

Micronutrient Supplementation as an Alternative Therapy for Managing ADHD Symptoms

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Abstract. The neurodevelopmental disorder known as Attention-Deficit/Hyperactivity Disorder (ADHD) is a long-term condition marked by impulsivity, hyperactivity, and inattention, affecting both children and adults. Although amphetamines and methylphenidate are prominent stimulant drugs used to treat similar symptoms, there are concerns about adverse effects, including potential reliance, appetite suppression, and disturbed sleep—have driven interest in alternative or complementary therapies. One emerging area of research focuses on micronutrient supplementation, which involves providing vitamins and minerals at higher doses than those typically consumed in a regular diet. Although the precise causal relationship between these deficiencies and ADHD symptoms remains unclear, it is hypothesized that correcting these imbalances might alleviate some of the condition's cognitive and behavioral challenges. Early findings suggest that micronutrient supplementation could be a valuable adjunct to traditional treatments, potentially offering a more holistic approach to managing ADHD symptoms. However, further research is needed to fully understand the therapeutic potential and establish clear guidelines for its use in clinical practice. Mendelian randomization studies have found no significant links between most micronutrients and ADHD, with some suggesting a potential connection to copper levels. Furthermore, the possibility of using omega-3 polyunsaturated fatty acids (PUFAs) to reduce the main symptoms of ADHD has been investigated. Ongoing studies indicate that consistent micronutrient therapy could yield results comparable to those of stimulants, often enhancing mood and reducing anxiety. Future research should prioritize personalized treatment approaches that integrate genetic, environmental, and dietary factors to optimize ADHD management.

Keywords: Attention-deficit/hyperactivity disorder, micronutrient supplementation, alternative treatment approaches.

1. Introduction

The developmental disease known as ADHD impairs a person's capacity to concentrate, control their behavior, and exercise self-control. It can impact daily functioning and relationships. While there's no cure for ADHD, treatments like medications, primarily stimulants and non-stimulants, can effectively manage symptoms. A comprehensive treatment plan also includes behavioral therapies and lifestyle changes. In addition, ADHD often leads to long-term challenges in academics, social interactions, and mental health. Conventional treatments, particularly those using psychostimulants, might have undesirable side effects in addition to their usual successes, including sleep disturbances, food suppression, and even growth-related issues [1]. Therefore, there is growing interest in alternative and complementary treatments that offer relief with fewer adverse effects. Recent research suggests that micronutrient supplementation, which involves the administration of vitamins and minerals at doses higher than the typical dietary intake, may be a promising approach for managing ADHD symptoms in children and adults.

Micronutrients play a crucial role in not only preventing diseases but also in promoting overall healthy growth and development. These essential nutrients, which include a wide range of vitamins and minerals, are fundamental to the body's proper functioning. Recent studies have found associations between certain mental health conditions, such as ADHD, and deficiencies in specific micronutrients like magnesium, iron, zinc, and vitamin D [2]. Research indicates that individuals with ADHD, both children and adults, tend to have significantly lower levels of these important nutrients compared to those in good health [2]. This raises the possibility of a connection between

micronutrient levels and mental health challenges. However, whether these correlations indicate a direct causal relationship remains unclear. Mendelian randomization (MR), a technique that examines genetic variation as an instrumental variable, can be used to investigate this and see whether there is a reliable causal relationship between mental health issues like ADHD and micronutrient shortages. Establishing this connection would provide valuable insights into potential interventions.

The efficacy of omega-3 polyunsaturated fatty acids (PUFAs) in the management of ADHD is still up for debate. Interest in omega-3 supplementation arose from studies showing that both children and adults with ADHD often have lower blood levels of key fatty acids, including DHA, EPA, and AA [3]. Researchers hoped to determine whether supplementation could help alleviate ADHD symptoms. However, a thorough examination of meta-analyses from studies that were double-blind and placebo-controlled, which assessed the outcomes based on teacher and parent evaluations, demonstrated only modest effect sizes [3]. Furthermore, recent trials, when combined with earlier data, have failed to show a statistically significant overall benefit of omega-3 PUFAs in reducing core symptoms of ADHD, such as impulsivity, hyperactivity, and inattention. This has led to growing skepticism about the potential role of omega-3 in ADHD treatment. While omega-3 PUFAs are recognized for their general health benefits, the current body of evidence provides limited support for their efficacy in directly addressing ADHD symptoms. As a result, further research is needed to better understand the potential impact of omega-3 supplementation and to clarify whether it can play a meaningful role in managing ADHD.

