



NUTRITIONAL STRATEGIES ADOPTED IN THE MANAGEMENT OF CHILDREN AND ADOLESCENTS WITH AUTISM SPECTRUM DISORDER

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ABSTRACT

Autistic Spectrum Disorder is defined as a neurological development disorder, improved by difficulties in communication, social interaction, restricted and repetitive structure with limited capacity for activities and interaction, in addition to gastrointestinal problems. Food has a major impact on the quality of life of an autistic spectrum patient, due to the greater food selectivity and, in many cases, total refusal of certain foods. Food also seems to have an influence on the behavior of children and adolescents with Autistic Spectrum Disorder. This integrative review sought to learn about the nutritional strategies adopted in the management of children and adolescents with Autistic Spectrum Disorder and to point out what are the positive impacts on the improvement of behavior and, consequently, on the quality of life of these adolescents. A survey of the articles published in the last ten years on the subject was carried out, in the scientific bases Biblioteca Virtual em Saúde and PUBMED. Among those found, the gluten-free and casein-free diet, the supplementation of probiotics and prebiotics, and micronutrients stood out. None of the diseases raised has evidence to be considered as a protocol in the nutritional treatment of children and adolescents with Autistic Spectrum Disorder. However, strategies such as the gluten and casein exclusion diet, the prebiotics and probiotics supplementation and the vitamin D and B complex vitamins supplementation can be applied safely, if this nutritional advice is carried out considering the individuality of each patient.

KEYWORDS: Autistic spectrum disorder; Behavior; Food.

ESTRATÉGIAS NUTRICIONAIS ADOTADAS NO MANEJO DE CRIANÇAS E ADOLESCENTES COM TRANSTORNO DO ESPECTRO AUTISTA: REVISÃO INTEGRATIVA

RESUMO

O Transtorno do Espectro Autista define-se como um transtorno do desenvolvimento neurológico, caracterizado por dificuldades de comunicação, interação social, comportamentos restritos e repetitivos com capacidade limitada de executar atividades e interação, além de problemas gastrointestinais. A alimentação tem uma grande interferência na qualidade de vida de um paciente espectro autista, por ele apresentar uma seletividade alimentar maior e em muitos casos, total recusa de determinados alimentos. A alimentação também parece exercer influência no comportamento de crianças e adolescentes com Transtorno do Espectro Autista. Esta revisão integrativa buscou conhecer as estratégias nutricionais adotadas no manejo de crianças e adolescentes com Transtorno do Espectro Autista e pontuar quais apresentam impacto positivo na melhoria do comportamento e conseqüentemente, na qualidade de vida desses indivíduos. Foi realizado um levantamento dos artigos publicados nos últimos 10 anos, sobre o tema, nas bases científicas Biblioteca Virtual em Saúde e PUBMED. Dentre as estratégias encontradas destacaram-se a dieta sem glúten e caseína, a suplementação de probióticos e prebióticos, e de micronutrientes. Nenhuma das estratégias levantadas possuem evidências suficientes para serem consideradas como protocolo no tratamento nutricional de crianças e adolescentes com Transtorno do Espectro Autista. Entretanto, as estratégias como a dieta de exclusão de glúten e caseína, a suplementação de prebióticos e probióticos e a suplementação de vitamina D e vitaminas do complexo B, podem ser aplicadas de forma segura, desde que esse aconselhamento nutricional seja realizado considerando a individualidade de cada paciente.

PALAVRAS - CHAVE: Alimentação; Comportamento; Transtorno do espectro autista.

INTRODUCTION

Autism or Autistic Spectrum Disorder (ASD) is a neurobiological disorder in which the individual has developmental difficulties in both communication and social interaction. In addition, there are restricted and repetitive behavior patterns with limited ability to perform activities and interactions (MELLO *et al.*, 2013).

According to the World Health Organization, in 2016, for every 68 children one had some level of autistic spectrum disorder, which is about 1% of the world's population (OPAS, 2017). This occurrence is increasing; however, its etiology is unclear. What is known is that environmental and genetic causes may be relevant. According to the Center for Disease Control and Prevention (CDC) of the United States (US) government, in March 2020, the prevalence of people with autism spectrum disorder has risen in that country, with one autistic child for every 54 children at the age of eight (CDC, 2020).

In 2019, law 13.861/2019 has been sanctioned by President Jair Bolsonaro. It mandates the inclusion of information about people with autism spectrum disorder in Brazilian demographic censuses. There is still no real data on how many autistic people there are in Brazil (BRASIL, 2020), however, according to the Pan American Health Organization (2017), the estimate is that one in every 160 children have autistic spectrum disorder in Brazil.

