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NUTRITIONAL ASPECTS OF CHILDHOOD CHRONIC RESPIRATORY DISEASES

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ABSTRACT

Chronic respiratory diseases compromise oxygenation to a variable degree and cause problems in the use of nutrients, the generation and use of energy by the different tissues and organs, with potential damage to respiratory function and non-respiratory systems. Available evidence indicates that both the available energy and some micronutrients, particularly with antioxidant activity, during pregnancy, are key for adequate lung development and therefore an adequate pulmonary function in preterm infants, infants and older children, particularly if they suffer from bronchopulmonary dysplasia. However, both maternal and fetal malnutrition, as well as deficiencies of certain nutrients and the presence of overweight or obesity in the child, would influence the development of asthma in childhood.

With regard to nutritional assistance, correction of nutritional deficit as well as micronutrients are essential in the treatment of diseases such as bronchopulmonary dysplasia, bronchiolitis obliterans and asthma. This review aims to establish how nutrition determines the development, evolution and prognosis of these pathologies and the need to consider nutritional assistance in the comprehensive care of these patients.

Key words: chronic respiratory diseases, childhood, nutrition.

INTRODUCTION

The provision of water, oxygen, energy and nutrients is vital for the survival of living beings. In this sense, any situation that affects this equation constitutes a risk factor for the survival and quality of life of an individual.

During the pediatric years, respiratory diseases, in general, and chronic respiratory diseases (CRD), in particular, compromise oxygenation to a variable degree and cause problems in the use of nutrients, energy generation and its use by the different tissues and organs, with potential damage to respiratory function and non-respiratory systems.

The purpose of this review is to describe, based on the available evidence, nutrition as a determinant in the development, evolution and prognosis of CRDs and consider nutritional assistance in the comprehensive care of these patients.

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ENERGY, OXYGEN AND NUTRIENTS

In a global view, a living organism needs the indemnity of all functional systems to provide adequate nutrition, this being, a convenient amount of water, oxygen and nutrients to meet demands both in physiological conditions and against adaptations triggered by pathologies. The use of these supplies, provided by the function of different systems, will allow cell multiplication, tissue growth and tissue repair after damage that occurs in the course of a disease and by extension the maintenance of the systemic functionality and viability of the individual.

In the well-known equation of cellular respiration: C6H12O6 + 6O2 = 6 CO2 + 6H2O + Energy, oxygen is the oxidizer of living organisms par excellence. Its function is to oxidize the organic energy macromolecules that, after a sequence of multiple chemical reactions, convert the energy contained in the carbon bonds, through electrochemical potentials, into energy molecules in the mitochondria. Oxygen is supplied to tissues and cells as a product of the interrelated joint work of the respiratory, cardiovascular, muscular and nervous systems.

Furthermore, water and nutrients are incorporated into the body by the digestive system and are distributed to the tissues, where they will be used to provide energy and allow cellular and systemic functioning. The defective function of any of these systems will compromise the availability of oxygen and other nutrients and, by extension, of tissue and systemic function.

NUTRITION IN THE PREVENTION OF CHRONIC RESPIRATORY DISEASES.

Nutrition plays an active role in the prenatal development of the lung, as it directly affects the growth mechanisms of the lung parenchyma. Some nutrients are determinants of epigenetic changes that modify lung development [1]. However, the influence on lung growth does not end at birth, as it extends to postnatal age, especially in early childhood [2].

Intrauterine growth restriction (IUGR) is the most common example of nutrient deficit during the period of fetal growth. One of the forms of IUGR is placental insufficiency that develops in the second half of pregnancy and being contemporary to the stages of acinar and alveolar development, mainly influences the development of the small airway and the pulmonary parenchyma [3,4 ,5]. Inadequate nutrition in newborns of extremely low weight (<1,000 g) in the neonatal period is related to the development of bronchopulmonary dysplasia (BPD) [6]. Intrauterine malnutrition involves the alveolization and development of the conductive airway, as a result of epigenetic changes. In animal models, malnutrition may not be the only causal mechanism of the structural alterations described. Pregnant mothers in the Western world who eat high-fat diets and develop hyperglycemia during pregnancy have delayed fetal lung development or deficiency in surfactant synthesis [7].

