of ?-lactalbumin along with tryptophane and phenylalanine. The results show that the effects of improved protein quality overcome the slight reduction of protein quantity (-0.2g/100ml). Protein quality and quantity are of key importance for the suitability and safety of an infant formula.

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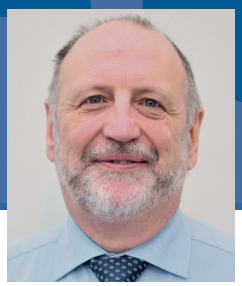

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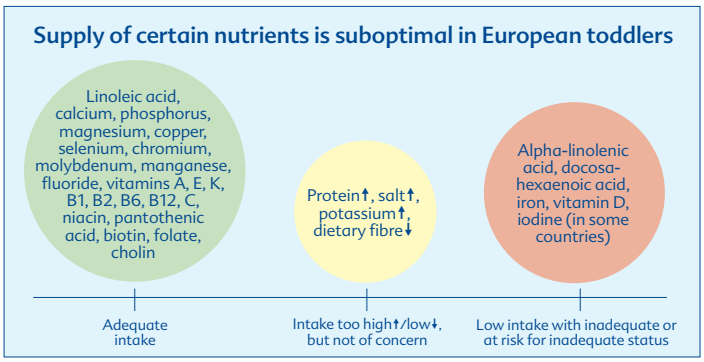
Growing-up milk: just a fancy trend?

Growing-up milks (GUM) are milk-based drinks with low protein, added minerals and vitamins intended for children 12-36 months old.
The statement of the European Food Safety Authority (EFSA) „Growing-up formula: no additional value to a balanced diet", did get a lot of attention in the press and often only the first part of the EFSA-statement was referred to: „Growing-up formula: no additional value according to EFSA". Nutritional requirements of toddlers are age specific. An unbalanced dietary intake during early life has a negative impact on long-term health. All studies on dietary intake in toddlers show that many toddlers do have an unbalanced diet with a high protein intake, high simple carbohydrate intake, low vitamin D and low iron intake. This is also stated in the EFSA-statement as well as the Panel notes that



Source: EFSA Panel on Dietetic Products, Nutrition and Allergies. Scientific opinion on nutrient requirements and dietary intakes of infants and young children in the European Union. EFSA Jorunal 2013; 11: 3408

„particular attention should be paid to ensure the appropriate supply of omega-3-fatty acids, iron, vitamin D, iodine to infants and young children who either have or are at risk of having inadequate status in these nutrients".

A literature search was done using the classic databases (Pubmed, Embase, Cochrane) on the use of GUM in 12-36 months old young children. GUM have a highly variable composition as their marketing is not regulated. Nevertheless, all papers conclude that GUM help to cover nutritional requirements of 12-36 months old infants. Appropriate intakes of macro- and micronutrients in 1-3 year old children have long-term health benefits. Present diets offered to toddlers do in general not meet the requirements. Supplemented foods are therefore helpful, of which GUM is one possibility. One to three year old healthy children should be fed solids for their four main meals (breakfast, lunch, four o'clock snack and dinner), including a variety of vegetables, fruits, and whole grain products. Toddlers should drink 300-500 ml whole milk or GUM. We calculated that in a Belgian population of toddlers a protein intake above the "safe upper limit" was reduced by 30 % by only changing standard milk consumption to GUM. For this purpose, we considered the mean protein content of all commercialised GUM. However, some GUM do not have a reduced protein content. In other words, by restricting this theoretical exercise to "low protein GUM", the effect would have been larger. GUM consumption increases the intake of vitamin D and iron, and lowers the intake of excessive protein. The authorities need to develop recommendations regarding the composition of "growing-up milks" (e.g.: no sweeteners, no taste modifiers, low protein, high iron, high vitamin D).

Take-home-messages:

1. Dietary intakes in 1-3 years old children do not cover dietary micronutrient requirements, and the protein intake is excessive
2. An unbalanced dietary intake during early life has a negative impact on long-term health
3. GUM is not required in a balanced diet of young children, but it is one possibility to contribute to an adequate nutrient intake

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