New insights on nutritional intervention in children on the autism spectrum

Novos desafios sobre intervenção nutricional em crianças autistas

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Artigo

Abstract

Currently, autism is a highly prevalent disorder worldwide. As the severity of autism increases, behavioral and dietary changes are often present. This study aimed to address the prevalence of obesity and frequent dietary changes in these patients, correlating them with food introduction and nutritional strategies commonly used in individuals with ASD. Nutritional interventions at different stages of life have been used to improve behavioral aspects of ASD, however, it is noted that more studies with a large sample are needed to make these strategies more concise and conclusive.

Resumo

Atualmente, o autismo é um transtorno de alta prevalência em todo o mundo. À medida que a gravidade do autismo aumenta, mudanças comportamentais e alimentares costumam estarem presentes. Este trabalho teve como objetivo abordar a prevalência da obesidade e alterações alimentares frequentes nesses pacientes, correlacionando-os com a introdução alimentar e estratégias nutricionais comumente utilizadas em indivíduos com TEA. Intervenções nutricionais em diferentes fases da vida vêm sendo utilizadas como melhoria de aspectos comportamentais do TEA, entretanto nota-se que ainda são necessários mais estudos de ampla amostra para tornar essas estratégias mais concisas e conclusivas.

Keywords: Autism; Child; Nutrition; Eating Disorders; Revision.

Palavras- chave: Autismo; Criança; Nutrição;Transtornos Alimentares; Revisão.

Área Temática: Nutrição.
Linha Temática: Percepção sensorial alimentar em crianças autistas.

Introduction

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), autism is a neurodevelopmental disorder characterized by difficulties in social interaction, communication and repetitive and restricted behavior. Autistic Spectrum Disorder (ASD) has these three characteristics that are essential for diagnosis along with the patient's medical history[1]. These changes lead to the development of adaptive difficulties that can be noticed before the age of three, However, many children are still diagnosed late, either due to misinformation or resistance from family and doctors[2].

The development of ASD is related to multiple etiologies. Recent studies suggest that genetic factors account for only 35-40% of the elements that contribute to the disorder [3]. The remaining 60-65% is due to other environmental factors, such as prenatal, perinatal and post-natal care[4]. Bearing this in mind, autism has become a global development disorder of high prevalence. Global epidemiological data estimate that one in 88 live births presents ASD, having a global prevalence of 0.62%[5,6].

In 2010, Brazil was estimated to own about 500.000 people with autism, with a higher prevalence in males[6]. Data from the Ministry of Health, taken from the 'Agência Saúde' program in the press service sector showed, in December 2014, that the prevalence of ASD in Brazil corresponds to 27.2 cases for every 10,000 inhabitants aged 5 to 18 years[7]. The exact number of children with ASD in Brazil is not yet available, however, an estimate can be made according to data from the American Psychiatric Association (APA) (2014) which predicts a prevalence of around 1% of the population with the disorder. According to the census of the Brazilian Institute of Geography and Statistics (IBGE) of July 2016, the Brazilian population is of approximately 200 million people, thus, the prevalence of individuals with ASD in Brazil can reach two million[8].

Food intake is a severe problem for autistic children due to the selectivity, which causes nutritional imbalance such as obesity[9]. This selectivity consists of the difficulty to try unfamiliar foods, regarded as food neophobia, making the mealtime frequently to be culminated by crying, restlessness and aggressiveness by the part of the child with ASD and emotional distress by the part of the caregiver, compromising body growth and nutritional status[10].

As the degree of severity of autism increases, gastrointestinal disorders such as diarrhea, constipation, bloating or abdominal discomfort become more frequent[11]. In addition, there is an increase in intestinal permeability in comparison with healthy subjects. Common behavioral changes in these individuals, such as irritability and aggressiveness can be consequences of these gastrointestinal disorders[12].

About 78%-90% of the children with ASD exhibit changes in sensory processing[13]. This symptomatology is constituted by an increase or decrease in reactivity to sensory

input, directly affecting food[14]. Some reports show that behaviors such as poor appetite, hesitation in eating food intake, not eat out of the house, refusing food because of the smell and temperature are observed[15].