2. Mendelian Randomization Analysis of Micronutrients

While the exact causes of ADHD are yet unclear, genetic and environmental factors are thought to have a role. Recent research has examined the relationship between food and micronutrient levels and the risk of ADHD, partly because deficiencies in particular nutrients have been connected to behavioral and cognitive problems. To determine the cause-and-effect link between micronutrients and ADHD, Mendelian randomization analysis was applied to two samples in a nutritional research study utilizing five distinct methodologies (weighted median, MR-Egger, inverse-variance weighted (IVW), and two modal-based estimates) [2]. IVW used information from many single-nucleotide polymorphisms (SNPs) to analyze the overall impact of genetic variations on ADHD risk. When just one SNP was available, the Wald ratio technique was utilized to assess the precise influence of each SNP on ADHD results. weighted median and MR-Egger methods for sensitivity analysis.. Cochrane's Q test was used to assess heterogeneity, and the multiplicative random effect IVW was used to treat excessive heterogeneity. While MR-PRESSO discovered horizontal pleiotropy, MR-Egger identified pleiotropy. R software (version 4.1.2) and leave-one-out sensitivity analysis were used for the final data analysis.

There was no indication of mild instrumental bias, according to the F-statistics ($F > 10$) [2]. The findings of the Wald ratio and IVW approaches used to assess the impact of circulating micronutrient concentrations on ADHD risk. Using the IVW technique, the primary MR analysis did not provide any indication of heterogeneity across studies according to Cochrane's Q test (iron: $Q = 9.506$, $p = 0.392$; magnesium: $Q = 6.387$, $p = 0.270$). Additionally, there were no indications of imbalanced horizontal pleiotropy in the MR-Egger intercept (Pintercept > 0.05). MR-PRESSO did, however, find outlier SNPs for vitamin B12 and D.

3. Effects of Micronutrient Supplementation in Children with ADHD

A randomized, placebo-controlled clinical trial was carried out over eight weeks at three sites, focusing on non-medicated children with ADHD aged six to twelve years. The Child and Adolescent Symptom Inventory-5 (CASI-5) was utilized to assess at least one impaired irritable symptom as reported by the parents. [4]. The parent-rated CASI-5 composite score, which included ADHD, and

the Clinical Global Impression–Improvement (CGI-I) score, which showed treatment response, were the study's predetermined primary outcomes.

135 children with a mean age of 9.8 years were randomized in the experiment, 126 of whom (93%) made up the modified intention-to-treat population. The blinding persisted the entire time. The CGI-I results showed that 18% of the placebo group and 54% of the micronutrient group were classified as responders (risk ratio = 2.97, 97.5% CI = 1.50, 5.90, $p < .001$). (4). The CASI-5 composite scores showed a mean change of -0.31 (95% CI = $-0.39, -0.23$) for the micronutrient group and -0.28 (95% CI = $-0.38, -0.19$) for the placebo group, indicating substantial improvements in both groups ($p < .01$). (4). The groups did not vary significantly, though (mean change = -0.02 ; 97.5% CI = $-0.16, 0.12$, effect size = 0.07, $p = .70$) [4]. Furthermore, the micronutrient group outgrew the placebo group by 6 mm ($p = .002$) [4]. There were no notable side effects or clinically noteworthy alterations in the results of the blood and urine tests.

4. Omega-3 Improves ADHD Symptoms

Fish's high content of polyunsaturated fatty acids (PUFAs), such as omega-3 and omega-6, which are critical for brain growth and function, makes it a popular choice for brain food. These polyunsaturated fatty acids, especially those present in phospholipids, are essential for the upkeep of neuronal cell membranes and the facilitation of neuron-to-neuron signal transmission. Furthermore, the development of the brain and cognitive performance are associated with micronutrients including iron, magnesium, and zinc. Recent studies point to a link between executive function, attention, and diet, especially in kids with ADHD. According to research, children with ADHD may have a decrease in symptoms when they consume omega-3 fatty acids, particularly docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), are taken together. However, DHA by itself does not appear to be as effective as EPA alone. Additionally, children with ADHD have been linked to inattentiveness due to low levels of zinc and magnesium, and attention has improved with supplementation.