Food plays an important role in the quality of life. According to the Food Guide for the Brazilian Population, the adequate intake of nutrients results in the prevention of diseases and nutritional deficiencies (BRASIL, 2014). However, people with autistic spectrum disorder may have some difficulties eating, such as neophobia of some foods, tantrums during feeding and food selectivity (SÁNCHEZ *et al.*, 2015).

Food selectivity is a term that refers to refusal to eat, little variety and restricted intake of foods consumed daily. The cause is still unknown; however, it is suggested to be due to neuromotor difficulties, different functioning of the sensory system, and gastrointestinal problems. It can also be caused by the restrictive interests of the person with ASD and the difficulty in following a routine. Children and adolescents with ASD have more eating problems and their choices are made based mainly on texture, with high energy density foods being preferred by them (SÁNCHEZ *et al.*, 2015).

Some behaviors that are common in individuals with ASD, such as obsession with details, fear of innovation, sensory deprivation, social isolation, and propensity for difficult situations, seem to be influenced by food. However, there is still no consensus about the way this influence occurs and whether it exists (BASPINAR; YARDIMCI, 2020).

In this context, to know which nutritional strategies have been adopted and evaluate which ones have had positive results in the treatment of children and adolescents with ASD is extremely relevant, to guide the conduct of professionals who assist this public.

DEVELOPMENT

This study is an integrative literature review. The following descriptors were used for the literature search in Portuguese, English, and Spanish, respectively: Transtorno do Espectro Autista, Alimentação e Comportamento, Autism Spectrum Disorder and Diet and Behavior, Trastorno del Espectro Autista e Dieta y Conducta. Inclusion criteria were full articles available electronically and published within the last 10 years, and the search was conducted in May 2020. The exclusion criteria were publications older than 10 years and that did not relate food with behavioral changes common to the autism spectrum disorder (ASD). The survey was carried out in two databases: Biblioteca Virtual em Saúde (BVS) and PubMed.

The study was carried out in three stages, the first consisting of an advanced search in databases, in which four articles were found in the BVS and 28 in PubMed, totaling 32. The second step was characterized by reading the abstracts, in which 15 articles were excluded because they met the exclusion criteria, resulting in 17 articles. The last step was the full reading of the remaining articles and the categorization into three groups according to the strategy they addressed: Gluten-free and casein-free diet; Probiotics and Prebiotics; Other nutritional strategies.

After reading the articles in their entirety, chart 1 which represents the relation of the studies that address gluten and casein, chart 2 that expresses the relation of those that address probiotics and prebiotics and chart 3 which represents those that address other nutritional strategies, were filled in.

CHART 1 - List of studies addressing gluten and casein organized by type.

Author/Year	Study Type/Sample	Objectives	Results	Limitations
PIWOWARCZYK <i>et al.</i> , 2018	Systematic review 6 randomized clinical trials	To systematically evaluate and update the evidence on the effectiveness of gluten-free and casein-free diets in children with ASD.	There is insufficient evidence of the benefits of gluten-free and casein-free diets for children with ASD, although more recent studies, though few and limited, have shown improvements.	Small sample size and lack of sample size calculations in all the analyzed tests.
NAVARRO <i>et al.</i> , 2015	Randomized, double-blind study 12 individuals with ASD	To make the association between diet type and intestinal permeability and behavioral disorders in children with the autistic spectrum.	There were no significant differences in intestinal permeability and behavior or IQ between the groups at baseline.	Small sample size.
GHALICHI <i>et al.</i> , 2016	Randomized clinical trial 80 children with ASD	To investigate the effect of gluten-free diet on gastrointestinal symptoms and behavioral indices in children with ASD.	The gluten-free diet appears to be beneficial, however, the same intervention needs to be done with larger numbers of individuals.	The sample size; the heterogeneity of the patients and the difficulty of the parents to apply the diet.
PUSPONEGORO <i>et al.</i> , 2015	Randomized controlled, double-blind clinical trial 74 children with ASD	To determine the effect of gluten and casein supplementation on maladaptive behavior and GI symptom severity in children with ASD.	There was no increase in maladaptive behavior after one week of supplementation.	Short intervention duration.
PEDERSEN <i>et</i>	Randomized	To evaluate the	The age of the	The relatively

<i>al.</i> , 2014	controlled trial 72 children	influence of gluten- and casein-free diet as an intervention for children diagnosed with autism spectrum disorder.	participants at the time of the dietary intervention is a highly significant variable. Children within the age range of 7 to 9 years are more likely to respond positively after 12 months of dieting.	small number of participants, and the asymmetry of participant numbers according to certain variables.
HYMAN <i>et al.</i> , 2016	Double-blind controlled clinical trial 14 Autistic Children	Evaluate the safety and efficacy of the gluten/casein-free diet.	The diet is safe if followed by a professional nutritionist, but no significant data has been found regarding its effectiveness in improving symptoms of ASD.	Small sample size.
MARÍ-BAUSET, 2016	Case-control study 131 patients	To verify the nutritional impact of gluten-free and casein-free diet in children with ASD.	Children in the diet had lower weight, BMI, total energy and micronutrient intake, but had a higher intake of fiber, legumes and vegetables. In addition, they showed higher fat intake, but needed Vit. D supplementation.	Relatively small sample size, which limited the statistical power to identify differences between groups.