Premature newborns with low weight for gestational age, have decreased lung function at later ages, even when they achieve postnatal weight recovery. In addition, newborns with low birth weight, with higher recovery weight gains (measured as normalization of z score), are associated with increased risk of childhood asthma and abnormal results in spirometric tests (low z scores of FEV1 and FEV1 / FVC ratio) [7], since it coincides with the period of greater differentiation of preadipocytes into adipocytes of white adipose tissue [8], a reserve of precursor fatty acids from inflammatory mediators and producers of proinflammatory adipokines.

Some studies conclude that water restriction could reduce the risk of developing BPD, however, the major problem with this restriction is the consequent limitation in the supply of energy and nutrients, since deficit nutrition increases the risk of BPD [7].

MICRONUTRIENTS IN CHRONIC RESPIRATORY DISEASES.

Not only energy and structural nutrients are involved in lung development. A group of micronutrients show a relevant effect on lung development, as determinants of growth through different mechanisms; in this group, vitamins A, D and E stand out, in addition to selenium and docosahexaenoic acid (DHA). Table 1 shows the recognized functions of these micronutrients in lung development and CRD as well as their dietary sources. The first 4, along with vitamin C and zinc, have often been called dietary antioxidants, as they participate in functions or enzymes that counteract oxidative damage to biomolecules and there is a possibility that increased consumption of these compounds protects against chronic diseases [10].

Vitamin A

Vitamin A supplementation in preterm infants of very low birth weight is associated with decreased incidence of BPD [11]. Likewise, vitamin A supplementation of deficient mothers, up to 6 months after gestation, in areas that have endemic vitamin deficiency, show better results in lung function between 9 and 11 years of age in their children, compared to children of mothers not supplemented [12].

Vitamin D

Vitamin D deficiency in pregnant women that persists after birth is associated with decreased lung function in offspring at 6 years of age [13,14]. Along these same lines, recent evidence shows that supplementation of pregnant mothers reduces the incidence of wheezing in their children at 3 years of age [15].

Vitamin E and Selenium

There is a strong association in the development of BPD in preterm infants with respiratory distress syndrome (RDS) associated with vitamin E and selenium deficiency [17,18], however, vitamin E supplementation has not shown conclusive results [19]. There is evidence that the deficit in selenium concentration in pregnant mothers is associated with a higher incidence of wheezing at 3 years of age and in low-weight premature infants it is associated with RDS, supplementation does not impact the incidence of BPD [7].

Docosahexaenoic Acid

In the long term, maternal supplementation with fish oil during pregnancy (with 2.4 g of DHA per day) evidences a relative reduction of 30% in the probability of persistent wheezing at 3 years of age and asthma at 5 [20].

DIET AND NUTRITIONAL STATE IN CHRONIC RESPIRATORY DISEASES

A recently published review [21] links different eating patterns with the development of CKD, identifying them as modifiable risk factors. These dietary patterns and some types of food facilitate or protect against its development.

Fruits and vegetables

Fruits and vegetables have a nutrient profile that includes antioxidants, vitamins, minerals, fiber and phytochemicals and would present possible benefits in association with respiratory conditions. [21]. Epidemiological evidence indicates that fruit intake is associated with a low prevalence of wheezing and that the intake of cooked green vegetables is related to a low prevalence of wheezing and asthma in schoolchildren aged 8 to 12. In addition, low consumption of vegetables in children was related to the development of current asthma [22].

Table 1. Some micronutrients with their function in CRD.