Children who were hyperactive and inattentive were advised to take ESPRICO, a supplement that contains magnesium, zinc, omega-3, and omega-6, by pediatricians in different research [5]. A high EPA-to-DHA ratio is stressed in the recipe since research indicates that it enhances mood, memory, and concentration. The effects of this supplement on emotional difficulties, sleep problems, impulsivity, hyperactivity, and general safety and acceptability were assessed throughout the course of a 12-week trial [5]. With SNAP-IV scores of 16 or higher, 308 children (38%) exhibited clinically significant APS for attention deficit at the beginning of the trial [5]. Of these kids, 227 (73.7%) had scores below this cutoff by the time of the last interview. The average reduction of 5.36 points, or 33.6% relative improvement from the baseline score, was seen in the APS for attention deficit from the beginning of the trial to the conclusion. More than 70% of the research group were male, and compared to the females, their attention deficit problems were somewhat more severe [5]. Throughout the trial, both boys and girls saw a substantial decrease in attention deficit symptoms, as evaluated by APS, according to the gender-specific analysis. The average drop for boys was 5.1 ± 5.2 points, and for girls, it was 5.6 ± 5.4 points (mean \pm SD). These reductions were similar for both genders [5]. Age-group-specific sub-analyses did not show any clinically meaningful variations in attention deficit recovery. 320 children (39.5%) initially had an APS of 13 or higher on the SNAP-IV Hyperactivity/Impulsivity subscale, indicating a clinically significant problem in this domain [5]. 202 of these kids (63.1%) had progressed to an APS below the 13-point cutoff at the study's conclusion [5]. The APS for hyperactivity/impulsivity dropped by an average of 3.65 points, representing a 28.2% relative improvement over the baseline score.

As research on ADHD progresses, it will be crucial to examine the long-term effects of micronutrient supplementation on behavior and cognitive development. Understanding how these nutrients influence neurological function and psychological well-being over time can provide valuable insights into effective management strategies. Additionally, investigating novel nutrients and bioactive compounds, such as polyphenols and probiotics, may open the door to new therapeutic

approaches that complement existing treatments [6]. This exploration could lead to more personalized care, tailoring interventions to the specific needs of individuals with ADHD based on their unique biochemical profiles. Enhanced understanding of the role of nutrition in mental health may also improve the overall quality of life for those affected by ADHD. By expanding the scope of nutritional interventions and integrating them into comprehensive treatment plans, future studies may help refine existing therapies, offering safer, more effective alternatives to traditional treatments. This could ultimately revolutionize the management of ADHD for children and adults alike [7,8].

5. Conclusion

While traditional ADHD treatments like psychostimulants are effective, their side effects have led to increased interest in alternative therapies. Supplementing with vital vitamins and minerals including magnesium, zinc, and vitamin D has become a viable supplemental strategy for treating symptoms of ADHD. However, recent research using Mendelian randomization methods, like IVW and MR-Egger, found no significant associations between most micronutrient levels and ADHD risk. Despite the possibility of a connection between copper levels and ADHD, these results lacked statistical significance. Similarly, omega-3 supplementation showed limited effectiveness in improving core ADHD symptoms, despite lower omega-3 PUFA levels found in ADHD patients.

To elucidate the function of micronutrients in the management of ADHD, future research should prioritize rigorous approaches with bigger sample numbers and longer durations. Personalized approaches that assess individuals' genetic profiles and nutrient deficiencies could enhance treatment effectiveness. Advances in nutrigenomics may provide insights into how specific individuals with ADHD respond to various micronutrient levels. Interestingly, sustained micronutrient therapy has demonstrated improvements in ADHD symptoms that are on par with or even higher than those brought on by stimulant medicine. Micronutrients are a potential therapeutic option for those who would rather not take medication since they have been associated to improvements in mood and anxiety, unlike stimulant drugs. This is especially true for children with ADHD who also struggle with mood or anxiety. Comprehending the ways in which these relationships impact results may help direct treatment approaches.

Further exploration of genetic, environmental, and social factors is also necessary to fully understand ADHD. Deficiencies and food sensitivities may result from genetic issues affecting enzyme synthesis or nutrient absorption, potentially worsening psychological symptoms. Multidisciplinary research is needed to investigate how these factors interact in a comprehensive, multimodal approach to optimize ADHD treatment. By considering genetics, nutrition, and environmental influences, future studies may uncover more effective ways to manage ADHD, addressing both the biological and psychosocial aspects of the disorder for more personalized and holistic treatment strategies.

As research on ADHD progresses, it will be crucial to examine the long-term effects of micronutrient supplementation on behavior and cognitive development. Additionally, investigating novel nutrients and bioactive compounds, such as polyphenols and probiotics, may open the door to new therapeutic approaches. These innovations could lead to more personalized treatment plans and improved quality of life for individuals with ADHD. By expanding the scope of nutritional interventions, future studies may help refine existing therapies, offering safer and more effective alternatives to traditional treatments. This could revolutionize the way ADHD is managed, benefiting both children and adults alike.

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