Source: Elaborated by the authors (2021)

CHART 2 - List of studies that address probiotics and prebiotics.

Author/Year	Study Type/Sample	Objectives	Results	Limitations
NG <i>et al.</i> , 2019	Systematic Review 8 clinical trials	Examine the clinical role of prebiotics and probiotics in the gastrointestinal and core symptom management of TEA.	There is limited overall evidence to support the use of prebiotics and probiotics in alleviating gastrointestinal or behavioral symptoms in children with autism spectrum disorder.	Limited amount of evidence.
	Randomized,			There was no

GRIMALDI, <i>et al.</i> , 2018	double-blind intervention study 26 autistic children	To understand the impact of diet on gut microbiota composition and metabolism in children with ASD; to investigate the potential of the intervention of prebiotic supplementation on these parameters; to evaluate the effect of the intervention on gut microbiota dysfunction, mood, behavior and sleep.	There was a significant impact of the diets on the gut microbiota, suggesting that they may be relevant to the improvement of several aspects, including psychological. Associated with probiotic supplementation there was an improvement in antisocial behavior and significant changes in fecal and urinary metabolites. Parents reported that their children slept 1 hour longer and had fewer problems falling asleep.	mention of limitations.
SANCTUARY <i>et al.</i> , 2019	Pilot Clinical Study 8 children with ASD and GI symptoms	To evaluate the tolerability of a probiotic (infant Bifidobacterium) in combination with a bovine colostrum product (BCP) as a source of prebiotic oligosaccharides and to assess GIT, microbiota, and immune factors in children with gastrointestinal comorbidities and ASD.	There was improvement in chronic gastrointestinal symptoms, however, more studies are needed to prove the effectiveness.	Small sample size and high symptom heterogeneity among participants.

Source: Elaborated by the authors (2021)

CHART 3 - List of studies that address other nutritional strategies.

Author/Year	Study Type/Sample	Objectives	Results	Limitations
DE CRESCENZO <i>et al.</i> , 2020	Systematic Review and Meta-Analysis 9 studies	Evaluate the effectiveness of PUFAs in children and adolescents with ASD.	No clinical recommendations can be suggested.	Low evidence.
HEALY; <i>et al.</i> , 2019	Systematic Review 12 studies	To report on the effect of weight management	There were no significant results in the comprehensive	Absence of subgroup analyses in most

		interventions in youth with ASD.	interventions, and there were also no significant changes in body weight.	studies and factors modifying intervention effectiveness. No intervention examines diet-based treatments alone, so it is not possible to differentiate between the effects of diet and other techniques.
LI <i>et al.</i> , 2018	Systematic review 15 studies	Provide current evidence on effective and safe supplements to treat nutritional deficiencies and improve symptoms in children with ASD.	Vitamin B6, B12 and Folic Acid may be helpful in improving behavioral symptoms of ASD. And Vit D provides improvement in self-care and skill development. Omega-3 fatty acid did not affect behaviors.	Several other nutritional deficiencies were not discussed. The number of studies included was limited.
CASTRO <i>et al.</i> , 2016	Systematic Review 11 studies	To evaluate whether folic acid supplementation might be associated with a higher incidence of autism.	The effect of folic acid supplementation, especially in pregnancy, shows contradictory and inconsistent results.	Limited to studies published from January 2003 to July 2013.
PARELLADA <i>et al.</i> , 2017	Randomized clinical trial 68 children and adolescents with ASD.	Investigate whether omega-3 supplementation improves erythrocyte membrane, plasma antioxidant status (TAS), and autistic behaviors.	Omega-3 treatment improved the erythrocyte membrane in the omega-6/omega-3 ratio, there was also significant improvement in subjects in social motivation.	The heterogeneity of the recruited sample. Cross-over designs, which can lead to confounding estimates of treatment effects.
VOIGT <i>et al.</i> , 2014	Randomized clinical trial 48 patients	To determine whether supplementation with decosa hexahenoic acid (DHA) improves behavior in children with autism.	There was no improvement in symptoms in the DHA group compared to the placebo group.	Small sample size.
SAAD <i>et al.</i> , 2016	Cross-Sectional Study	To evaluate vitamin D in	The patients presented vitamin D deficiency.	They included only males, and

	122 patients	autistic children compared to controls and the relationship between vitamin D deficiency and the severity of autism.	After supplementation, there was significant improvement in irritability, lethargy/social withdrawal, hyperactivity, and stereotypic behavior.	the control groups were all suffering from acute inflammation, which can affect plasma vitamin D levels.
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Source: Elaborated by the authors (2021)

The 17 articles selected are foreign journals and are available in English. Considering the time restriction, it was possible to verify that the theme is recent in the literature and most of them present significant limitations, requiring further research.