Micronutrient	Function in CRD	Main Sources*
Vitamin A	Retinoids of vitamin A regulate the expression of extracellular matrix proteins (airway development and alveolization) [9].	Beef liver, milk, butter, cheeses, egg yolk, fatty fish. Dark green leafy vegetables, yellow or orange fruits and vegetables.
Vitamin D	Type II pneumocytes development, responsible for the synthesis of surfactant, its component production and its release into the alveolar lumen [7].	Fatty fish (cod), fish liver oil, egg yolk, red meat, beef liver. Foods fortified with vitamin D.
Vitamin E	Liposoluble vitamin that has an active protective role against oxygen toxicity [7].	Vegetables rich in polyunsaturated fats (palm oil, soybean oil, wheat germ), nuts (peanuts, raw almonds), vegetables and fruits (potatoes, spinach, peaches, carrots, tomatoes, lettuce).
Selenium	Trace element that is mainly present in selenoproteins, in particular glutathione peroxidase, an enzyme with definite antioxidant action [7].	Garlic, mushrooms, broccoli fish and intestines, muscle meats, cereals, grains, dairy products.
DHA	N-3 long chain polyunsaturated fatty acid that improves lung development and modulates inflammation [5].	Fatty fish, salmon, trout, vegetable oils (canola, olive, soy, flaxseed), fortified foods

Sources: Essentials of Human Nutrition. Mann J., Truswell S. Eds. Oxford University Press 2007: 138-143, 163-184, 201-214, 214-222.

Obesity

From another perspective, overfeeding and obesity resulting from this, are clearly related to asthma, although the mechanisms involved are still under investigation. Several hypotheses have been proposed to explain the link between obesity and asthma, such as a chronically increased inflammatory state, restrictive effect of obesity on lung volumes and genetic predisposition [23]. It is known that in obese people, the intake of dietary lipids leads to an increase in circulating free fatty acids, which activate immune responses, such as the activation of the Toll-like receptor 4 (TLR4), which increase inflammatory phenomena both at a systemic level as in the airways. Furthermore, adipose tissue secretes adipokines, cytokines with influence on inflammatory cascades, procoagulant, antifibrinolytic and vasoactive, suggesting a direct action on inflammation [8]. Asthmatic subjects have higher concentrations of circulating leptin (an adipokine) than healthy controls. Bronchial and alveolar epithelial cells possess leptin receptors and this induces the activation of alveolar macrophages and has indirect effects on neutrophils, promoting airway inflammation [21].

Malnutrition

Malnutrition problems are probably more related to the development and evolution of patients with chronic obstructive pulmonary disease (COPD) observed in adults with a history of chronic smoking [21] and, by extension, occurs in diseases that arise with high energy consumption or difficulty for sufficient provision of it to the individual [24]. As previously mentioned, there is a general consensus that malnutrition in pregnant women has adverse effects on fetal lung development. The findings include impaired alveolarization (be it smaller or larger alveoli), as well as interalveolar septa and a thicker alveolus- capillary barrier. Likewise, epithelial maturation can also be affected by factors that restrict fetal growth. IUGR has been shown to alter surfactant protein expression [25].

NUTRITION AS A TREATMENT

Nutritional therapy is an important part of treatment in all diseases: water and energy along with different nutrients are necessary in allowing the body to contract the necessary adjustment, start the repair and finally survive.

Each pathology has a particular characteristic and therefore a specific approach. Within the heterogeneous group of childhood CRDs, we could approach the focus with 4 pathogenic models that may be useful: bronchopulmonary dysplasia (BPD), cystic fibrosis (CF), Post-infectious bronchiolitis obliterans (BO) and bronchial asthma (BA). In this review, CF will be excluded, a pathology in which nutritional treatment is a key element and prognostic factor and exceeds the extent of this article.

Bronchopulmonary Dysplasia

The evolution of premature carriers of BPD depends, among other factors, on nutritional assistance [26]. Preterm infants per se have a high nutritional risk due to insufficient nutrient reserves and increased nutritional demands and therefore more committed when they suffer from BPD. Infants with severe BPD have respiratory difficulties that interfere with oral feeding, so standard feeding regimens may not provide adequate energy or protein intake [26]. For this reason, nutritional strategies used to prevent BPD include optimization of nutrient administration, including vitamin A and antioxidants to support healthy lung tissue growth and development. Likewise, nutritional management in the newborn with CRD must meet the different needs of premature babies, whether extreme or late, and the necessary correction of nutritional disorders that often accompany drug therapy [26].

