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REVIEW ARTICLE

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Major clinical implications of adequate nutrition in children and adolescents with attention-deficit/hyperactivity disorder: a concise systematic review

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Abstract

Introduction: Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by inappropriate levels of impulsive behavior, hyperactivity, and/or inattention, with a worldwide prevalence estimated at around 7% in childhood and adolescence, and around 3 % in adulthood, with a higher prevalence in boys than in girls. **Objective:** It was to present the main clinical implications of adequate nutrition in children and adolescents with attention-deficit/hyperactivity disorder. **Methods:** The PRISMA Platform systematic review rules were followed. The research was carried out from January to March 2024 in the Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** A total of 84 articles were found, 21 articles were evaluated, and 14 were included in this systematic review. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 19 studies with a high risk of bias and 30 studies that did not meet GRADE. Most studies showed homogeneity in their results, with X^2=62.8%>50%. Intake of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) fatty acids daily for 8 weeks is associated with less impulsive behavior in children with ADHD. Dietary supplementation with omega-3 fatty acids reduces ADHD symptoms in both individuals with ADHD and typically developing children. A Mediterranean diet may improve BIS results, although our results are not conclusive in this population. The daily intake of calories and nutrients in patients taking methylphenidate is generally lower than in a healthy population of similar age. Co-supplementation of vitamin D and magnesium over 8 weeks may improve behavioral function and mental health in children with ADHD.

Keywords: Attention-deficit/hyperactivity disorder. Impulsive behavior. Hyperactivity. Nutrology. Nutrition.

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by inappropriate levels of impulsive behavior, hyperactivity, and/or inattention **[1]**, with a worldwide prevalence estimated at around 7% in childhood and adolescence, and around 3% in adulthood, with a higher prevalence

in boys than in girls. Although ADHD is a common disorder in childhood, adolescence, and adulthood, this review focuses on childhood ADHD, as the adult form has other characteristics. Along with schizophrenia, autism, and epilepsy, ADHD is one of the most studied neurodevelopmental disorders. Depending on the definition and study, this disorder is relatively common, affecting approximately 5% to 12% of school-age children **[2]**.

In this scenario, ADHD is associated with an increased risk of several other mental health problems, including depression, anxiety, oppositional defiant disorder, antisocial behavior, and substance abuse. It is a heterogeneous and multifactorial behavioral phenotype, involving genetic susceptibility, environmental risk factors, and gene-environmental interactions **[3]**. The physiology underlying ADHD is not yet fully understood, but alterations of brain monoaminergic systems and reduced connectivity of brain neural networks have been linked to challenges in executive functioning and reward processes **[4]**.

Associations mentioned in the etiology and pathology of ADHD include genetic factors, interaction of genes and nutrition, epigenetics, and environmental elements, along with stress. Nutrition and diet were also reviewed as influencing factors, as restriction and elimination diets have been tested in ADHD treatments. Supplements, herbal and nutritional products and their effects on the disorder have been extensively discussed **[1]**. As potential causes of ADHD in children, oxidative stress, metal toxicity, decreased methylation of relevant genes, cerebral hypoperfusion, and mitochondrial dysfunctions have been mentioned as potential causes. Gut microbiota has recently been linked to dietary patterns and linked to susceptibility to ADHD. Dietary immunomodulation and antioxidant treatment have been discussed by our research group in some preliminary articles. An etiological classification of ADHD and food sensitivities for this disorder have been reviewed **[5]**.

In this context, it is necessary to analyze the dosages of Fe, Cu, Zn, Mg, and Se in children and adolescents with ADHD **[5]**. Therefore, the present study aims to present the main clinical implications of adequate nutrition in children and adolescents with attention-deficit/hyperactivity disorder.

Methods

Study Design

The present study followed the international systematic review model, following the rules of PRISMA (preferred reporting items for systematic reviews and meta-analysis). Available at: http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1. Accessed on: 02/16/2024. The methodological quality standards of AMSTAR-2 (Assessing the methodological quality of systematic reviews) were also followed. Available at: https://amstar.ca/. Accessed on: 02/16/2024.

