

The Effects of Omega-3/6 Fatty Acids and Vitamin D on Children with Attention-deficit/hyperactivity Disorder (ADHD): A Narrative Review

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ABSTRACT

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Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental syndrome very common among children. The main cause of this disorder is unknown, and it seems that a combination of genetic, biological, environmental, psychosocial, neurochemical, and nutritional factors are involved. Diet seems to be one of the etiological factors for ADHD, as lower levels of long-chain omega-3 fatty acids have been reported in children with ADHD. In the present study, we reviewed the studies on the relationship of omega-3/6 fatty acid and vitamin D supplementation with ADHD. A literature search was conducted in different databases including Google Scholar, Science Direct, SID, PubMed, and MagIran using the following keywords: omega-3/6 fatty acid, PUFA, ADHD, Vitamin D, and Nutrient. Fifty-two records were retrieved and 30 articles were finally included in the review. It was concluded that omega-3/6 fatty acids and vitamin D supplements have potential efficacy in decreasing the ADHD symptoms among children, but further studies are needed to find the underlying mechanisms of such treatments and to determine the optimal dose of these treatments and if it is better to be used as a single treatment or in combination with other medication.

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental syndrome very common in children. Studies have reported an estimated prevalence rate of 2% to 18% for ADHD [1-3]. The prevalence of ADHD is higher in boys than in girls, and some studies have reported that its prevalence in boys is 2 to 9 times that in girls [4]. In Iran, more than 50% of referrals to psychiatric clinics are children, and 33% of referrals to mental therapy centers have ADHD. Studies conducted in Iran have reported the prevalence of ADHD to be 3% to 6% [5-6]. Kouchakzadeh Talami et al [7], in their study of the symptoms of ADHD in children aged 3-6 years in a city in northern Iran, reported a frequency of 67.3% and also found that the 5-year-olds had the highest percentage of symptoms.

The main cause of ADHD is unknown, and it seems that a combination of genetic, biological, environmental, psychosocial, neurochemical, and nutritional factors are involved [8]. Therefore,

timely diagnosis and treatment of ADHD symptoms is very important for preventing further disorders, as ADHD children have a higher risk for criminal behavior and drug abuse [9-10]. Since ages 3-4 have been reported to be the peak ages for the emergence of ADHD [11], early diagnosis and treatment is crucial to preventing the occurrence of further behavioral and learning disorders [12].

One of the etiological factors for ADHD may be diet. Children with ADHD seem to have lower levels of omega-3 long-chain fatty acids in their blood [13-14]. According to Germano et al [15], "linoleic acid (LA, omega-6) and α -linolenic acid (ALA, omega-3) cannot be synthesized in our body and must be introduced with foodstuffs." On the other hand, "the omega-3 polyunsaturated fatty acids have a wide range of beneficial effects in several human health conditions."

This article reviews various papers published on the efficacy of omega-3/6 fatty acids and vitamin D in children with ADHD to provide an insight into how such supplements may be useful in the

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prevention and treatment of ADHD in children.

The only criterion for including the papers in the study was using screening/diagnostic tests for hyperactivity in children, such as the Statistical Manual of Mental Disorders (DSM-IV), the Abbreviated Symptom Questionnaire (ASQ), the ADHD Rating Scale, the Clinical Global Impression (CGI). Papers were excluded if supplements other than omega-3/6 fatty acids and vitamin D were used.

A review of 22 papers published on the relationship between omega-3 fatty acids and ADHD by Farhud and Shalileh [16] found that 18 of the 22 studies had reported an association between omega-3 fatty acids and ADHD and that insufficient iron was correlated with ADHD symptoms [16].

A review article by Jafarian et al [17] on the effects of omega-3 supplementation on hyperactivity and other developmental behavior in children with autism spectrum disorders reported that children with autism tended to have lower levels of omega-3 when compared with their non-autistic peers and suggested that using omega-3 to treat hyperactivity in autistic children with more severe symptoms seems to be very effective as proven by biochemical tests. Also, as some studies have reported, omega-3 fatty acids have potential efficacy in decreasing aggressive-impulsive behaviors in autistic children, yet the mechanisms by which omega-3 fatty acids exert such effects are not fully understood [17].

According to meta-analysis and literature reviews, supplementation with omega-3 fatty acids in the form of fish oil supplements is worth a trial for most of the patients. The supplementation with iron and zinc is indicated for patients with documented deficiencies. Elimination diets such as the Feingold diet or the oligoantigenic diet may be beneficial for patients with intolerance for specific foods. However, nutritional interventions should rather be considered as complementary therapies than as alternative to pharmacological therapies for ADHD [18].

The study by Hosseini et al [19] on the effects of oral prescription of salmon oil on avoidance learning in male mature rats found that the minimum and maximum dosage of Salmon oil ($p < 0.01$) and the average dosage ($p < 0.001$) significantly increased learning ability and recommended further studies to consider salmon oil for treatment of memory and learning disorders.