Inadequate eating practices and early food introduction may result in health complications for the child, as well as in adult's health. In addition, they can lead to less efficient microbiota, resulting in inflammatory reactions related to several complications, including autism[16].

Among the various factors related to autism, this study aimed to address the prevalence of obesity, frequent dietary changes in these patients, correlating them with the introduction of food, finally, showing nutritional strategies aimed at improving physical health and wellbeing. -being of these individuals.

Method

For the elaboration of this literature review, the literature search included books, theses, dissertations and scientific articles on the subject, produced worldwide during the period from 2009 to 2020. The material collection process was carried out in a non-systematic way. Considering the object of the study, initially the articles referring to the topic addressed were searched in the database of the electronic libraries SciELO, PUBMED, CAPES Journal, Scholar Google and Medline. The database was being complemented with materials indicated by specialists in the subject. Finally, these materials were read in full, categorized and critically analyzed.

Obesity in Autism

The prevalence of obesity is growing, and is considered a worldwide epidemic. Brazilian society of Endocrinology data shows that in the age group of 5 to 9 years, obesity levels have been increasing (51.4% boys; girls 43.8%)[17]. Moreover, data from the Ministry of Health show that almost one in every five adults (18.9%) are obese and more than half of the adult population of the Brazilian capitals (54.0%) are overweight[18]. The big concern is the development of obesity-related diseases such as diabetes, cardiovascular diseases, cancers, reduced functional capacity, quality and life expectancy, mechanical limitations, shortness of breath and skin problems[19].

One of the alarming issues for children and adolescents with autism is the greatest risk of overweight and obesity. In the study of Kummer et al. (2016) showed a higher percentage of obesity in groups of patients with ASD (21.7%) than in the control group (5.3%)[20]. A study conducted in northeastern Brazil found that 38.5% of the children evaluated were overweight or obese by BMI/I (Body Mass Index for Age), in conjunction with the energy consumption value (EER) which was above the recommended for 53.85% of autistic individuals[19]. In order to explain this higher caloric consumption, in the study by Rodrigues et. al (2020), children with ASD had greater food preference (31.1%) for the unhealthy food groups (sweets, snacks, sweets and industrialized beverages)[21]. Similarly, Almeida et. al (2018) analyzed the presence of a higher consumption of ultra-processed foods in overweight children with ASD than without excess weight (34.2% versus 19.4%)[22].

On the other hand, there is a greater repulsion for raw and/or cooked vegetables in this child's eating behavior, which has a positive correlation with difficulties in sensory-oral processing. The lower consumption of healthy foods is positively correlated with difficulties at meal times[21,22]. A survey in Denmark revealed that the nutritional intake of 414 children with ASD with a mean age of 9.63 years, who have eating rituals did not meet the recommended intake of fiber, choline, potassium, vitamin D and K in most children, compromising child development.

One of the reasons for this result is due to the food selectivity, which consists in having difficulty in trying new experiences with food, so the use of a restricted diet generates an impact on the nutritional state, causing a problem in the short and long term, such as diabetes, cardiovascular disease and psychosocial difficulties[24]. This behavioral characteristic is termed as food neophobia, which will be discussed in detail later.

Another cause associated with obesity in patients with ASD is the use of medications, such as risperidone, the most prescribed antipsychotic to these patients, which increases the appetite and therefore the body mass[25]. A study found that children who used this drug showed a sharp increase in weight, from two to eighteen kilos, while the control group of the same age range had a gain of one to seven kilos, in the same period[26].

Parenthood obesity of autistic children is considered a risk factor. Krakowiak et al. (2012) evaluated the association between the incidence of metabolic diseases during pregnancy and the prevalence of the risk of autism in children and found that the risk of autism, as well as other developmental disorders, increases when mothers present obesity and type II diabetes[27].

Surén et al. (2014) present a differential perception of the paternal body mass index (BMI). Before this study, there was an overestimation of the risk associated with maternal BMI, however, it was observed that the risk of autistic disorder was 0.27% in children of obese parents and 0.14% in children of parents with an ideal BMI, showing a genetic association between the body mass of the father and his offspring[28]. This association may be mediated by a pleiotropic gene, that is, variants of genes associated with different disorders of variable manifestations.

