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Does supplement intake play a role in managing Attention-Deficit/Hyperactivity Disorder symptoms in children and adults? – An overview of recent literature

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ABSTRACT

Introduction and objective: This review examines the role of supplements, such as vitamin D, zinc, magnesium, iron, polyunsaturated fatty acids, and probiotics, in managing various ADHD symptoms. It aims to identify possible alternatives or additions to commonly used treatments to improve the alleviation of the physiological signs of ADHD. *Description of the state of knowledge:* Attention-Deficit/Hyperactivity Disorder is one of the most common diagnoses made by psychiatrists in children and adolescents. Its symptoms can vary between patients but most often include inattentiveness, distractibility, hyperactivity, and impulsiveness. Many medications registered for the treatment of this disorder can induce unpleasant side effects. The broad spectrum of supplements may be beneficial for ADHD patients and alleviate troublesome symptoms. Supplementation intake has been previously proven helpful in managing various psychiatric disorders. This instills optimism that they may also have a positive impact on people with ADHD. *Summary:* The reviewed studies found many indications that oral intake of the supplements mentioned above may be beneficial for patients with ADHD. Nevertheless, this is still a fairly novel area, and more research is required to fully explore the potential advantages they may bring to managing this disorder.

Keywords: Attention-deficit hyperactive disorder; supplements; vitamin D; zinc; magnesium; iron; polyunsaturated fatty acids; probiotics

1. INTRODUCTION

Attention-Deficit/Hyperactivity Disorder (ADHD) is a neurodevelopmental disturbance defined by behaviors such as inattentiveness, hyperactivity, emotional imbalance, and impulsivity. The prevalence differs based on age, gender, race, and ethnicity; however, it was established to be between 10.08% and 10.47% among children and adolescents aged 4 to 17 (Li et al., 2023). Its development cannot be attributed to any specific risk factor. Genetic and environmental factors contribute to the increased risk of ADHD (Thapar and Cooper, 2016). The most widely employed pharmacological treatment of ADHD consists of the use of stimulant drugs such as methylphenidate and amphetamine, as well as non-stimulant medicaments atomoxetine, guanfacine, and clonidines (Groom and Cortese, 2022). However, they can induce many unpleasant side effects, such as loss of appetite, trouble sleeping, mood disturbance, nausea, and headaches (Cascade et al., 2010).

Aim

The present study focuses on evaluating specific supplementation intake for managing ADHD symptoms in children and adolescents. It aims to provide an invaluable perspective on alternative treatments for symptom management among ADHD patients.

2. METHODOLOGY

Using freely available databases such as PubMed and keywords like "ADHD supplements", "ADHD diet", and "ADHD treatment", relevant articles were selected. Initially, the selection was based on titles and abstracts. Articles suitable for the study, written in English and published between 2006 and 2023, were then included.

3. RESULTS AND DISCUSSION

Vitamin D

Vitamin D is important for our well-being not only because it influences the skeletal system but also because it can reduce the risk of many chronic disorders such as heart, autoimmune, infectious diseases, type 2 diabetes, and more (Holick, 2012). Kotsi et al., (2019) assessed the levels of this vitamin in children and adolescents with attention-deficit hyperactivity disorder. They found that there is a significant difference in serum concentration of D vitamin metabolite (25(OH)D) in patients diagnosed with ADHD compared to healthy controls, establishing that there is an association between lower vitamin D levels and ADHD. In 2018, Elshorbagy et al., (2018) demonstrated that there is a higher prevalence of vitamin D deficiency in ADHD children compared to the control group. Furthermore, they found that the group receiving vitamin D supplementation revealed improvements in cognitive functions.

Another study concerning the impact of vitamin D supplementation in children with ADHD found that oral supplementation leads to an alleviation of ADHD symptoms, particularly inattentiveness. This suggests that vitamin D treatment for children with ADHD could be a beneficial consideration (Dehbokri et al., 2019). Not only could supplementation alone potentially bring good results, but it may also have a positive impact on patients treated with methylphenidate. Mohammadpour et al., (2018) found that vitamin D intake, in conjunction with methylphenidate, mitigated ADHD evening symptoms. Hemamy et al., (2021) assessed the effects of vitamin D and magnesium supplementation in ADHD children and found that the one receiving supplement showed a significant reduction in emotional, conduct, and peer problems compared to the placebo group.