An 8-week randomized double-blind clinical

trial in 6- to 12-year-old children with ADHD found that omega-3 fatty acids supplementation (635 mg of eicosapentaenoic acid and 195 mg of docosahexaenoic acid per day) significantly reduced the plasma levels of C-reactive protein and interleukin-6 and significantly improved ADHD symptoms in the participants [20].

The study by Crippa et al [21] on the relationship between polyunsaturated fatty acids (PUFAs) status and cognitive and behavioral traits of ADHD in 73 school-aged children with and without ADHD found that children with ADHD had lower levels of Docosahexaenoic acid, omega-3 index, and total PUFA. PUFAs were positively associated with behavior but not consistently related to cognitive domains. The study concluded that children with ADHD display abnormal fatty acid profiles [21].

Another study on the correlation between PUFA intake and neurocognitive functions in ADHD children found that ADHD symptoms had a negative relationship with n-3 PUFA intake and a positive association with Essential fatty acid deficiency [22]. The study concluded that EFA deficiency may play a role in the clinical manifestation and neurocognitive performance of children with ADHD [22].

Mortimer-Cawley and Mushtaq [23] reviewed the strength of the evidence gathered by NICE for a review of its ADHD guidance and suggested that further studies were needed to “support the idea that either ‘few food’ diets or dietary supplements are an effective treatment for ADHD, or to add weight to the research evidence against their use in a robust and comprehensive way.”

According to Patrick and Ames [24], “omega-3 fatty acids play a very important role during brain development, partly through their regulation of the serotonin system” and “omega-3 fatty acid deficiency also affects the structure and wiring of the developing brain as it is associated with a decrease in neurogenesis, dendritic arborization, synaptogenesis, selective pruning, and myelination” [24]. Their extensive review paper on the effect of omega-3 fatty acids and vitamin D on ADHD, bipolar disorder, schizophrenia, and impulsive behavior suggested that vitamin D may modify the severity of brain dysfunction and that the timing of vitamin D deficiency may exacerbate brain dysfunction. They argued that serotonergic dysfunction was a common denominator in a wide range of neuropsychiatric illnesses including ADHD and proposed a mechanism whereby vitamin D regulates

serotonin synthesis, EPA influences serotonin release, and DHA improves membrane-embedded serotonin receptor accessibility, thereby contributing to improved cognitive function and health in ADHD patients [24]. It is worth noting that vitamin D and omega-3 fatty acid supplements are safer than serotonin-enhancing drugs, which have known side effects [25].

An exploratory study by Barragán et al in 2014 compared the efficacy of omega-3/6 fatty acids with methylphenidate (MPH) and combined MPH + omega-3/6 in children with ADHD and found significant differences favoring combined omega-3/6 and MPH over omega-3/6 alone for ADHD total and Hyperactivity-Impulsivity subscales [26].

A meta-analysis of the treatment efficacy of different omega-3 fatty acid compositions in ADHD concluded that there was not enough evidence to recommend omega-3 fatty acid supplementation as the sole treatment in children with significant ADHD symptoms [27], noting that most studies were not of high methodological quality.

A review of the studies on ADHD treatment with omega-3 fatty acids from 2000 to 2015 reported that although findings were not consistent, there was evidence suggesting that omega-3 supplementation is a successful treatment for ADHD symptoms [28]. There was a high tolerance for such supplements, and side effects were very mild. The article concluded that treatment with omega-3 PUFA positively affects ADHD and that patients with mild ADHD can benefit from this treatment more. Moreover, the dosage of stimulant medication could be reduced when used in combination with omega-3 PUFA supplements [28]. Several arguments, based on the biochemical and physiological functions of omega-3 PUFAs, have been presented in the literature to explain how these supplements are successful in the treatment of ADHD [28].

The results of a double-blind randomized clinical trial in 6- to 12- year-old ADHD patients receiving PUFAs along with methylphenidate could not recommend adding PUFAs to the therapeutic regimen of ADHD patients because the findings did not confirm beneficial effect of PUFAs in the treatment of ADHD. The study recommended future randomized clinical trials with greater sample size and longer follow-up period for more robust results [29].

Johnson et al [30] reported that, compared with placebo, 3 months of treatment with omega-3/6

improved reading ability in mainstream schoolchildren, as measured with the Logos test. The study also found significant improvements in several cognitive parameters in children with ADHD symptom scores above the median and concluded that children with attention problems can specifically improve with omega-3/6 supplementation. [30].

Conclusion

Some studies support the effectiveness of vitamin D and omega-3 fatty acid supplements in decreasing the aggressive-impulsive behaviors in autistic and ADHD children, but the mechanisms by which omega-3 fatty acids and vitamin D produce these effects are not fully understood. In line with other studies, the present paper concludes that further studies are needed to identify the underlying mechanisms of omega-3/6 and vitamin D actions in reducing ADHD symptoms, to determine the optimal doses of these treatments, and to determine whether it is better to use these supplements as a single treatment or in combination with other medication.

Conflict of interest

None of authors have conflict of interests.

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