The prevalence of obesity has been increasing among adults. According to the World Health Organization (WHO), it is estimated that at least 1 billion people present overweight and 300 million are obese[29]. This fact occurs as the number of children with autistic spectrum grows as the first studies indicated a prevalence of 4 to 5 cases of infantile autism for 10,000 births, however, in more recent investigations, there was an estimated drastic increase in cases, reaching an average of 40 and 60 cases every 10,000 births[30].This occupies the third position of prevalence among developmental disorders, surpassing congenital malformations and down syndromes[6].

Food Specifics in ASD

Food Neophobia

One of the best-known features of ASD is the difficulty that these individuals have in relationships and social interaction. This characteristic comes from the theory of super selectivity, which is responsible for the difficulty to interact socially, learn to speak and difficulty eating[31].

In the first two years of life, children experience a set of food, textures and different flavors. However, children with ASD end up creating barriers to new food experiences because of their selectivity to the new [32]. This behavior and the restrict interest to new food lead to dietary selectivity, known as food neophobia, observed by the insistence of the compliance with the routines during the meal, as in the use of the same dishes or cutlery[33].

Bandini et. al (2010) suggested that children with ASD showed a greater denial of food and a more limited repertoire compared with the children of typical development, despite the refusal have been observed in both groups. It is important to note that food selectivity also occurs in neurotypical children, but persistence in diverging food and prolonged food neophobia, beyond early childhood, is characteristic of children with ASD[15].

Parents of the autistic children describe that in response to novel foods or unfavorite food, the child with ASD answers through oro-motor skills, reflecting on gagging and/or difficulty chewing, swallowing and language movement, which is not observed in their siblings without the spectrum. As a result, the timing of meals is often marked by exhaustion and irritation, being related to something unpleasant, hampering adequate nutrition[34]. To this, children with ASD tend to be nutritionally vulnerable, among which we can emphasize: malnutrition, predisposition to carious lesions and other lesions in the oral cavity and micronutrient deficiencies[35].

Zimmer et al. (2012) signaled that ASD patients who present selectivity were more likely to develop at least one severe nutritional deficiency, this finding associated with lower consumption of fruits and vegetables being encouraged[36]. The most common micronutrient deficiencies in ASDs are vitamins B1, B3, B5, B6, B9, B12, A and the minerals calcium (Ca), zinc (Zn), selenium (Se) and magnesium (Mg). In the study by Caetano et al. (2018) it was possible to observe a possible inadequacy (50%) of calcium (Ca), which is directly associated with several organic functions, such as modulation of transduction signals, metabolism of energy production and cell proliferation, being symptoms resulting from their disability associated with: anxiety, depression, hyperactivity, agitation, hallucinations, irritability, nervousness, aggression, chronic stress, learning difficulties and memory loss[37]. Concomitantly with the lower intake of vitamin D in children with spectrum, the lack of this vitamin and calcium can culminate in the presence of rickets in childhood or adolescence[38].

Food neophobia is commonly presented in autism and can generate protein-calorie malnutrition, besides contributing to a poor diet. These two factors cause great concern since the intake of micronutrients is related to the energy supply. The lack of these micronutrients explains the large presence of diseases such as anemia and gastrointestinal problems related to the spectrum[39].

In order to consolidate these characteristics, Suarez et al. (2014) interviewed parents of children with autistic spectrum, where 19% reported that their sons eat less than 10 types of foods as part of your regular diet; 26% reported between 11-20 types of foods; and 55% reported that their children eat more than 21 types of foods[41]. In addition, a significant higher score was perceived regarding sensory hypersensitivity, especially tactile, in children who accept less than 20 types of foods in their diet. Hence, there is an association between food neophobia and sensory sensitivity that exists in autistic children[41].

Sensory sensitivity

About 78-90% of autistic children have sensory abnormalities[13]. According to DSM-5, "this is a symptom that is constituted by the increase or decrease in reactivity to the sensory input or unusual interest in sensory aspects of the environment"[1]. Patients with the spectrum have different degrees of sensory sensitivity and can be identified as hyper and/or hypo-reactivity[10]. The hyper-reactivity occurs when the child responds to sensory input with greater intensity if compared the children neurotypical ones. On the other hand, in the hypo-reactivity pattern, the response to sensory input is less intense or does not occur[42].