Search Strategy and Search Sources

The literary search process was carried out from January to March 2024 and was developed based on Scopus, PubMed, Science Direct, Scielo, and Google Scholar, covering scientific articles from various eras to the present. The descriptors (MeSH Terms) were used: *"Attention-deficit/hyperactivity disorder. Impulsive behavior. Hyperactivity. Nutrology. Nutrition"*, and using the Boolean "and" between the *MeSH terms* and "or" between historical discoveries.

Study Quality and Risk of Bias

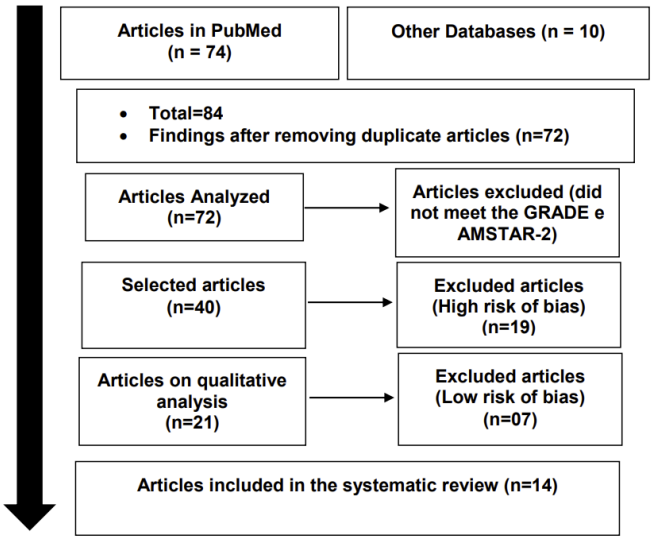
Quality was classified as high, moderate, low, or very low in terms of risk of bias, clarity of comparisons, precision, and consistency of analyses. The most evident emphasis was on systematic review articles or meta-analyses of randomized clinical trials, followed by randomized clinical trials. The low quality of evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. The risk of bias was analyzed according to the Cochrane instrument by analyzing the Funnel Plot graph (Sample size versus Effect size), using the Cohen test (d).

Results and Discussion

Summary of Findings

As a corollary of the literary search system, a total of 84 articles were found that were subjected to eligibility analysis and, subsequently, 14 studies were selected to compose the results of this systematic review. The studies listed were of medium to high quality (Figure 1), considering in the first instance the level of scientific evidence of studies such as meta-analysis, consensus, randomized clinical, prospective, and observational. The biases did not compromise the scientific basis of the studies. According to the GRADE instrument, most studies showed homogeneity in their results, with X^2=62.8%>50%. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 19 studies with a high risk of bias and 30 studies that did not meet GRADE.

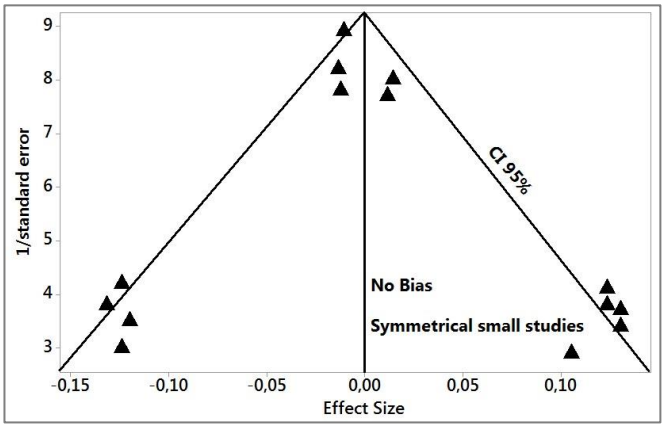
Figure 1. Flowchart showing the article selection process.



Source: Own authorship.

Figure 2 presents the results of the risk of bias of the studies using the Funnel Plot, showing the calculation of the Effect Size (Magnitude of the difference) using the Cohen Test (d). Precision (sample size) was determined indirectly by the inverse of the standard error (1/Standard Error). This graph had a symmetrical behavior, not suggesting a significant risk of bias, both between studies with a small sample size (lower precision) that are shown at the bottom of the graph and in studies with a large sample size that are presented at the top.