Among the presented articles, six were systematic reviews, and of these, one also included a meta-analysis. It is important to highlight that the theme related to the autistic spectrum disorder and food has been the focus of several studies, with the purpose of designing nutritional strategies to improve the clinical and behavioral status of these individuals. Among the articles, seven reported the association of ASD with a gluten- and casein-restricted diet, three addressed probiotics and prebiotics, and the others, other nutritional strategies.

Autism Spectrum Disorder and Eating

The use of nutritional strategies to improve the quality of life of people with ASD is a topic of much discussion. Especially because studies on the effectiveness of these strategies are still scarce and have many limitations. One of the relevant factors in this topic is the manifestation of gastrointestinal problems, which are very frequent in individuals with ASD. Sintomas como diarreia, constipação, refluxo ou intolerância a determinados alimentos são extremamente comuns. Além disso, a desnutrição e/ou intoxicação por substâncias não nutritivas também ocorre devido à seletividade alimentar que é recorrente na alimentação do autista (SILVA *et al.*, 2020). Essa seletividade, acontece quanto à textura, a neofobia e a variedade restrita de alimentos (SÁNCHEZ *et al.*, 2015).

Attempts to reverse this can lead to situations that only worsen the response of the child or adolescent with ASD, as they may exhibit behaviors such as aggression, crying, pushing food as a protest, self-mutilation, and even throwing objects at parents or caregivers (SHARP *et al.*, 2019).

It is theorized that behaviors such as these may be the result of negatively affected brain function, being a consequence of the fullness of the affected intestinal and blood-brain barrier. It is believed that damage to the intestinal barrier associated with poor digestion of some foods leads to increased release of pro-inflammatory cytokines, peptides, and toxins that eventually reach the central nervous system, which would lead to the aggravation of these behaviors in the autistic (BASPINAR; YARDIMCI, 2020).

In this context, some nutritional strategies have been adopted in an attempt to improve the quality of life of autistic patients. Among these are the gluten- and casein-free diet, the use of probiotics and prebiotics, and the supplementation of micronutrients and essential fatty acids, which will be addressed in this review.

Gluten and Casein

Gluten is characterized by a set of proteins found in wheat, oats, barley, malt, and rye (BRASIL, 2002) and casein is a phosphoprotein a type of protein that comes from mammalian milk (KUNZ; LÖNNERDAL, 1990).

The diet including these proteins can lead to symptoms such as intestinal inflammation, colitis, gastrointestinal changes, and some types of allergies in autistic children and adolescents, probably due to impaired intestinal permeability. Physical and behavioral symptoms are also commonly observed in these individuals (HYMAN *et al.*, 2016). The gluten and casein exclusion diet was developed to evaluate the hypothesis that it may bring benefits and improvement of these symptoms (PUSPONEGORO *et al.*, 2015).

In order to follow the gluten exclusion diet, it is necessary to remove from the diet all foods and cooking ingredients that contain traces of wheat, oat, barley, rye and other cereals that contain these ingredients, such as flours, breads, pies, pastas and sweets. To remove casein from the diet it is necessary to exclude dairy products such as milk, including breast milk, yogurt, cheese, butter, cream, ice cream, and others that contain this ingredient in their formulation (MARÍ-BAUSET *et al.*, 2016).

One of the articles, a systematic review, documents that in general, there is little evidence that the gluten-free diet is completely safe from a nutritional standpoint. However, there was improvement in symptoms, and no side effects of the diet in children with ASD. This review points out that although the diet appears to have benefits, further studies are needed to validate this recommendation (PIWOWARCZYK *et al.*, 2018).

The randomized controlled trials that were presented indicated that the diet may be safe for some children with ASD, but only one reported a significant role in decreasing gastrointestinal symptoms. With regard to behavior, these studies concluded that the gluten- and casein-free diet did not promote a significant decrease in behavioral disturbances; however, intervention time and sample size were presented as limitations. It was also possible to observe that children and adolescents who consumed the gluten-free and casein-free diet had a higher intake of fiber, legumes, and vegetables, in addition to better quality of fat intake (GHALICHI *et al.*, 2016; PUSPONEGORO *et al.*, 2015; HYMAN *et al.*, 2016).

