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Early programming

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Abstract

Nutrition is an important factor for early programming as well as the maternal nutrition is an important determinant in the early nutrition programming during the first 1500-2000 days of life. This term includes beyond the pre and postnatal nutrition, includes 500 days before conception (1500 days) and 500 days after 2 years of age (2000 days), to the beginning of the preschool period. The nutrient supplies to the fetus could initially be modulated by placental transfer with the mothers’ diet, being a “window of opportunity” to modulate the infant growth, the neurodevelopment, and the visual, cognitive and immune functions during the first 1500-2000 days of life to prevent chronic non-communicable diseases as well as food allergies and even mental illness in the offspring.

Key message

Nutrition is an important factor for early programming. The nutrient supplies to the fetus could initially be modulated by placental transfer with the mothers’ diet, being a “window of opportunity” to modulate the infant growth, the neurodevelopment, and the visual, cognitive and immune functions during the first 1500-2000 days of life to prevent chronic non-communicable diseases as well as food allergies and even mental illness in the offspring.
of opportunity” to modulate the infant growth, the neurodevelopment, and the visual, cognitive and immune functions during the first 2000 days of life and also to prevent chronic non-communicable (NCDs) and mental illness, as well as food allergies in the offspring.

Early Nutrition Programming

Infant nutrition could be affected by the pre-conceptional nutritional status of the parents, maternal body composition, gestational weight gain, gestational diabetes, maternal diet during pregnancy, birth mode, birth weight, breastfeeding, complementary feeding, and the environmental factors such as: physical activity, sleep, stress, socio economic status, antibiotics use, and the exposition to smoking, alcohol, heavy metals and endocrine disruptors.

The key nutrients to achieve a balance diet from preconceptional period has been previously recommended by the International Federation of Gynecology and Obstetrics FIGO. Studies have demonstrated the preconceptional maternal diet influence over the offspring DNA methylation; the relationship between the maternal nutritional status, weight gain during pregnancy, gestational diabetes and the maternal food intakes during pregnancy with the offspring’s body composition.
A high energy diet, high in carbohydrates and fats, which is more common in obese pregnant women than in normal weight pregnant women, can induce permanent changes in adipose tissue metabolism and in consequence, linked with an increased risk of obesity and type 2 diabetes in the offspring. This is related to the placenta function to transport nutrients to the fetus and the risk of cardiovascular and metabolic disease in adult life. On their behalf, the appropriate weight gain during pregnancy is associated with lower levels of adiposity in the offspring, as the infants born to overweight and obese women have higher birth weight and higher percentage of fat mass. For instance, a direct association between maternal meat intake in the third trimester of pregnancy and offspring’s fat mass during the adolescence has been found. In the same way, it has been also found that a higher protein intake during the early life is related with the weight gain during the first years of life and this is strongly related with obesity in later life. This can be explained because the exposure to an increased energy and protein supply before birth and in the early infancy as during the complementary feeding period, alters the development of the systems regulating appetite, and could interact to promote excess intake and thus, predispose the infants to weight gain and obesity.

Nowadays, Latin America needs a strategic design of new clinical and practical guidelines to allow the primary care health professional to offer adequate dietary recommendations, not only during the pre-conceptional period and during the pregnancy in order to prevent the excess gestational weight gain, but also during complementary feeding period, to prevent food allergies in early life, and the NCDs and mental illness in the adult life.
Human milk oligosaccharides: current clinical evidence

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Key message

In vitro and observational studies document the prebiotic and protective nature of human milk oligosaccharides (HMOs). Recent technological advances have allowed the supplementation of infant feeding with defined HMOs for non-breastfed infants. The clinical evidence accumulated so far shows potential benefits in microbiota composition, protection from infections, and immune responses in infants.

Abstract

Human milk remains the ideal form of sole source nutrition for infants in early life. Beyond its nutritional composition, its non-nutritive components play a key role in supporting infant health. Unique among these components are human milk oligosaccharides (HMOs), which are particularly high in amount and complexity in human compared to other mammalian milks. More than 150 different HMOs, amounting to 10-15 g/L of milk have been identified so far.
In vitro and animal studies have documented a number of physiologic and clinical effects of HMOs. Amongst the best described is the prebiotic effect of several HMOs, which promote the growth of certain bifidobacteria. In addition, several HMOs have been shown to have antiadhesive and antimicrobial effects towards pathogens including bacteria and viruses, which may in part explain the lower incidence of intestinal, respiratory and urinary tract infections in breastfed compared to formula-fed infants. Animal and invitro studies have also shown a direct effect on modulation responses of immunocompetent cells at a gut mucosal and systemic level. Certain HMOs have been shown in vitro to block norovirus from binding to histo-blood group antigens, inhibiting rotavirus infectivity in animals, and reducing *E. histolytica* attachment or intestinal cell destruction.

