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Protective effect of breastfeeding against childhood obesity

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Abstract

Objective: To review the literature concerning the hypothesis that breastfeeding has a protective effect against obesity. The biological plausibility of this hypothesis and the potential mechanisms involved are discussed.

Sources of data: Articles published in indexed scientific journals, books and graduate theses and dissertations. Most articles were obtained from the Medline and Scielo databases using the keywords "breastfeeding," "overweight," "obesity," "children" and "adolescents" for the period between 1980 and 2002. Some articles were identified from the references cited in the first articles.

Summary of the findings: Most studies report a protective effect of breastfeeding against childhood obesity. Some studies found no association between breastfeeding and obesity. One study including a small sample reported greater adiposity in breastfed children. Different definitions of exposure and outcome were used in different studies, making comparison difficult. Metabolic imprinting is suggested as a potential mechanism to explain the association. Behavioral aspects may also be involved.

Conclusion: Breastfeeding seems to have a protective effect against childhood obesity, but this issue still deserves further investigation.

J Pediatr (Rio J). 2004;80(1):7-16: Children, adolescents, overweight, obesity, breastfeeding.

Introduction

A remarkable increase in the prevalence of obesity has been observed in several countries and in different age groups (including the pediatric population) in the last few years.[1-13] In the United States, obesity affects 20 to 27% of children and adolescents.[7] In Brazil, Monteiro et al.[5] reported a prevalence of obesity in children younger than five years of 2.5% among low-income families and 10.6% in economically privileged families. A secular study, conducted in the northeast of Brazil, revealed an upward trend of overweight and obesity prevalence rates in male adolescents in all states comprised by the region, between 1980 and 2000.[13] In Recife, a 17.4% prevalence of obesity was noted in preschool children from high-income families, whereas a prevalence of 10.1% was found in those from low-income families.[14]

The increase in the prevalence of childhood obesity is alarming due to the increased risk of these children becoming obese adults, and due to several obesity-related morbid conditions.

Serdula et al.[15] found a risk at least twice as high for adult obesity in obese children, comparatively to nonobese ones. Around one third of preschool children and half of obese students become obese adults.

The effects of childhood obesity may be observed in the short and long term. Short-term complications include orthopedic disorders, respiratory problems, diabetes, hypertension, and dyslipidemia, in addition to psychosocial disorders. In the long term, a high mortality due to multiple causes and to coronary heart disease has been described for individuals who used to be obese in their childhood or adolescence.[16-25]

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Among the complications caused by obesity, we highlight a recently described entity known as nonalcoholic steatohepatitis (NASH).[26-35] It was initially described in adults, but it has now been observed in children and adolescents.[27-32,35] The prevalence of NASH has increased, probably due to the increase in the prevalence of obesity, and also because health professionals are more alert to its diagnosis.[26] This disease is characterized by its silent development – it may be incidentally diagnosed in asymptomatic children or in those with vague symptoms, such as intermittent abdominal pain – and by its wide variation in nature, that is, it goes from benign cases to cirrhosis, which is potentially deadly.[26,28-32] The treatment options are limited; gradual weight loss seems to be the most effective measure.[30,31,34,35]

As obesity is a chronic disease that is difficult to treat and is associated with various morbid diseases, and whose prevalence has been increasing, special attention should be paid to preventive measures. Simple measures without potential adverse effects and a low cost are particularly appealing. In this regard, several authors have formulated the hypothesis that breastfeeding has a protective effect against obesity, but controversial results have been obtained.[36-53]

In the present study, the authors review the literature on this topic by analyzing several epidemiological studies that investigated a possible relationship between breastfeeding and obesity, as well as studies that demonstrate the biological plausibility of this relationship and that seek to explain the mechanisms that are potentially involved.