Determining the energy needs of patients with BPD is a key problem. The use of predictive formulas seems appropriate against the gold standard represented by indirect calorimetry, to determine the resting energy expenditure of these patients [28]. Infants with BPD require intakes of 3.5 to 4 g per kg / day of protein to achieve normal growth and energy intake up to 15 to 25% higher than healthy premature infants, although intake greater than 125-135 kcal per kg / day may not be beneficial [26]. Table 2 lists the recommendations for energy and some nutrients in preterm infants [27].

Frequently, these infants have feeding problems, so the assistance of a professional expert (speech therapist, speech pathologist or occupational therapist) is necessary to reduce harmful stimuli on the face and mouth, encourage attachment and non-nutritive breastfeeding by maternal breast and detect in timely manner signs of hunger and satiety [26].

Pharmacological therapy is not without interaction on the metabolism of nutrients, being necessary to monitor the serum levels of sodium, potassium, chloride, calcium and phosphorus when diuretics, aminoglycosides and / or vancomycin are used, and correct them when necessary. Special emphasis should be placed on the detection of imbalances that may lead to the development or accentuation of osteopenia, including the measurement of vitamin D levels and timely supplementation[26}.

Post-infectious bronchiolitis obliterans (BO).

A Brazilian study shows high percentages of malnutrition and risk of malnutrition among patients with BO considering the parameters weight for age and height for age, with evidence of less commitment when using weight for height, which could indicate the time extent of the nutritional involvement [24]. In the same study, the analysis of body composition detected patients with low muscle reserves (51% of patients), with a preserved fat compartment. Likewise, there was no association between spirometry and nutritional variables [24].

Regarding nutritional support, maintaining adequate nutritional support is essential. Patients with BO have a higher caloric expenditure due to respiratory compromise, and adequate nutritional support could improve the efficacy of respiratory musculature [28].

Bronchial asthma

Asthma is one of the most common chronic diseases in children. Its incidence has increased in recent decades. The parallel increase in the prevalence of obesity and asthma in recent decades has raised concerns about the relationship between both pathologies [29]. Several hypotheses raise the relationship to explain the increase of asthma in childhood: from the deficit intake of certain nutrients, such as vitamin D, magnesium, foods rich in antioxidants [29], the increase in foods with n-6 polyunsaturated acids and a lower adherence to the Mediterranean diet [35]. It has also been linked to intrauterine malnutrition. Maternal diets rich in antioxidants (including zinc and selenium), as well as a more favorable relationship towards long-chain n-3 polyunsaturated fatty acids (PUFA), compared to those of type n-6 (PUFA), are most likely to be beneficial for asthma prevention [29]. This is due to the fact that n-3 PUFA derive in eicosanoids that have direct anti-inflammatory effects and n-6

Table 2. Recommendations of oral/enteral daily food intake for preterm infants and infants with BPD [33].

Nutrients	Recommendations (*)	Nutrients	Recommendations(*)
Energy	110–135 kcal	**Carbohidrates**	11.6–13.2 g per kg/day
Infants w/ BPD	15-25% additional	**Lipids**	5,3–8,4 g
Proteins		**LA**	385–1.540 mg
<1 kg	3,8–4,2 g	**ALA**	0,7–2,1 % kcal day
1,0-1,8 kg	3,4–4 g	**DHA**	12–30 mg
1,8-2,5 kg	2,8–3,4 g	**AA**	18–42 mg
>2,5 kg	1,8–2,2 g	**Vitamin A**	1.332–3.330 UI
Infant w/BPS	3,5-4 g	**Vitamin D**	800–1.000 UI per day
Calcium	120–230 mg	**Vitamin E**	6–12 UI
Phosphorus	60–90 mg	**Selenium**	1,3–10 μg
Iron	2–3 mg	**Zinc**	1,1–2 mg

(*) Recommendations per kg / day except AAL and vitamin D.
LA: linoleic acid. ALA: α-linolenic acid. DHA Docosahexaenoic acid. AA: arachidonic acid.