The results point out that the gluten-free and casein-free diet seems to be beneficial in some cases, and that despite being indifferent in others, it is not possible to state that children who consume diets without restriction suffer nutritional losses. If properly implemented and monitored for nutritional adequacy, respecting individuality, it is not harmful to the health of these individuals. However, given the many limitations and small number of studies, it is not possible to state that this strategy should be adopted with the purpose of behavioral improvement (PUSPONEGORO *et al.*, 2015; HYMAN *et al.*, 2016; GHALICHI *et al.*, 2016; MARÍ-BAUSET, 2016; PIWOWARCZYK *et al.*, 2018).

The results found in this review agree with the findings of the review conducted by Baspinar and Yardimci (2020), in which the authors state that the gluten-free and casein-free diet does not have sufficient scientific support to be recommended as a nutritional strategy in the treatment of ASD, and that despite being safe, in the long term it may offer nutritional risks if not followed by a professional nutritionist. The authors also

pointed out as limitations the small number of studies on the subject and their low quality.

Probiotics and Prebiotics

Probiotics are live microorganisms that when given in adequate amounts can benefit the gut microbiota of individuals with autism spectrum disorder. Common symptoms reported by patients with ASD include constipation, diarrhea, and abdominal pain characteristic of an imbalance in the gut microbiota (BINNS, 2013).

Prebiotics are substrates selectively used by living host microorganisms that offer health benefits (NG *et al.*, 2019). Thus, prebiotics and probiotics have been suggested for people with ASD with the intention of reducing symptoms related to gastrointestinal changes (GRIMALDI *et al.*, 2018).

Among the three articles presented, the intervention, double-blind, randomized study conducted by Grimaldi *et al.* (2018), concluded that prebiotic supplementation in children with ASD generates positive results in both improving gut microbiota and antisocial behavior.

The other two studies, one of them a pilot study with only eight children, showed that the use of prebiotics and probiotics was well tolerated and that there was an improvement in gastrointestinal symptoms. The only side effect was flatulence. The pilot study found no relationship between probiotic supplementation and behavioral improvement but did find an improvement in gut microbiota. The randomized, double-blind intervention study with 26 autistic children, in addition to finding improvement in gastrointestinal parameters, detected improvement in antisocial behavior when supplementation was associated with the exclusion diet.

However, the systematic review in which eight clinical trials were included concluded that there is still insufficient evidence regarding the benefit of prebiotic and probiotic supplementation for improving GI and behavioral symptoms in individuals with ASD. In fact, research has increased to evaluate the benefits of using prebiotics and probiotics to ensure the balance of the gut microbiota of autistic individuals, but is still insufficient (NG *et al.*, 2019).

The recent study by Sivamaruthi *et al.* (2020), pointed out that the use of probiotics in autistic individuals has shown promising results in alleviating autism progression and reducing gastrointestinal problems, as well as improving cognitive and behavioral deficits. However, as noted in this review, the study led to the conclusion that although supplementation seems to influence symptoms associated with ASD, most papers show inconclusive results and several limitations, such as sample size and intervention time. Thus, more studies need to be conducted before this intervention can be recommended.

Other nutritional strategies

In addition to the strategies previously presented, it was possible to detect six more nutritional interventions commonly adopted in the treatment of ASD, as follows: weight loss, supplementation of vitamins D, B6, B9 (folic acid), B12, omega-3, omega-6, and docosahexaenoic acid (DHA) (VOIGT *et al.*, 2014; CASTRO *et al.*, 2016; PARELLADA *et al.*, 2017; SAAD *et al.*, 2016; LI *et al.*, 2018; CRESCENZO *et al.*, 2020).

Out of the seven studies found, three showed positive results regarding the intervention adopted, while four showed negative or inconclusive results.

The interventions that showed positive results were supplementation with B vitamins (6, 9, 12), vitamin D, and omega 3. The systematic review that included studies with all these interventions pointed out that they promoted behavioral improvement, especially self-care (PARELLADA *et al.*, 2017). The cross-sectional study in which 122 autistic children were included, also reported positive results with vitamin D supplementation. It was found that there was a decrease in irritability, lethargy, social withdrawal, hyperactivity, and stereotypic behavior (SAAD *et al.*, 2016).

In the systematic review conducted by Jiang Li *et al.*, (2018), it was pointed out that vitamin D generated improvement only in self-care and skill development. Among the negative or inconclusive results, folic acid supplementation, especially during pregnancy, stands out. In this study children with autism had higher serum homocysteine levels due to this supplementation (CASTRO *et al.*, 2016).

Weight loss was also shown to be an ineffective strategy. In the systematic review conducted by Healy *et al.*, (2019), which included 12 studies, they pointed out the absence of subgroup analyses in most of the studies reviewed. Furthermore, no intervention examines diet-based treatments in isolation, making it impossible to differentiate between the effects of diet itself from other techniques for both weight loss and possible behavior change.