Energy balance regulation

Our body's energy balance is regulated by a complex neuroendocrine system, yet not fully understood, which consists of an afferent system, a processing unit in the central nervous system located in the ventromedial hypothalamus, and an efferent system.[54]

The afferent system conveys information on hunger versus satiety and on body energy stores. Afferent signals may be short or long-term and may be generated peripherally or centrally.[54]

Among peripheral hunger signals we have low blood glucose levels, cortisol, and grelin, a recently discovered hormone.[54-56] Grelin is produced in the stomach and was identified in 1999, initially as a growth hormone stimulator and, later, as a regulator of the energy balance. Fasting causes an increase in grelin secretion, while eating reduces it.[54-56] Grelin was already found in umbilical cord blood , but its effects on eating behavior of neonates still have to be clarified.[57]

Peripheral satiety signals include gastric distension, action of nutrients and several hormones, such as insulin, cholecystokinin and peptide YY_{3-36} (PYY_{3-36}), to cite a few.[54,58] PYY_{3-36}, an intestinal hormone, is released after the meals, proportionately to the caloric content of the meal. The infusion of normal postprandial PYY_{3-36} levels significantly reduces the appetite and decreases food intake by approximately 33% during 24 hours.[58]

Identified in 1994, leptin is a long-term peripheral afferent signal. Leptin is mainly produced by adipocytes and informs the hypothalamus about the energy stores available in the adipose tissue.[54,59,60] Leptin inhibits the appetite and metabolic pathways and stimulates the catabolic pathways.[59,60] In addition to the adipose tissue, other sources of leptin have been described, e.g.: liver, stomach, and placenta.[60] Vatten et al.[61] found a positive association between leptin levels in umbilical cord blood and weight and length at birth. Sandoval & Davis,[62] in their review article, reported an integrated regulation between leptin and insulin, suggesting that abnormal leptin levels might be implicated in the pathophysiology of diabetes.

Besides the peripheral signals mentioned here, the ventromedial hypothalamus receives information from other parts of the brain. Dopamine, gamma-amino butyric acid, neurotensin and corticotropin-releasing hormone provide information on stress, state of alert and pain, with an inhibitory effect on appetite. Serotonin and norepinephrine seem to play a key role in inducing satiety. The effect of serotonin on the induction of satiety seems to have a central and also peripheral component, with intestinal secretion of serotonin.[54,63] On the other hand, metenkephalin, orexins A and B, melanin-concentrating hormone and galanin stimulate food intake and energy storage.[54]

Peripheral and central afferent signals reach the neurons of the ventromedial hypothalamus, where they will be integrated by a "central processing unit" designed to promote or reduce food intake and energy expenditure. This central processing unit has an anorexigenic branch, which contains the neurons that express the POMC (proopiomelanocortin) peptide, with its alpha-MSH (alpha-melanocyte-stimulating hormone) cleavage product and the CART (cocaine-amphetamine-regulated transcript) peptide, and an orexigenic branch, which contains the neurons that express NPY (neuropeptide Y) and AgRP (agouti gene-related protein). These two branches compete for melanocortin receptors.[54]

Overfeeding and leptin infusions induce POMC and alpha-MSH syntheses. Alpha-MSH induces anorexia, binding to the melanocortin receptor. CART synthesis also is induced by leptin and reduced by fasting.[54]

NPY is the major orexigenic peptide and has specific receptors. Fasting and weight loss stimulate NPY expression, whereas leptin inhibits it. The AgRP peptide is a competitive melanocortin receptor antagonist, which blocks the binding of alpha-MSH to the receptor, preventing it from inducing satiety.[54]

For Kalra et al.,[64] rhythmicity and synchronism in the secretion of leptin, grelin and NPY are important for the

daily meal pattern. According to these authors, subtle and progressive problems with this mechanism lead to a positive energy balance, causing excessive weight gain and obesity.

The efferent system is concerned with appetite and storage versus energy expenditure. The sympathetic nervous system stimulates energy expenditure, whereas the parasympathetic nervous system stimulates storage.[54] Total daily energy expenditure contains three components: resting energy expenditure (usually represents 50 to 65% of total expenditure), thermogenesis (around 10% of total expenditure) and voluntary energy expenditure (which ranges from 5 to 50% of total expenditure).[54] Bachman et al.[65] showed that rats submitted to ablation of the three types of adrenergic receptors developed obesity, due to a food-induced deficiency in the thermogenic mechanism.