The problem of sensory modulation directly affects the relationship of the child with food, since a meal is a full sensory experience that contains sets of appearances, odors, textures, flavors, motor planning and the conversation that encompasses the food environment[13]. Children with ASD are characterized by having the repetitive habit of always choosing the same meal and aversion to certain tastes and textures, refusing some foods by smell and refuse to eat foods that are at the extremes of temperatures[15].

The children more selective with the number of foods ingested feature higher values of hyper-reactivity in modulating sensory tactile, showing problems of salivation, social behavior at meal, as well as unusual food preferences with regard to specific recipes, color, texture and/or temperature of the food[41]. In the study carried out by Nadon et. al (2011), children with palliative modulation and olfactory changes presented these same issues at meal time, however with more pronounced food preferences[13].

The sooner is the experience of food introduction, the lower the rejection and, also, the frequency of exposure to foods is related to their preference. In order to increase the preference for new food, five to 10 exposures are necessary. In this way, the initial rejection of food can be considered as an exercise of adaptation and, therefore, cannot be considered a permanent rejection for food. Hence, it should not be excluded from the diet of children[43].

The sensory information is primarily formulated by an external point of view, once most of the children who have sensory changes fail to describe them due to the severe impairment of speech and cognitive skills. Thus, the sensory changes negatively affect the lives of individuals with ASD and their families[14].

The presence of a modified sensory modulation and, consequently, the food neophobia, makes the food habits of children with ASD restricted and monotonous[24]. Thus, these factors result in changes in the gut-brain axis, leading to intestinal dysbiosis, which aggravates the symptoms of autistic behavior [44].

Gut Microbiota

Generally, the gut microbiota of neurotypical individuals consists of anaerobic bacteria, such as *Bacteroides*, *Bifidobacterium* e *Lactobacillus*, being those responsible for production of butyrate, propionate, acetate and lactate, that strengthen the immune system [45]. However, in autistic individuals, there is an imbalance of the gut microbiota, having a reduction of bacteria of the *Bifidobacterium* genus and abnormal growth of pathogenic micro-organisms such as *Clostridium* species, causing inflammation and mucous membranes symptoms that is commonly noticeable in those patients, such as diarrhea, constipation, reflux, allergies or food intolerances[44].

Theije et. al (2014) studied intestinal microbiota's comparison of autistic animals with healthy animals. A murine model with ASD behavior-like had changes similar to humans, with a reduction of the phylum *Bacteroidetes* parallel to a raise of phylum *Firmicutes*. In addition, these animals showed an impaired intestinal barrier[47]. In order to restore the intestinal barrier and the normal microbiota composition, a treatment with *Bacterioides fragilis* was applied, which resulted in the improvement of communicative behavior, motor planning, and repetitive movements, being a potential probiotic therapy for behavioral symptoms[48].

Specific Changes in diet may alter gut microbiota. For this reason, the food and nutrients consumed are potential instruments of alert[49]. The gluten and casein are elements that present exogenous opioids peptides, which act directly in the intestinal lumen or in peripheral organs. These peptides have the ability to pass through the mucosa and the blood-brain barrier, affecting the central nervous system and affecting brain function, leading to social isolation and apathy[45].

In the study of Parletta et al. (2016), 85 children with ASD showed lower blood values of Docosahexaenoic acid (DHA) and Eicosapentaenoic Acid (EPA) in comparison with the control group[50]. Accumulating evidence suggested that polyunsaturated fatty acids (PUFA) deficiency may be linked to some neurodevelopmental disorders, including ASD[51,52]. Omega 3 and omega 6 fatty acids are two of the most well-known PUFAs, play an important role in brain functioning because of their anti-inflammatory properties and their ability to maintain appropriate function of brain cell membrane and myelin sheath[53]. Since PUFAs cannot be produced by the human body, some studies have suggested that changes in dietary behaviors that caused an imbalance in PUFAs' consumption may provide an explanation for recent increase in ASD prevalence[52].