This may suggest that vitamin D and magnesium co-supplementation may improve behavioral function and mental health in children with ADHD. There are several possible explanations why supplementing vitamin D may have a positive effect on patients with ADHD. One of them is the link between dopamine and vitamin D levels in the brain (Mohammadpour et al., 2018). Seyedi et al., (2019) investigated the impact of vitamin D intake on serum levels of Brain-Derived Neurotrophic Factor (BDNF), dopamine, and serotonin in school-aged children with ADHD. It concluded that vitamin D supplementation in children with ADHD was associated with increased serum dopamine levels; however, it had no impact on BDNF and serotonin levels. Concluding, several studies suggest that supplementing vitamin D alone or with other medication can be beneficial for patients with ADHD; however, further research is still needed.

Zinc

Zinc is one of the essential trace elements in the human body, and its health significance is increasingly appreciated. Its deficiency may play an essential role in the appearance of many diseases. It has a significant biological role as a catalyst, while zinc ions have structural and regulatory functions. Its insufficiency can lead to anorexia, loss of appetite, and other symptoms, and it may also affect the immune system, triggering arteriosclerosis and anemia. The deficiency of this element can also have a significant effect on a patient's mental health. It can alter behavior, learning, and cognitive function. The meta-analysis conducted by Ghoreishy et al., (2021) assessed the association between hair and serum/plasma zinc levels and attention-deficit/hyperactivity disorder.

The results suggest that there may be a link between lower zinc levels and ADHD. Another study Skalny et al., (2020) found that children with ADHD had lower levels of chromium, magnesium, and zinc by 21%, 4%, and 7%, respectively, compared to healthy controls, and that altered essential trace elements may contribute to the risk and severity of ADHD. Yoldaş et al., (2020) found that low zinc levels can be associated with an increased risk of ADHD symptoms, and evaluating zinc levels could be valuable in managing ADHD symptoms in preschool children. Knowing that there may be a link between zinc levels in a patient's organisms and ADHD symptoms, there is potential that zinc supplementation can be beneficial in its treatment.

Noorazar et al., (2020) studied the benefits of zinc augmentation in children with ADHD already treated with methylphenidate and found a significant difference between the mean inattention scores between the case and control groups. This may suggest that augmentation with zinc can enhance the improvement of inattention in children with ADHD. As interest in the role of zinc in treating mental health disorders rises, the need for further studies is becoming more vital. Although there are promising results in patients treated with zinc as an addition to other treatments, its significance is still widely unknown, and additional research needs to be conducted.

Magnesium

Magnesium is essential for human health. It plays a crucial role in the physiological function of the brain, heart, and skeletal muscles. Low serum magnesium levels have been associated with various neurological conditions, such as migraines, depression, and epilepsy. Insufficiency of this element can also be linked to cardiovascular diseases, diabetes, and lung cancer. Supplementation with magnesium is considered a potential treatment for many diseases (De-Baaij et al., 2015). Huang et al., (2019) explored the connection between serum magnesium levels and ADHD in children. Their analysis found that children diagnosed with ADHD exhibited lower levels of magnesium in peripheral blood (plasma, serum, or whole blood) compared to their peers without ADHD.

This can suggest a potential association between lower magnesium levels and ADHD in children. Botturi et al., (2020) aimed to assess the relationship between magnesium levels and psychiatric pathology, as well as to evaluate the effectiveness of magnesium supplementation as a therapeutic intervention. While their findings were not consistent, there is evidence suggesting a correlation between low magnesium levels and ADHD. Not only that, but also the evidence provided suggests potential benefits of magnesium supplementation in psychiatric disorders. Studies have estimated that Restless Leg Syndrome (RLS) is prevalent in patients with ADHD, which can indicate a potential link between magnesium deficiency and ADHD symptoms (Villagomez and Ramtekkar, 2014).

This is based on magnesium's role in various enzymatic reactions, muscle relaxation, protein synthesis, and energy production. In multiple studies, researchers investigated the effects of magnesium supplementation in combination with other supplements believed to be beneficial for patients with ADHD. Huss et al., (2010) suggest that combining omega-3 and omega-6 fatty acids with magnesium and zinc may have a promising influence on attentional, behavioral, and emotional problems in children and adolescents with ADHD. Hemamy et al., (2021) found that combining vitamin D and magnesium supplementation in children with ADHD may be effective in reducing conduct problems, social problems, and anxiety scores compared to placebo intake.