Obesity: multicausality

Obesity is a multifactorial disease in which genetic and environmental factors are involved [7,66-74] (Figure 1). A family trait is noted, which means that children whose parents are obese are at a greater risk of becoming obese.[68] However, evaluating to which extent genetics and environmental factors are implicated is not an easy task, since parents and children often have similar eating habits and physical activity.[68,70,71] Moreover, there is some evidence that genetic factors can modulate the body's response to changes in environmental factors, such as diet and physical activity.[74]

It has already been documented, for instance, that there exists a considerable variation between individuals as to their serum fat levels in response to changes in the amount of fat and cholesterol in the diet. Some individuals are poorly sensitive to changes in their diet, while others have a greater sensitivity.[74]

Interventional studies with monozygotic twins also demonstrate a modulation of genetic response to environmental changes.[74] In a study with 12 pairs of monozygotic twins submitted to a hypercaloric diet, the response in terms of weight gain, increase in body fat and increase in visceral fat varied remarkably between individuals, in which the between-pair variation was greater than the within-pair one. A study with monozygotic twins submitted to a negative energy balance, based on a program of physical exercises, also revealed a greater within-pair agreement as far as variations in weight, body fat, subcutaneous fat and visceral fat were concerned.

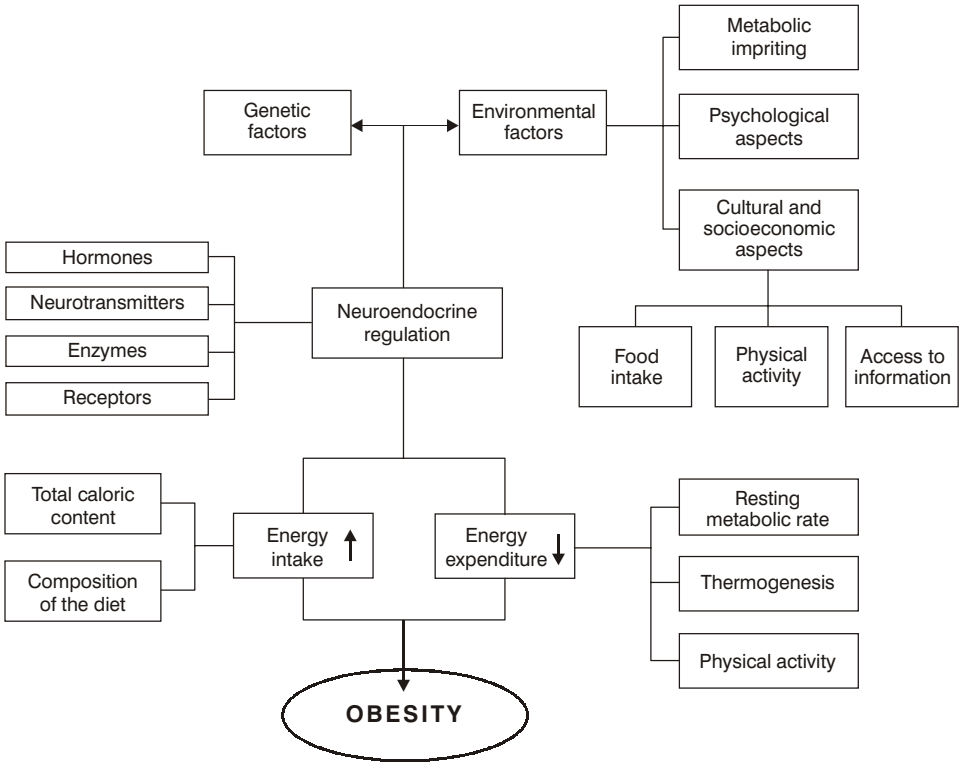

Figure 1 - Causal model for obesity.

If on the one hand there appears to be a genetic modulation of the response to changes in environmental factors, on the other hand, there is some evidence that certain environmental conditions that act during a critical period of development, could cause mutations in the expression of certain genes, as discussed further ahead in "metabolic imprinting."[75,76] An individual's first nutritional experiences are believed to influence his/her susceptibility to certain chronic diseases in adulthood, including obesity.[75-85]

Hoffman et al.[85] reported, for instance, that children with a prior history of malnutrition, classified as stunted, have a deficiency in lipid oxidation, and are therefore at higher risk for obesity. These authors suggest that this could be one of the mechanisms that may explain the increase in the prevalence of obesity in developing countries.