PUFA give rise to the main eicosanoids of the proinflammatory pathways [30]. A recent meta-analysis concluded that a high body mass index (BMI, calculated in kg / m2) during childhood, is associated with a statistically significant increase in the relative risk of asthma [31], and this association is independent of socioeconomic factors and ethnicity [32].

Several recent studies also demonstrated that adherence to a Mediterranean diet (Table 3) was also associated with a lower risk of asthma symptoms in children [32]: a cross-sectional study with 700 Greek children showed that greater adherence to a Mediterranean diet was inversely associated significantly with wheezing, wheezing with exercise, asthma diagnosis or any asthma symptom [33].

Food intake with certain micronutrients may be beneficial for a more favorable course of asthma; in this sense, some vitamins such as cyanocobalamin (vitamin B12), pyridoxine (vitamin B6) and calciferol (vitamin D) are included, as well as minerals such as zinc, selenium and magnesium.

Other factors involved in asthmatic patients, such as food allergies, gastroesophageal reflux and possible interactions between food and medication, contribute to aggravate their symptoms.

An important issue is food preparation: for example, vegetable antioxidants lose much of their properties if they are boiled.

While it may be beneficial to look for micronutrient deficiencies and intervene with an individual supplement, it can be more effective when this supplement is taken along with others and incorporated with a healthier whole-food diet. Additional research in this field should continue as it has the potential for a significant non-pharmacological intervention that could be added to current asthma therapy and obtain good results [29].

CONCLUSION

Adequate nutrition has been increasingly recognized in the assistance of the various prevalent and emerging pathologies of today, both in the general and pediatric population. Nutrition influences from pregnancy in the development of pulmonary pathology in preterm and term infants, as well as in older children. During pregnancy the maintenance of an adequate maternal nutrition, a healthy diet and the inclusion of antioxidant nutrients could be beneficial to prevent the development of respiratory distress syndrome of the newborn, BPD and wheezing and asthma in older children.

Rapid weight recovery in premature infants in the first 18 months of life and obesity developed in older children fed with high-fat diets (Western diet) show an increased risk of asthma. The Mediterranean diet in children is inversely associated with the presence of wheezing, wheezing when exercising and asthma diagnosis.

Nutrition is an important part of the treatment of children with CRD. Throughout the life cycle, adequate nutritional assistance is needed to facilitate its recovery in the short and long term, as in BPD, to avoid malnutrition and its consequent involvement in the respiratory musculature and pulmonary function in BO. In asthmatic patients it is essential to promote a healthy weight, diet and lifestyle, which could be reflected in the prevention of diseases and clinical improvement.

Table 3. Characteristics of the Mediterranean diet.

Frecuency	Type of food	Daily rations
	Agua	5 (vasos)
In each food	Fruits Vegetables: variety of colors/textures, cooked/raw Olive Oil Bread/Pasta/Rice/Couscous/Other cereals/Potatoes (preferably whole grain)	1-2 ≥2 1-2
Daily	Dairy Products (preferably low in fat) Olives / Nuts / Seeds Herbs / Spices / Garlic / Onion (less salt added) Variety of aromas Legumes	2 1-2
Weekly	White meat Fish / Seafood Eggs Red meat Processed meats Candy	2 ≥2 2-4 <2 ≤1 <2

Adapted from: Serra-Majem L., Ortiz-Andrellucchi A .: The Mediterranean diet as an example of sustainable food and nutrition: a multidisciplinary approach (La dieta mediterránea como ejemplo de una alimentación y nutrición sostenibles: enfoque multidisciplinario) Nutr Hosp 2018; 35 (Suppl 4): 96-101.

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