It was also possible to infer that there is little evidence to support the efficacy of fatty acid supplementation for improving symptoms of ASD. The same is true for the use of DHA for behavioral improvement purposes, so these strategies cannot yet be considered effective (VOIGT *et al.*, 2014; PARELLADA *et al.*, 2017; CRESCENZO *et al.*, 2020).

According to Monteiro *et al.*, (2020), in a systematic review that included 18 clinical studies, although some authors expose progress in symptoms associated with autism in individuals undergoing nutritional interventions, there is little scientific evidence to support their use in children and adolescents with autism. These findings corroborate the results of this review.

In a 12-month randomized controlled trial, Adams *et al.* (2018) evaluated the effectiveness of nutritional and dietary intervention in 67 patients with ASD and aged 3 to 58 years. They were supplemented with vitamins and minerals, polyunsaturated fatty acids (PUFAs), digestive enzymes, and prescribed a healthy gluten-, casein-, and soy-free diet. The treatment group showed significant improvement in non-verbal intellectual ability and behavioral symptoms related to ASD. These findings are extremely relevant, as they infer that perhaps, for nutritional strategies in the treatment of ASD to be effective, they need to be adopted in the long term.

FINAL CONSIDERATIONS

Evidence on the efficacy of nutritional strategies in the treatment of ASD is still very scarce and limited. All systematic reviews included in this study pointed out as a limitation the small number of studies to include in their analysis and the low quality of most of the research. This reinforces the need for more studies along these lines to be conducted to remedy the lack of studies for systematic reviews and meta-analysis.

It was observed that none of the strategies raised have sufficient evidence to be considered as a protocol in the nutritional treatment of children and adolescents with ASD, and that more clinical trials with larger populations and that follow rigorous criteria of methodology and execution are necessary to better elucidate this issue.

In summary, strategies such as the gluten and casein exclusion diet, prebiotic and probiotic supplementation, and vitamin D and B-complex supplementation can be safely applied, if this nutritional counseling is done considering the individuality of each patient.

REFERENCES

ADAMS, J. B.; AUDHYA, T.; GEIS, E.; GEHN, E.; FIMBRES, V. et al. Comprehensive nutritional and dietary intervention for autism spectrum disorder—a randomized, controlled 12-month trial. **Nutrients**, v. 10, n. 3, p. 369, 2018. Doi: 10.3390/nu10030369.

BASPINAR, B.; YARDIMCI, H.; Gluten-Free Casein-Free Diet for Autism Spectrum Disorders: Can It Be Effective in Solving Behavioural and Gastrointestinal Problems?. **The Eurasian Journal of Medicine**, v. 52, n. 3, p. 292, 2020. Doi: 10.5152/eurasianjmed.2020.19230.

BINNS, N. **Probióticos, prebióticos e a microbiota intestinal**. São Paulo, Brasil. International Life Science Institute (ILSI Europe), 2013. 33 p. Disponível em: <<https://ilsi.eu/publication/probiotics-prebiotics-and-the-gut-microbiota/>>.

BRASIL. Ministério da Saúde; **Guia Alimentar para a População Brasileira** promovendo a alimentação saudável. Normas e manuais técnicos: Brasília, 2014. Disponível em: <https://bvsms.saude.gov.br/bvs/publicacoes/guia_alimentar_populacao_brasileira_2ed.pdf>.

BRASIL. **Resolução RDC nº 40, de 8 de fevereiro de 2002**. Aprova o “Regulamento técnico para rotulagem de alimentos e bebidas embalados que contenham glúten” constante do anexo desta Resolução. Órgão emissor: ANVISA - Agência Nacional de Vigilância Sanitária Disponível em: <http://bvsms.saude.gov.br/bvs/saudelegis/anvisa/2002/rdc0040_08_02_2002.html>. Acesso em 11 de abril de 2021.

BRASIL. Câmara dos deputados. **Sancionada lei que inclui dados sobre autismo no Censo 2020** Fonte: **Agência Câmara de Notícias**. Disponível em: <<https://www.camara.leg.br/noticias/562740-sancionada-lei-que-inclui-dados-sobre-autismo-no-censo-2020/>>. Acesso em: 07 ago. 2020.

CASTRO, K.; KLEIN, L. S.; BARONIO, D.; GOTTFRIED, C.; RIESGO, R. et al. Folic acid and autism: what do we know? **Nutritional Neuroscience**, v. 19, n. 7, p. 310-317, 2016. Doi: 10.1179/1476830514Y.0000000142.