Increased energy intake and reduced energy expenditure have been described as the major causes of obesity.[7,86,87] However, some authors have not found any difference between the energy intake of obese and nonobese individuals. The information provided by the individual about his/her energy intake might not be a valid evaluation parameter.[7,88] The interaction between genetic and environmental factors is another plausible explanation to this fact.[74] In addition to the total caloric content, the composition of the diet is also important, as a diet rich in simple carbohydrates and lipids is a risk factor for obesity.[7,89-91]

Recently, the role of lipids in the etiology of obesity has been argued. Willett[92], in a recent review article, argues that in the United States there has been a considerable reduction in the amount of dietary energy consumed as fat, in the last 20 years, and that during this period, there has been a large increase in the prevalence of obesity. For this author, there is no consistent evidence that a high content of lipids in the diet plays an important role in the etiology of obesity; this author suggests that the effect of confounding variables, including physical activity, might have been responsible for the wrong results in the study of this association. For other authors, however, there is enough scientific evidence for the recommendation of a low-fat diet. Astrup[93], for example, underscores that the three meta-analyses of randomized clinical trials that investigated this issue showed that a 10% reduction in dietary fat causes a remarkable weight loss that is enough to reduce the incidence of diabetes by approximately 50%.

With regard to energy expenditure, several studies have revealed that it tends to be lower in obese individuals, in whom any of its three components may be altered – resting metabolic rate, thermogenesis, or physical activity[7,94,95].

Obesity has been classified as endogenous (secondary to genetic syndromes and endocrinopathies, e.g.: Prader-Willi syndrome, Down's syndrome, hypothyroidism, etc...) and exogenous (caused by excessive energy intake compared to energy expenditure). Currently, endogenous obesity is believed to account for only around 1% of the cases.[96]

However, recent advancements in the understanding of the neuroendocrine regulation of energy balance, of the genetics of obesity and of the interactions between genetics and environment make us believe this classification should be revised in the future and that this rate shall change considerably. Very likely, this low prevalence of endogenous obesity is due to our poor understanding of these phenomena. As new hormones, neurotransmitters, receptors, and genes are discovered, the etiology of obesity assumes another dimension. In the future, patients formerly placed in a single group of obesity (endogenous) may have the cause for their obesity determined at the endogenous level.

Lustig[54] has described childhood obesity as a phenotype of several diseases, most of which have not been identified yet. According to Warden & Warden,[97] approximately 15 chromosomal loci related to weight, body fat, and other obesity-related traits have already been identified in humans and over 90 of these loci have been identified in animal models. According to these authors, seven genes have been identified as the cause of obesity in humans and, in most cases, obesity results from the interaction of multiple genes, and not from the action of a single gene.

Cases of childhood obesity secondary to leptin deficiency have been described. Nonetheless, human obesity is more frequently associated with resistance to leptin than with its deficiency.[97]

MC4R mutations have been regarded as the most frequent genetic cause of obesity in humans.[97] Children with syndromic cases have been described, characterized by obesity, adrenal insufficiency and red hair, attributed to proopiomelanocortin gene mutations, which inhibit the production of alpha-MSH. Alpha-MSH affects hair color by binding to MC1R in the skin and influences food intake and energy expenditure by binding to MC3R and MC4R in the hypothalamus; adrenal insufficiency in these children may be explained by the fact that alpha-MSH consists of the first 13 amino acids of adrenocorticotrophic hormone.[97]

Some authors have suggested an association between MC4R mutations and certain mental diseases characterized by eating disorders and obesity.[98]

Obesity caused by mutation in prohormone convertase 1, an enzyme that converts POMC into its components, including alpha-MSH, also has been identified.[97]

The identification of multiple causes of obesity may contribute to the future implementation of safer, efficient, and personalized treatments for obese individuals.[97]

Breastfeeding versus obesity: epidemiological studies

The hypothesis that breastfeeding has a protective effect against obesity is not recent. Nevertheless,

controversial results have been found, and the issue is still up-to-date, especially because of the increase that has been observed in the prevalence of obesity.

Different definitions of exposure and outcome hinder the comparison between several studies. In addition, outcome was assessed at different ages. Another important aspect, related to the methodology, and pointed out by Dewey[36] in a recent review article, is that studies which present the outcome as prevalence of overweight and obesity should be highly valued, instead of those which just show mean body mass index. Dewey[36] underscores that breastfeeding possibly reduces both overweight and underweight, which would result in a lower prevalence of overweight, but not in a difference in mean BMI. Therefore, we should concentrate on the right-hand end of the distribution and not on the central trend.