Vitamin D plays a crucial role in the regulation of serotonin, through the tryptophan. The level of serotonin in the brain depends on the blood levels of tryptophan, which, unlike serotonin, crosses the blood-brain barrier[54]. EPA increases serotonin release of pre-synaptic neurons by reducing inflammatory signaling molecules such as prostaglandins E2 series. DHA also participates in the process, making the serotonin receptors more sensitive to this molecule, therefore, increasing your collection and promotion of the effects[55]. It is known that depletion of tryptophan causes a rapid and temporary reduction in brain serotonin in normal individuals and has major effects on their social behavior. In individuals with autism, further decreasing their brain serotonin by acute depletion of tryptophan exacerbates symptoms such as repetitive behaviors and facial recognition patterns revealing a continuing requirement for serotonin in modulating these behaviors. Furthermore, tryptophan supplementation has been shown to reduce social anxiety, which could be relevant to individuals with ASD[56].

Food Introduction

The care of children in the early years of life is critical, for being an extremely vulnerable phase. One of the basic needs for survival, nutrition takes an important role, ensuring good nutritional status, growth, good school performance and preventing the development of chronic non-communicable diseases [16].

The Ministry of Health of Brazil, in the food guide for children under two years of age, advises that breastfeeding is exclusive until 6 months of free demand[57]. The introduction

of food before the sixth month of life increases the risk of gastrointestinal infections, food allergy infant morbidity and mortality and higher incidence of chronic-degenerative diseases in adulthood. Frequent and excessive consumption of foods rich in empty calories in the first year of life can affect the health of children and adults[16].

The first months of a baby's life are known as the phase of microbiota colonization. In this way, the early introduction of foods to the child may lead to a less efficient microbiota, affecting its functions [58]. The onset of nutritional deficiencies reduces in children when breastfeeding is maintained and the introduction of food is done correctly[59]. A diet high in refined carbohydrates and lipids, mostly saturated and trans fatty acids, favors the proliferation of some species of microorganisms in the gut microbiota that can lead to inflammation reactions related to several disorders, including autism.

Consequently, the patients with autism are called "gut fragile" because food allergies are more common in these children than in same age control children.This can be evidenced by morphological tests that estimate that the gastrointestinal structure is altered, revealing that there is a proliferation of cells of the crypt, the basolateral membrane of the intestinal epithelium thickening, and increased intestinal permeability [60].

Nutritional Intervention

Effective treatments for the main symptoms of autism spectrum disorders (ASD) are lacking, but some studies show a positive relation between commonly reported autistic disorders and eating habits[11,61]. Therefore, nutritional intervention aims to get better skills development, improving physical health and well-being of these individuals [32].

As already mentioned, in the first six months, the newborn must be exclusively breastfed[57], as it contains essential nutrients and secretes immunoglobulins responsible for ensuring the child's healthy growth and development, ensuring intestinal maturation and immune defense. Therefore, breastfeeding is considered one of the main ways to prevent diseases that affect the central nervous system[33].

Currently, the gluten and casein free diet (GFCF) is commonly used for the treatment of ASD in children. Piwowarczyk et al. (2017) gathered data from randomized trials, it could be observed that compared to the control group, in the GFCF group there were significant improvements in scores for the 'communication' subdomain of the Autism Diagnosis Observation Schedule and for the subdomain of 'social interaction' of the Gilliam Autism Rating Scale, significant improvements in scores for the 'daily living skills' subdomain of the Vineland Adaptive Behavior Scale, as well as for the 'inattention' and 'hyperactivity' subscales of the ADHD-IV scale , in favor of the GFCF group. However, in general, the clinical importance of the results cannot be reliably established, as no individual data were provided. There is still little evidence that following a GFCF diet is beneficial in controlling ASD symptoms in children and adolescents[62].

Micronutrient supplementation was analyzed as effective to correct nutritional deficiencies in ASD, however its clinical aspects of improvement in neurobiological symptoms still need to be better investigated. The use of nutritional supplements as complementary therapy for ASD is highly prevalent, but little evidence supports their effectiveness. Among the five supplements reviewed by Li et. al (2017), Vitamin B6/Mg, Methyl-B12, Vitamin D,

Omega-3 fatty acids and folic acid, none were recommended for improvement of behavioral symptoms of ASD according to the best current evidence[63].