CDC, Centro de controle de prevenção de doenças. Prevalência de Autismo nos EUA sobre 10%: agora é 1 para 54, **Revista Autismo**. Disponível em: <[https://www.revistaautismo.com.br/destaque/prevalencia-de-autismo-nos-eua-sobe-10-agora-e-1-para-54/#:~:text=2020\)%20pelo%20CDC%20\(Centro%20de,sempre%20de%204%20anos%20atr%C3%A1s](https://www.revistaautismo.com.br/destaque/prevalencia-de-autismo-nos-eua-sobe-10-agora-e-1-para-54/#:~:text=2020)%20pelo%20CDC%20(Centro%20de,sempre%20de%204%20anos%20atr%C3%A1s)>. Acesso em: 28 jul. 2020.

CRESCENZO, F.; D'ALÒ, G. L.; MORGANO, G. P.; MINOZZI, S.; MITROVA, Z. et al. Impact of polyunsaturated fatty acids on patient-important outcomes in children and adolescents with autism spectrum disorder: a systematic review. **Health and quality of life outcomes**, v. 18, n. 1, p. 1-12, 2020. Doi: 10.1186/s12955-020-01284-5.

GHALICHI, F.; GHAEMMAGHAMI, J.; MALEK, A.; OSTADRAHIMI, A. Effect of gluten free diet on gastrointestinal and behavioral indices for children with autism spectrum disorders: a randomized clinical trial. **World Journal of Pediatrics**, v. 12, n. 4, p. 436-442, 2016. Doi: 10.1007/s12519-016-0040-z.

GRIMALDI, R.; GIBSON, G. R.; VULEVIC, J.; GIALLOUROU, N.; CASTRO-MEJIÁ, J. L. et al. A prebiotic intervention study in children with autism spectrum disorders (ASDs). **Microbiome**, v. 6, n. 1, p. 1-13, 2018. Doi: 10.1186/s40168-018-0523-3.

HEALY, S.; PACANOWSKI, C. R.; WILLIAMS, E. Weight management interventions for youth with autism spectrum disorder: a systematic review. **International Journal of Obesity**, v. 43, n. 1, p. 1-12, 2019. Doi: 10.1038/s41366-018-0233-8.

HYMAN, S. L.; STEWART, P. A.; FOLEY, J.; CAIN, U.; PECK, R. et al. The gluten-free/casein-free diet: a double-blind challenge trial in children with autism. **Journal of autism and developmental disorders**, v. 46, n. 1, p. 205-220, 2016. Doi: 10.1007/s10803-015-2564-9.

KUNZ, C.; LÖNNERDAL, B. Human-milk proteins: analysis of casein and casein subunits by anion-exchange chromatography, gel electrophoresis, and specific staining methods. **The American journal of clinical nutrition**, v. 51, n. 1, p. 37-46, 1990. Doi: 10.1093/ajcn/51.1.37.

LI, Y. J.; LI, Y-M; XIANG, D. Supplement intervention associated with nutritional deficiencies in autism spectrum disorders: a systematic review. **European journal of nutrition**, v. 57, n. 7, p. 2571-2582, 2018. Doi: 10.1007/s00394-017-1528-6.

MARÍ-BAUSET, S.; LLOPIS-GONZÁLEZ, A.; ZAZPE, I.; MARÍ-SANCHIS, A.; SUÁREZ-VARELA, M. M. Nutritional impact of a gluten-free casein-free diet in children with autism spectrum disorder. **Journal of autism and developmental disorders**, v. 46, n. 2, p. 673-684, 2016. Doi: 10.1007/s10803-015-2582-7.

MELLO, A. M.; ANDRADE, M.; CHEN HO, H.; DIAS, I. **Retratos do autismo no Brasil**. São Paulo: Associação dos Amigos do Autista, 2013. Disponível em: <<https://www.ama.org.br/site/wp-content/uploads/2017/08/RetratoDoAutismo.pdf>>.

MONTEIRO, M. A.; SANTOS, Andressa; GOMES, Lidiane; RITO, Rosane. Autism spectrum disorder: A systematic review about nutritional interventions. **Revista Paulista de Pediatria**, v. 38, 2020. Disponível em: <<https://doi.org/10.1590/1984-0462/2020/38/2018262>>.

NAVARRO, F.; PEARSON, D. A.; FATHEREE, N.; MANSOUR, R.; HASHMI, S. S. et al. Are 'leaky gut' and behavior associated with gluten and dairy containing diet in children with autism spectrum disorders? **Nutritional Neuroscience**, v. 18, n. 4, p. 177-185, 2015. Doi: 10.1179/1476830514Y.0000000110.

NG, Q. X.; LOKE, W.; VENKATANARAYANAN, N.; LIM, D. Y.; SOH, A. Y. S. et al.; A systematic review of the role of prebiotics and probiotics in autism spectrum disorders. **Medicina**, v. 55, n. 5, p. 129, 2019. Doi: 10.3390/medicina55050129.