In 1981, Kramer[37] published the result of two case-control studies conducted with adolescents aged between 12 to 18 years in Canada. One of the studies included 639 patients from a clinic for adolescents and the other one consisted of 533 students of a Canadian school; both studies reported a protective effect of breastfeeding against obesity. The adolescents were considered obese when their relative weight exceeded 120% and the measurement of one of the skinfolds (triceps or subscapular) exceeded the 95th percentile or when both exceeded the 90th percentile. The breastfeeding period was considered to have ended when the child was bottle-fed more than once a day. In these studies, a long time elapsed between exposure and outcome, predisposing to a recall bias. In a subsample of approximately 10% of the adolescents, the authors compared the information provided by the mothers on their children's diet in the first months of life, including information supplied by the physician who had followed up the child, and the information matched in all cases. The protective effect of breastfeeding persisted even after the control of confounding variables, such as parental nutritional status, ethnicity and socioeconomic class.

In 1985, Kramer et al.[38] published the results of a prospective cohort study carried out with 462 children, in which the length of breastfeeding was considered to be one of the determinants of weight and BMI at 12 months. In a second publication, these authors reported that the protective effect of breastfeeding persisted when these children were reassessed at 24 months.[39]

Fomon et al.,[40] in a cohort study conducted with 469 children, did not find any difference in adiposity parameters (BMI, triceps and subscapular skinfolds) and in serum cholesterol levels, at the age of eight years, between breastfed and formula-fed children. Some authors claim that some children were not on exclusive breastfeeding, but they do not clearly define the exposure variable, which is a limitation to this study.

Agras et al.[41] reported that breastfeeding for longer than five months was associated with greater adiposity, determined by way of BMI, at the age of six years. This result was obtained from a cohort study, in which the small sample size, worsened by the losses to follow-up, translated into remarkable limitation. Of the 99 patients included in the study, only 54 concluded it.

Zive et al.[42] did not find any association between the length of breastfeeding and adiposity at four years, determined by BMI and the sum of triceps and subscapular skinfold measurements, in a study with 331 children. Birthweight, ethnicity, socioeconomic class, and maternal adiposity (BMI and sum of skinfold measurements) were assessed. Maternal adiposity was the major determinant of adiposity in children.

O' Callaghan et al.[43] did not observe any association between the length of breastfeeding and the prevalence of obesity at five years, in a prospective cohort with 4,062 Australian children. Several variables were taken into consideration, such as BMI, educational level, family income, birthweight, and gestational age.

Wadsworth et al.[44], in a study published in 1999, did not find any significant association between breastfeeding and the prevalence of overweight and obesity at six years, after assessing 3,731 children in the United Kingdom. The authors pointed out that the children in their study had been born in 1946, and that the prevalence of breastfeeding in the United Kingdom, as a whole and within different socioeconomic classes, changed a lot over time.

In a longitudinal study conducted in Sweden with 781 adolescents, Tulldahl et al.[45] described lower prevalences of overweight, defined as a BMI greater than or equal to the 85th percentile, among those children who had been breastfed for longer than three months.

In a cross-sectional study with 9,357 German children aged between five and six years, published in 1999, von Kries et al.[46] found a 4.5% prevalence of obesity among children who had never been breastfed and a 2.8% prevalence among breastfed ones. A dose-dependent effect was observed for the length of breastfeeding, with a 3.8% prevalence of obesity for those children on exclusive breastfeeding for two months, 2.3% for 3 to 5 months, 1.7% for 6 to 12 months and 0.8% for longer than 12 months. Similar results were observed as to the prevalence of overweight. After adjustment for possible confounding factors, breastfeeding persisted as a protective factor against obesity and overweight. Obesity was defined as a BMI above the 97th percentile and overweight as a BMI above the 90th percentile.

The findings of the study conducted by Liese et al.[47] corroborate those found by von Kries. In a cross-sectional cohort study with 2,108 children aged between nine and ten years, from two German cities, Lise et al.[47] observed a lower prevalence of overweight (defined as a BMI greater than or equal to the 90th percentile) among breastfed children, even after the control for confounding variables, such as nationality, number of siblings, and socioeconomic class.

Gillman et al.,[48] in a large study with 8,186 girls and 7,155 boys aged from 9 to 14 years, found a lower risk for overweight in individuals who had been on exclusive or predominant breastfeeding in the first six months of life than in those who had been formula-fed. The protective effect of breastfeeding persisted after the control for several confounding variables. These authors also described a dose-dependent effect, and observed a lower risk for overweight in individuals breastfed for at least seven months comparatively to those breastfed for three months or less. Overweight was defined as a BMI above the 95th percentile.