However, there was no significant impact on psychosomatic problem scores. Another study focused on the effectiveness and tolerability of L-threonic acid Magnesium Salt (LTAMS) supplementation in adults with ADHD (Surman et al., 2021). There were significant improvements observed via changes in the scores on the various scales used in the study. The supplementation demonstrated effectiveness and good tolerability in adults with ADHD; nonetheless, further evaluation in a larger sample group is needed.

Iron

The role of iron in the human organism is diverse and essential for various metabolic processes. It participates in various complex mechanisms, including oxygen transport, DNA synthesis, and electron transport. Iron deficiency usually manifests as anemia, which can lead to functional impairments affecting cognitive development, immunity mechanisms, and work capacity. It can also reduce learning ability and is associated with increased rates of morbidity (Abbaspour et al., 2014). Iron is also essential for the synthesis of catecholamines and dopamine, neurotransmitters involved in ADHD (Botturi et al., 2020). A study exploring the association between iron deficiency and attention-deficit/hyperactivity disorder in children Wang et al., (2017) reviewed 11 articles and found that lower serum ferritin (a marker of peripheral iron stores) levels correlate with ADHD.

It can suggest a potential link between iron deficiency and this disorder. Another study Percinel et al., (2016) found that hyperactivity scores in ADHD patients were negatively correlated with serum ferritin levels, suggesting a potential link between hyperactivity symptoms and iron levels. Fiani et al., (2023) stated that iron deficiency is commonly found in patients with ADHD. This can be associated with more severe symptom manifestation and a worse response to psychostimulants. Another study Calarge et al., (2010) found that children with lower iron stores may require a higher dose of psychostimulant medication. It means that iron supplementation could be investigated as a potential tool to optimize the response to psychostimulants in individuals with low iron stores and ADHD.

Polyunsaturated fatty acids

Polyunsaturated fatty acids (PUFAs) are crucial in the human body. Particularly, omega-3 (n-3) and omega-6 (n-6) fatty acids have been shown to provide various benefits, including lipid-lowering effects, antihypertensive properties, and cardio protection. They regulate inflammatory processes, influence gene expression, and are essential for maintaining overall well-being. They can also be associated with various medical conditions, such as metabolic syndrome, cardiovascular diseases, depression, and neurodegenerative illnesses. PUFAs are shown to have a significant impact on patients' mental health. Omega-3 PUFAs, in particular, play an essential role in brain function and mood regulation (Akbar et al., 2021). They are considered essential for brain development, and increasing evidence suggests a connection to various psychiatric and neurodevelopmental disorders (Richardson, 2006).

In the meta-analysis conducted by Hawkey and Nigg, (2014), it was found that patients with ADHD had overall lower blood levels of omega-3. Apart from that, it was stated that omega-3 supplementation can show modest improvements in ADHD symptoms, particularly hyperactivity. Bos et al., (2015) found that omega-3 supplementation may be a beneficial addition to ADHD treatments, although there was no observed effect on cognitive control measured by fMRI. Contrary to this, Carucci et al., (2022) have shown in the study that there is a limited role of omega-3/6 dietary products in treating inattentive-type ADHD in children. Although it is known that deficiency in polyunsaturated fatty acids is linked to an increased risk of many psychiatric disorders, including attention-deficit/hyperactivity disorder, there is still a need for high-quality studies to assess their efficacy fully (Lange, 2020).

Probiotics and the gut microbiota

Probiotics are non-pathogenic microbes found in a wide variety of foods and supplements. The growing interest in them comes from their potential to significantly enhance overall human health. They have been studied for their potential beneficial effects on gut health, the prevention of diseases such as obesity and diabetes, and the treatment of other various health conditions. Research has indicated that the supplementation of probiotics can significantly improve the prognosis and management of many disorders (Bodke and Jogdand, 2022). Studies of the gut microbiome have shown its significant impact on mental health through the microbiota-gut-brain axis. It can influence it by producing neurotransmitters, regulating the immune system, and producing metabolites affecting brain function.

The composition and abundance of the gut microbiota can be linked to several mental disorders, such as anxiety, depression, and bipolar disorder (Xiong et al., 2023). This influence on mental health has prompted investigations into the use of probiotics to regulate the gut microbiota and potentially alleviate the symptoms of many mental disorders. A study Bundgaard-Nielsen et al., (2023) has shown that children and adolescents diagnosed with ADHD and ASD exhibit distinct gut microbiota patterns when compared to the control group. The changes in microbiome diversity were associated with the imbalance between pro- and anti-inflammatory signals. With the emerging understanding of the gut microbiome's influence, targeting it could offer promising therapeutic effects for ADHD.