Figure 2. The symmetric funnel plot suggests no risk of bias among the small sample size studies that are shown at the bottom of the plot. High confidence and high recommendation studies are shown above the graph (n=14 studies).



Source: Own authorship.

Major Clinical Findings

According to the results collected, it was observed that the Barratt Impulsiveness Scale (BIS) is a self-administered instrument developed to assess the personality/behavioral construct of impulsivity. Impulsivity is associated with attention-deficit/hyperactivity disorder (ADHD). In this sense, a cross-sectional clinical study evaluated the progression of impulsive behavior in children with ADHD after an 8-week dietary intervention with a Mediterranean diet and/or omega-3 fatty acid supplementation, using an 11-item version of the BIS adapted for children (BIS-11c). A total of 60 children with ADHD were included and divided into 4 groups, with a control group and 3 intervention groups (Mediterranean diet; omega-3 supplementation; and Mediterranean diet plus omega-3 supplementation). The supplementation group showed a very significant decrease in total BIS-11c. Total cognitive scores decreased slightly in the diet and supplementation groups. Only the control group showed a considerable decrease in the total motor score. Therefore, ingestion of 550 mg of eicosapentaenoic acid (EPA) fatty acid and 225 mg of DHA fatty acid per day for 8 weeks is associated with less marked impulsive behavior in children with ADHD. A Mediterranean diet may improve BIS results, although our results are not conclusive in this population **[6]**.

Also, a case-control study evaluated caloric and nutrient intake in a group of patients diagnosed with ADHD undergoing treatment with extended-release methylphenidate (MPH-ER) and analyzed the need to design nutritional intervention strategies. A total of 100 patients diagnosed with ADHD were treated with MPH-ER and 100 healthy children (control group). The nutritional status in the ADHD group was significantly lower than in the control group. Caloric intake at morning snack, lunch, and afternoon snack was significantly higher in the control group. Calorie intake at dinner was significantly higher in the ADHD group. There were no significant differences in breakfast. Total calorie intake, as well as intake of proteins, carbohydrates, fats, fiber, calcium, iron, magnesium, zinc, selenium and phosphorus, thiamine, niacin, vitamin B6, and folate, in the control group, was significantly higher than in the group ADHD. Thus, the daily intake of calories and nutrients in patients undergoing MPH-ER treatment is generally lower than in a healthy population of similar age **[7]**.

A systematic review study analyzed the relationship between Mg, Fe, Zn, Cu, and Se and ADHD. The associations observed between concentration levels of the elements Mg, Fe, Zn, Cu, and Se and ADHD symptoms are contradictory. This is partly due to the heterogeneity and complexity of the disorder. As a trend, lower levels of ferritin and zinc can be observed. However, this correlation is not causal, as illustrated by placebo-controlled trials that report conflicting evidence about the effectiveness of supplementation **[8]**.

One study evaluated the association between

changes in sugar consumption between 6 and 11 years of age and the incidence of ADHD. A food frequency questionnaire (FFQ) was used to estimate sugar consumption and the Developmental and Well-Being Assessment (DAWBA) was administered to mothers to assess the presence of ADHD. Only children without ADHD at age 6 and with complete FFQ and DAWBA information at ages 6 and 11 were included in the analyses (n = 2,924). The incidence of ADHD between 6 and 11 years old was 4.6% (3.6-5.6%) among boys and 1.8% (1.2-2.5%) among girls. Adjusted analyses showed no association between always high sucrose consumption between 6 and 11 years of age and the incidence of ADHD, compared to individuals who always had low consumption, both among boys and girls. The results suggest that there is no association between sucrose consumption between 6 and 11 years of age and the incidence of ADHD **[9]**.

Furthermore, a randomized controlled clinical study examined the effect of vitamin D and magnesium supplementation on the mental health of 66 children with ADHD. Participants were randomly allocated to receive vitamin D supplements (50,000 IU/week) plus magnesium (6 mg/kg/day) (n = 33) or placebo (n = 33) for 8 weeks. After eight weeks of intervention, serum levels of 25-hydroxyvitamin D3 and magnesium increased significantly in the intervention group compared to the control group. Additionally, children who received vitamin D plus magnesium showed significant reductions in emotional problems, conduct problems, peer problems, prosocial scores, total difficulties, externalizing scores, and internalizing scores compared to placebo-treated children. Co-supplementation of vitamin D (50,000 IU/week) and magnesium (6 mg/kg/day) for 8 weeks can improve behavioral function and mental health in children with ADHD **[10]**.