In a cross-sectional cohort study with 2,565 American children aged between three and five years, Hediger et al.[49] noted that children who had been breastfed showed a lower prevalence of "overweight risk," defined as a BMI between the 85th and 95th percentiles, compared to those who had never been breastfed. However, the authors did not observe any protective effect against obesity, defined as a BMI equal to or greater than the 95th percentile. Confounding variables such as birthweight, ethnicity, and maternal BMI were taken into consideration.

By assessing 32,200 Scottish children aged from 39 to 42 months, Armstrong et al. [50] found lower prevalences of obesity among those who had been on exclusive breastfeeding in the first six to eight weeks of life, comparatively to those who had been exclusively formula-fed, after adjustment for socioeconomic class, birthweight and gender. Similar results were obtained with two different definitions of obesity (BMI greater than or equal to the 95th percentile and BMI greater than or equal to the 98th percentile).

Toschke et al.,[51] in a cross-sectional cohort study with 33,768 individuals aged from 6 to 14 years, in the Czech Republic, found a lower prevalence of overweight (defined as a BMI above the 90th percentile) and of obesity (defined as a BMI greater than the 97th percentile), among breastfed ones. Parental educational level and obesity, birthweight, number of siblings, and physical activity were taken into consideration. The authors highlighted the homogeneity of socioeconomic conditions of the studied population, as it is a socialist society.

Breastfeeding and metabolic imprinting

Epidemiological and experimental animal studies have suggested that an individual's first nutritional experiences may affect his/her susceptibility to chronic diseases in adulthood, such as obesity, hypertension, cardiovascular disease and type 2 diabetes, known as metabolic imprinting.[75-85] Metabolic imprinting refers to a phenomenon through which an early nutritional experience during a critical and specific period of development (opportunity window) could result in a long-lasting, lifelong effect that predisposes to certain diseases.[75]

A classic epidemiological study is the one carried out by Ravelli et al.[79] with Dutch 19-year-olds exposed to an *in utero* period of hunger and deprivation, between 1944 and 1945. Those individuals whose mothers were nutritionally deprived during the first two terms of pregnancy had a prevalence of overweight 80% higher than those who had not been exposed to such conditions. The explanation for this, as the authors suggest, is that these individuals were nutritionally deprived during a critical period of hypothalamic differentiation, therefore modifying the development of hypothalamic centers in charge of appetite regulation. On the other hand, those individuals who had been exposed to nutritional deprivation during the last term of pregnancy or during the first five months after birth had a prevalence of overweight 40% lower than nonexposed individuals. The authors attribute this phenomenon to the fact that nutritional deprivation occurred in a critical period of adipocyte replication in this group.

Waterland & Garza[75] proposed some potential mechanisms through which metabolic imprinting could occur, among which were the induction of changes to the structure of certain organs (changes in vascularization, innervation or in the juxtaposition of different cell types inside the organ), changes in the number of cells and metabolic differentiation (changes in the expression of certain genes, causing changes in the production of enzymes, hormones, hormone receptors, transmembrane transporters, etc.).

Breastfeeding represents one of the earliest nutritional experiences of newborns, giving continuity to intrauterine nutrition. The nutrient content of breastmilk is qualitatively and quantitatively different from baby formulas. In addition, several bioactive factors are found in human milk, such as growth hormones and growth factors, which act on growth, differentiation, and functional maturation of specific organs, affecting several aspects of development.[99-101]

Wagner[99] draws attention to the fact that the amniotic fluid and breastmilk share some common characteristics, such as bioactivity, emphasizing the concept of continuity between intrauterine and extrauterine growth. Hirai et al.[100] demonstrated the importance of certain growth factors found in the amniotic fluid and breastmilk for perinatal gastrointestinal adaptation.

The unique composition of breastmilk could be implicated in metabolic imprinting, changing, for instance, the number and/or size of adipocytes or inducing metabolic differentiation. The complexity of the neuroendocrine network that regulates energy balance, with its multiple components and a large number of bioactive factors in human milk, suggests an infinity of possible effects of human milk on this process.

Insulin, adrenal steroids, T3 and T4 are some of the hormones found in breastmilk.[101] Casabiell et al.[102] detected leptin in human milk, which may have a regulatory role in infants, since this hormone inhibits appetite and anabolic pathways, and stimulates catabolic pathways.[61]

Lucas et al.[103] found different endocrine responses to the release of pancreatic and intestinal hormones among breastfed and formula-fed newborns.