There is still little evidence to support the effectiveness of omega-3 supplementation in improving basic ASD symptoms. One study reported a significant improvement in parental ratings of stereotypy and lethargy in children receiving omega-3 supplements compared to those receiving placebo; teacher ratings were not significantly different. Three randomized controlled trials of omega-3 versus placebo reported no significant differences between groups on most measures of challenging behavior, communication, language, and adaptive behavior[64].

Vitamin D consumption plays an important role in normal brain development. Studies have shown positive responses to micronutrient supplementation during pregnancy[65]. A meta-analysis of prospective studies suggested that children with reduced maternal or neonatal vitamin D were 54% more likely to develop ASD[66]. Vitamin D deficiency during periods of neurodevelopment can result in brain structure changes and behavioral problems. Vitamin D also has anti-inflammatory and antioxidant properties; for example, vitamin D supplementation decreased serum interleukin 10 and 12 concentration and increased total antioxidant capacity[67].

Autism is considered a condition that affects the brain, and growing evidence indicates that oxidative stress and inflammation are involved in the pathogenesis of autism, which may be related to vitamin D deficiency. Vitamin D can have significant effects in the prevention and treatment of autism. More studies are needed to investigate the causal relationship between vitamin D and autism and to elucidate its mechanism[66].

Currently, there is a growing number of studies on the effectiveness of a gluten-free and casein-free diet in autism. Whiteley et al. (2012) reported that autistic children, who have had a diet restricted in gluten and casein, showed improvements in behavior after 8 to 12 months of diet[68]. Hyman et al. (2016) tested the effects of a diet without GFCF diet in 30 autistic children and has not demonstrated positive effects on physiological and behavioral symptoms, justified by the absence of gastrointestinal problems in the childrenstudied[69]. In this way, diets free of opioid peptides should be introduced when there is the presence of gastrointestinal symptoms or the diagnosis of intolerance or allergy to these foods[45].

Concerning prevention, vitamin D supplementation during pregnancy (125mcg/day) and in early childhood (25mcg/day) significantly reduces the incidence of autism in mothers of infants who already have a child with autism, a reduction from 20% to 5% incidence. However, one must be cautious with the development of toxicity. However, in the last 15 years, the Poison Control reported that there were around 15,000 cases of overdose of the micro-nutrient, but only three of them developed clinical toxicity and no death. Given this, during the vitamin D supplementation, it is recommended a serum measurement every 3 months [72].

Despite their widely reported use, little evidence supports the effectiveness of nutritional supplements or the GFCF diet in improving ASD symptoms. The harm reported in studies was generally considered mild, but the long-term effects of these therapies are not well understood. Evidence remains insufficient for most interventions, given small sample sizes, lack of long-term follow-up, and heterogeneous populations and agents. However, various supplements can be helpful and further research is encouraged.

Conclusion

Autism is a developmental disorder that has a high prevalence worldwide, which is growing as it increases the rate of obesity in parents of children with autistic spectrum. It is a disorder often associated with eating disorders and studies have shown that it is linked with inadequate food introduction, therefore, reflecting in an altered microbiota, generating diarrhea, constipation, flatulence, allergies and food intolerances, as well as behavioral changes like agitation, irritation, and aggression.

Nutrition plays a fundamental role in improving the quality of life of these individuals. Scientific studies show that nutritional interventions still need more large sample studies to become an effective and concise strategy for improving the behavioral issues present in the ASD.

Above all, it is essential the interaction between the family and the nutritionist for the success of interventions applied to the autistic patients, through daily and continuous observations of the clinical and laboratory signs and symptoms, considering that the improvement is so cautious and individualized. In addition to dietary adaptations, it is valid to highlight the encouraging of physical activity, psychological, medical and educational follow up.

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Conflict of interest statement

Nothing to declare.

Author contributions

IMLV-M and ECBAG proposed the study. IMLV-M performed the research. IMLV-M, ECBAG and VS-M wrote the first draft. All authors contributed to the design and interpretation of the study and to further drafts. ECBAG and VS-M critically revised the work.

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