Probiotics may impact brain activity related to cognitive performance and ADHD symptoms by modifying the gut microbiota (Cenit et al., 2017).

In a randomized controlled trial carried out by Elhossiny et al., (2023), findings have suggested that *Lactobacillus acidophilus* LB supplementation, when combined with atomoxetine (a noradrenaline reuptake inhibitor used to treat ADHD), may have a beneficial impact on managing ADHD symptoms and can positively influence patients cognitive performance. Although certain factors can be associated with ADHD and changes in the gut microbiome, the exact influence of the microbiome on ADHD development requires further investigation. There is a need for more extensive, well-designed studies to establish definitive correlations between gut microbiota composition and ADHD (Bull-Larsen and Mohajeri, 2019).

Table 1 Selected nutrients and the principal findings of the review

Nutrient	Key Findings
Vitamin D	Higher prevalence of vitamin D deficiency in ADHD children (Elshorbagy et al., 2018) Supplementation may improve cognitive functions and alleviate ADHD symptoms (Dehbokri et al., 2019) Combined with magnesium supplementation can reduce emotional, conduct, and peer problems in ADHD children (Hemamy et al., 2021)
Zinc	Lower zinc levels are linked to ADHD (Ghoreishy et al., 2021) Zinc supplementation with methylphenidate may enhance improvement in inattention in ADHD children (Noorazar et al., 2020)
Magnesium	Magnesium deficiency is linked to various neurological conditions, including ADHD (De-Baaij et al., 2015) Supplementation of this nutrient shows effectiveness and tolerability in adults with ADHD (Surman et al., 2021)
Iron	Iron deficiency in ADHD can be associated with more severe symptoms and worse response to psychostimulants (Fiani et al., 2023) Children with lower iron levels may require higher doses of psychostimulant medication (Calarge et al., 2010)
Polyunsaturated Fatty Acids (PUFAs)	ADHD patients have lower blood levels of omega-3 fatty acids (Hawkey and Nigg, 2014) Omega-3 supplementation shows modest improvements in ADHD symptoms, particularly hyperactivity (Hawkey and Nigg, 2014)
Probiotics	Probiotic supplementation with atomoxetine may benefit ADHD symptom management and cognitive performance (Elhossiny et al., 2023)

Given the previous account of problems relating to the worldwide manifestation of ADHD syndrome in the human population as well as the consequences thereof in social relations, it seems that recommendations of proper dietary habits and, if need be, nutritional supplements are likely to alleviate the situation of the ADHD-affected people within their social environments. A broad spectrum of food ingredients has already been considered beneficial for patients with ADHD. The ingredients or additives include vitamin D, zinc,

magnesium, and iron, as well as probiotics, which enhance the activity of the intestinal flora (Table 1). However, further research is necessary to broaden the scope of means available for the mitigation of ADHD-induced behavior.

4. CONCLUSION

The literature review points to the association between various nutritional components and ADHD symptoms. However, research should continue to identify the underlying mechanisms. The addition of a focused supplement to standard treatment could provide overall better therapeutic outcomes with ADHD. The restrictions, including various sample sizes, study designs, and potential confounding factors, suggest a need for further research in this area. Large-scale and well-designed clinical trials are crucial to developing clear guidelines on the application of nutritional interventions in the treatment of ADHD.

Authors Contributions

Emilia Nagórska and Sylwia Mazur: Conceptualization

Aleksandra Kublińska and Krzysztof Marcinkowski: Methodology

Emilia Nagórska: Software

Karolina Strus, Aleksy Bizan and Krzysztof Marcinkowski: Check

Karolina Strus: Formal analysis

Magdalena Madera and Aleksandra Kublińska: Investigation

Roksana Zdunek, Agata Mazur: Resources

Roksana Zdunek, Emilia Nagórska and Natalia Dąbrowska: Data curation

Sylwia Mazur, Aleksandra Kublińska and Emilia Nagórska: Writing - rough preparation

Krzysztof Marcinkowski, Roksana Zdunek and Agata Mazur: Writing - review and editing

Aleksy Bizan: Supervision

Natalia Dąbrowska: Project administration

All authors have read and agreed with the published version of the manuscript.

Informed consent

Not applicable

Ethical approval

Not applicable

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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