Some authors have pointed out that the higher consumption of proteins by formula-fed infants, compared to breastfed ones, could be one of the factors responsible for the greater risk of obesity. The high protein intake leads to an increased secretion of IGF-1 (*insulin-like growth factor type 1*), which in its turn stimulates the multiplication of adipocytes. However, this hypothesis has not been confirmed yet, and further investigation is necessary.[36,83]

Breastfeeding: behavioral aspects

As we know, breastfeeding does not consist only of biological aspects (e.g.: composition of the breastmilk), but it also includes psychological and behavioral aspects that constitute the mother-child relationship. The same can be said of eating habit formation in children.

It is widely known that breastfeeding contributes towards strengthening the link between mother and child.[104-106] The increase in oxytocin levels in the mother's brain during breastfeeding is believed to strengthen this link.[104] It has been described that UNICEF Baby-Friendly Hospital Initiative, which encourages breastfeeding and closer contact between mother and child, has reduced the rates of child abandonment in several countries, such as Russia, Philippines, Costa Rica and Thailand (in the latter one, a decrease from 33 per 10,000 live births to1 per 10,000 was described).[104] Adolescents aged from 15 to 18 years who had been breastfed see their mothers as more caring and report a closer parent-child relationship.[106] An association has been reported between breastfeeding and a higher frequency of interactive behaviors between mother and child, as well as the maternal perception of a feeling of competence and of more flexibility in child care, in addition to seeing their children's temper as "easier."[107,108] These positive behavioral aspects of breastfeeding may contribute to a smoother dietary transition and to the formation of healthier eating habits.

The development of eating habits is a complex process, which involves several factors. In general, children have an inborn predisposition for sweet and salty foods and reject acidic and bitter ones.[109] Neophobia, tendency towards rejecting new foods, is also observed, and offering the food repeatedly tends to increase its acceptance.[109, 110] The association with the context in which the food is eaten also influences the development of food preferences.[109] Parents influence their children's development of food preferences through their own preferences, their attitudes to eating, and by interfering in the availability of food.[109-114]

Possibly, breastfed infants may develop more efficient mechanisms for the regulation of their energy intake. It has been reported that in situations in which parents have a greater control over their children's diet the development of self-regulating mechanisms may be impaired, since external control mechanisms may subdue internal hunger and satiety signals.[111-115] Therefore, bottle-feeding, for instance, could favor the development of overweight by stimulating an excessive milk intake or by harming the development of self-regulating mechanisms.

It is common knowledge that the maternal diet affects the flavor of breastmilk and that different tastes interfere with milk intake. There is evidence that experience with several flavors (tastes) during breastfeeding facilitates the acceptance of new and varied foods by the child in the future.[115]

Final remarks and conclusions

Given the several morbid conditions associated with obesity, as well as its increasing prevalence and its difficult treatment, it is necessary that efficient preventive measures be found. Simple measures, without potential adverse effects and a low cost, should be a priority.

The hypothesis that breastfeeding could have a protective effect against obesity is supported by epidemiological evidence, being biologically plausible, but literature data are still controversial. If this hypothesis is confirmed, it will represent one more advantage of breastfeeding, as well as a new "weapon" to fight obesity.

Different definitions of exposure and outcome hinder the comparison between several studies. The long time elapsed between exposure and outcome also interferes with the analysis of this possible association, by producing a recall bias or incurring in elevated costs, long duration, and operational difficulties in case of longitudinal studies, or by not allowing all confounding variables to be taken into consideration.

The potentially implicated mechanisms still have to be clarified. Breastfeeding involves several aspects, such as the amount of food intake, composition of the food (nutrients and bioactive factors), time of introduction of solid foods, development of regulatory eating mechanisms, as well as behavioral aspects related to the mother-child relationship and formation of eating habits.

Metabolic imprinting is an appealing explanation. However, this phenomenon requires further investigation, in order to clarify the level at which breastfeeding plays a key role, either in changing the number and/or size of adipocytes, interfering in regulatory hypothalamic mechanism, modulating endocrine responses, interfering in gene expression or by means of another mechanism yet to be defined.

Obesity, with its multicausality and multiple consequences, is a challenge to pediatricians and other health professionals that work with children. In many cases, preventive measures may avoid long-term adverse effects in the organic and psychosocial context.

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