The most abundant HMO is 2 fucosyl lactose (2’FL), comprising close to 30% of all the oligodaccharide present in human milk. The presence and abundance of this particular oligosaccharide and other fucosylated HMOs varies in human milk depending on the mother’s genetically determined ‘secretor’ or ‘non-secretor’ status, and has allowed comparison of clinical outcomes in infants of these different populations. The presence of 2’FL and its abundance seems to confer an additional level of protection to infants of secretor mothers. In observational studies, higher levels of 2’FL in human milk have been documented to increased levels of bifidobacteria (and not bifidobaterial), lower the risk of diarrheal disease including Campylobacter diarrhea. HIV-infected women with total HMOs above the median for the population studied were less likely to transmit the disease to their infants via breastfeeding. Among HIV-exposed, uninfected children, higher maternal breast milk concentrations of 2-linked fucosylated HMOs were significantly associated with
reduced mortality during, but not after, breastfeeding. Higher levels of fucosylated oligosaccharides have been shown to inversely correlate with the incidence of allergic disease (IgE-associated disease, eczema, and IgE-associated eczema) in C-section infants up to two years of age, not later.

Technological and manufacturing advances have recently opened the possibility of assessing the safety and the clinical effects of supplementation of HMOs to formula fed infants. The clinical evidence accumulated so far, in randomized controlled trials indicate similar effects and potential benefits to those in observational studies. 2’FL and a combination of 2’FL and LnNT appear to have positive bifidogenic effects in intestinal microbiota, to have an immunologic effect, in terms of cytokine profiles, and protection from acute infections in infants. The safety profile of supplemental HMOs from infant feeding has so far been well documented. Further work is needed and is ongoing in better characterization of the various functions HMOs may serve, as well as their application in the clinical setting.
The role of microbiota in functional gastrointestinal disorders

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Abstract

The role of the intestinal microbiota in health and disease has been the focus of intensive research during the two past decades. Healthy gut microbiota consists of many different microbes, but before the age of 3 years, the microbiota has a lower diversity compared to adults. Various chronic gastrointestinal disorders such as functional gastrointestinal disorders (FGID), inflammatory bowel disease, and celiac disease have been associated with perturbations in gut microbiota composition. An imbalance and/or reduced microbial diversity has been associated with a wide variety of FGIDs in children such as colic, irritable bowel syndrome...
(IBS), constipation and diarrhea. Only a few studies reported on microbiota in children with constipation, with different results, which might be caused by the differences in study populations. Multiple risk factors have been linked to functional abdominal disorders, including hypersensitivity to food products, psychological factors such as child abuse, stress, depression and anxiety, genetic factors, and alterations of the gut microbiota. In terms of microbiological differences in children with irritable bowel syndrome compared to healthy children; apparently, they have a significantly greater percentage of $\gamma$-Proteobacteria and reduced Bifidobacterium and Verrucomicrobiunm members. Although the pathophysiological mechanisms underlying infant colic remain largely unclear, several studies were performed to investigate the difference in gut microbiota between healthy infants and infants with colic, showing that children with colic might have less beneficial bacteria like bifidobacteria and lactobacilli. Other studies found that the presence of certain intestinal microorganisms was associated with increased amounts of crying in infants up to 3–4 months of age, including microorganisms belonging to the Proteobacteria phylum. The relative abundance of microorganisms belonging to the genera Escherichia and Klebsiella was increased in stool samples from infants with colic. These alterations indicate that a state of intestinal dysbiosis (defined as a microbial imbalance in the gastrointestinal tract) might play a role in the expression of infant colic symptoms. Because of this dysbiosis, crying behavior would be facilitated by the microbiota–gut–brain axis, affecting central and enteric neuronal function, such as detection of pain in infants. Intestinal dysbiosis might contribute to colic symptoms by increased fermentation of lactose, carbohydrates and proteins, resulting in increased gas production. Increased gut
permeability might facilitate increased low-grade gut mucosal and systemic inflammation. Low-grade gut inflammation can result from elevated amounts of Gram-negative bacteria. Several mechanisms of action are proposed for the effectiveness of probiotics in reducing infant crying, including the reduction of gut inflammation or the increase production of short-chain fatty acids, improving epithelial barrier function. A systematic review and meta-analysis, pooling results from seven RCTs, concluded that *L. reuteri* DSM 17938 could be considered in the treatment of infant colic, mainly breastfed infants. Other probiotic strains have also been investigated in the clinical trial setting. In one study in infants with colic, *L. rhamnosus* GG found no difference in daily crying time between infants receiving placebo or probiotic.