Authors conducted a 12-week, double-blind, placebo-controlled study comparing the effects of high doses of eicosapentaenoic acid (EPA, 1.2 g) and placebo on cognitive function (continuous performance test) in n = 92 young people (ages 6 to 18) with ADHD. Blood erythrocyte endogenous polyunsaturated fatty acids (PUFAs) were measured before and after treatment, to examine the effects of basal endogenous EPA levels on treatment response and the effects of EPA treatment on PUFA levels. Overall, the EPA group improved more than the placebo group in focused attention; furthermore, among youth with the lowest baseline levels of endogenous EPA, the EPA group improved more than the placebo group on another measure of focused attention and vigilance. Interestingly, the EPA group improved less than the placebo group in impulsivity, both overall and in the youth with the highest baseline EPA levels, who also showed less improvement in other ADHD and emotional symptoms. Therefore, EPA treatment improves cognitive symptoms in youth with ADHD, especially if they have a low baseline endogenous EPA level, while youth with high EPA levels may be negatively affected by this treatment **[11]**.

A study investigated the effects of dietary omega-3 fatty acid supplementation on ADHD symptoms and cognitive control in boys with and without ADHD. A total of 40 boys with ADHD, ages 8 to 14 years, and 39 matched, typically developing controls participated in a 16-week, double-blind, randomized, placebo-controlled study. Participants consumed 10 g of margarine daily, enriched with 650 mg of eicosapentaenoic acid (EPA)/docosahexaenoic acid (DHA) each or placebo. Baseline and follow-up assessments addressed ADHD symptoms, cognitive control fMRI, urine homovanillic acid, and cheek cell phospholipid sampling. EPA/DHA supplementation improved parent-rated attention in both children with ADHD and typically developing children. The DHA phospholipid level at follow-up was higher in children receiving EPA/DHA supplements than in placebo. There was no effect of EPA/DHA supplementation on cognitive control or fMRI measures of brain activity. Thus, dietary supplementation with omega-3 fatty acids reduces ADHD symptoms, both in individuals with ADHD and in typically developing children **[12]**.

The authors did not identify a significant difference between the body mass index and energy intake of the two groups. Hyperactive children have been shown to have a higher rate of physical activity than non-hyperactive children. The consumption of vitamin B12 and riboflavin in hyperactive children was significantly lower than in the healthy group. The intake of refined grains in the case group was significantly higher compared to the control group. Healthy children consumed more fruits and vegetables, skimmed milk, and eggs than children with ADHD. Therefore, hyperactive children consume fewer fruits and vegetables, skim milk and eggs, as well as food sources containing B vitamins, while consuming higher levels of refined grains **[13]**.

Finally, a recent meta-analysis study was conducted to explore the association between ADHD and the risk of overweight/obesity in children and adolescents. According to the meta-analysis, children with ADHD were at a significant risk of co-occurring overweight and obesity, especially boys, people in Asia and Europe, and patients not taking medication. ADHD has a significant association with overweight and obesity in children and adolescents, which can be altered by factors such as geography, gender, and medication use **[14]**.

Conclusion

It was concluded intake of EPA and DHA fatty acids daily for 8 weeks is associated with less impulsive behavior in children with ADHD. Dietary supplementation with omega-3 fatty acids reduces ADHD symptoms in both individuals with ADHD and typically developing children. A Mediterranean diet may improve BIS results, although our results are not conclusive in this population. The daily intake of calories and nutrients in patients taking methylphenidate is generally lower than in a healthy population of similar age. Co-supplementation of vitamin D and magnesium over 8 weeks may improve behavioral function and mental health in children with ADHD.

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Ethical Approval

Not applicable.

Informed consent

Not applicable.

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Data sharing statement

No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

Similarity check

It was applied by Ithenticate@.

Peer review process

It was applied.

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