OPAS, Organização Pan-Americana da Saúde. **Folha Informativa - Transtorno do Espectro Autista**, 2017. Disponível em: <<https://www.paho.org/bra/index.php?Itemid=1098#:~:text=Estima%2Dse%20que%2C%20em%20todo,que%20s%C3%A3o%20significativamente%20mais%20elevados>>. Acesso em: 3 ago. 2020.

PARELLADA, M.; LLORENTE, C.; CALVO, R.; GUTIRREZ, S.; LÁZARO, L. et al. Randomized trial of omega-3 for autism spectrum disorders: effect on cell membrane composition and behavior. **European Neuropsychopharmacology**, v. 27, n. 12, p. 1319-1330, 2017. Doi: 10.1016/j.euroneuro.2017.08.426.

PEDERSEN, L.; PARLAR, S.; KVIST, K.; WHITELEY, P.; SHATTOCK, P. Data mining the ScanBrit study of a gluten-and casein-free dietary intervention for children with autism spectrum disorders: behavioural and psychometric measures of dietary response. **Nutritional Neuroscience**, v. 17, n. 5, p. 207-213, 2014. Doi: 10.1179/1476830513Y.0000000082.

PIWOWARCZYK, A.; HORVATH, A.; LUKASIK, J.; PISULA, E.; SZAJEWSKA, H. Gluten-and casein-free diet and autism spectrum disorders in children: a systematic review. **European journal of nutrition**, v. 57, n. 2, p. 433-440, 2018. Doi: 10.1007/s00394-017-1483-2.

PUSPONEGORO, H. D.; ISMAEL, S.; FIRMANSYAH, A.; SASTROASMORO, S.; VANDENPLAS, Y. Gluten and casein supplementation does not increase symptoms in children with autism spectrum disorder. **Acta Paediatrica**, v. 104, n. 11, p. e500-e505, 2015. Doi: 10.1111/apa.13108.

SAAD, K.; ABDEL-RAHMAN, A. A.; ELSEROGY, Y. M.; AL-ATRAM, A. A.; CANNEL, J. J. et al. Vitamin D status in autism spectrum disorders and the efficacy of vitamin D supplementation in autistic children. **Nutritional Neuroscience**, v. 19, n. 8, p. 346-351, 2016. Doi: 10.1179/1476830515Y.0000000019.

SÁNCHEZ, S. S.; LORENTE GARCIA, A.; PINEDA LOPEZ, O.; CANDIDO FERNANDEZ-CAO; J.; ARIJA VAL, V. Selectividad alimentaria en los trastornos del espectro autista: una revisión sistemática. **Revista Española de Nutrición Comunitaria**, v. 21, n. 2, p. 13-19, 2015. Disponível em: <<https://pesquisa.bvsalud.org/portal/resource/pt/ibc-163583>>.

SANCTUARY, M. R.; KAIN, J. N.; CHEN, S. Y.; KALANETRA, K.; LEMAY, D. G. et al. Pilot study of probiotic/colostrum supplementation on gut function in children with autism and gastrointestinal symptoms. **PloS one**, v. 14, n. 1, p. e0210064, 2019. Doi: 10.1371/journal.pone.0210064.

SHARP, W. G.; BURRELL, T. L.; BERRY, R. C.; STUBBS, K. H.; MCCRAKEN, C. E. et al. The autism managing eating aversions and limited variety plan vs parent education: a randomized clinical trial. **The Journal of pediatrics**, v. 211, p. 185-192. e1, 2019. Doi: 10.1016/j.jpeds.2019.03.046.

SILVA, D. V.; SANTOS, P. N. M.; SILVA, D. A. V. Excesso de peso e sintomas gastrointestinais em um grupo de crianças autistas. **Revista Paulista de Pediatria**, v. 38, n. 5, p. 1-6, 2020. Disponível em: <<http://dx.doi.org/10.1590/1984-0462/2020/38/2019080>>.

SIVAMARUTHI, B. S.; SUGANTHY, N.; KESIKA, P.; CHAIYASUT, C. The role of microbiome, dietary supplements, and probiotics in autism spectrum disorder. **International journal of environmental research and public health**, v. 17, n. 8, p. 2647, 2020. Doi: 10.3390/ijerph17082647.

VOIGT, R. G.; MELLON, M. W.; KATUSIC, S. K.; WEAVER, A. L.; MATERN, D. et al. Dietary docosahexaenoic acid supplementation in children with autism. **Journal of Pediatric Gastroenterology and Nutrition**, v. 58, n. 6, p. 715-722, 2014. Doi: 10.1097/MPG.0000000000000260.