A large RCT including 589 healthy full-term breastfed and formula-fed infants evaluated the prophylactic use of *L. reuteri* DSM 17938 in preventing functional gastrointestinal disorders. Daily administration of *L. reuteri* DSM 17938 from birth reduced crying time by ~51 min per day at 1 month and ~33 min per day at 3 months compared with infants receiving placebo. This study also shows that the intervention group showed less regurgitations and more adequate quantity of bowel movements compared to placebo group.

In conclusion, we currently have some information that suggests that dysbiosis exists to a greater or lesser extent in gastrointestinal functional disorders. The use of certain probiotic strains, specifically *L. reuteri* DSM 17938, as a way to modulate existing dysbiosis, may be useful.
Nutrition in toddlerhood: challenges and opportunities

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Abstract

Nutrition in children after the stage of breastfeeding has become a dark box in which several confusing factors may be playing a relevant role. In pediatric groups, the identification of the child in English includes the older infant and the preschooler, who for identification, in Mexico at least, has been categorized as the young toddler.

This stage in which the complementary feeding has already been completely established and the digestive maturation no longer represents a major replica, resulting both for the clinician
and for the parents a vein of important information. The focus on other essential components of neurodevelopment seems to distract attention in the child’s feeding conditions.

Gait stabilization, verbalization and achievement of motor development goals seem to be the most relevant component of the interaction with the child. An otherwise fun and fundamentally enriched stage of endless physical and emotional experiences. The process of language development, together with the complex processes of expressing affections, likes, dislikes, makes food quality and diet properties a secondary priority.

In this stage there’s also a conflict between the expectations of growth and feeding patterns that parents have in relation with the child. The experience of seeing triple the weight and growing 50% of the height in 12 months, generates a great disappointment in parents who observe the child drastically change their appetite and thereby fall into one of the most common failures in feeding Children, condescension. This is established in a very natural way to see that the child accepts with great pleasure sweetened beverages and foods of low nutritional quality in substitution of healthy foods, which a few months before consumed with pleasure. In the mind of the troubled parents, the transfer of a healthy food, such as milk, can occur, for a wide variety of foods that should be included in the repertoire of the family diet. In Mexico, for example, the complementary feeding that begins in the first year of life has drastically changed by a high consumption of a sweet feeding pattern, low amount of fruits and vegetables and a decreasing consumption of milk and dairy products. This feeding pattern remains with the same characteristics throughout virtually all childhood. Worryingly, this eating pattern involves high calorie intake (almost 250 kcal / day above the daily recommendation), poor intake of iron, vitamin D and other essential nutrients in development. These transgressions in the diet of Mexican preschoolers may largely correspond to the two most prevalent
nutritional conflicts in the Mexican population, iron deficiency anemia and the severe epidemic of overweight and obesity.

In many Latin American countries, the transition from complementary food to real integration into the family diet suffers from many deficiencies in the nutritional content. In Mexico, for example, 50% of babies still use a bottle at 24 months. However, most of these bottles do not contain adequate fortification of iron, vitamin D and calcium. We found that up to 60% of Mexican children 12 to 24 months of age do not achieve their daily goals of iron or vitamin D consumption. The bottle is unfortunately occupied by inadequate substitutes for age-appropriate milks. There is a great variety of drinks with high caloric content and low nutritional value. Among these drinks we will find from juices, soda, to dairy drinks with added sugars.

This difficult transition from ceasing to be a baby to enter the world of young children (toddlers), involves the acquisition of achievements from the motor point of view (both thick and thin), language development, development of emotions, and cognitive development. For parents, these achievements displace in many occasions, those related to good nutrition, including healthy lifestyle habits.

The use of cutlery and achieve attention throughout the time of feeding should be a feeding goal. Similarly, the consumption of simple water in a glass and without spilling is another habit that can be used for the rest of life. Keep a wide variety of fruits, vegetables and whole grains inside the food arsenal. The consumption of these foods in at least 5 servings a day has been shown to be effective in maintaining a diverse and healthy intestinal microbiota. The exercise of consuming them in their most complete forms despite the incomplete and inefficient chewing process at this age is a challenge that clinicians and parents should encourage.
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