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Omega-3 Fatty Acid Supplementation: A Natural Way to Lessen Symptoms of ADHD

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Introduction

Attention Deficit/Hyperactivity Disorder (ADHD) is a widely diagnosed neurodevelopmental disorder affecting approximately 8% of children in the United States.[1] To date, the most common and effective treatment is prescription-only stimulant medication. Despite significant efficacy, stimulant medications can cause multiple health and potential legal risks for patients and the population in general. Such risks have led researchers to investigate alternative methods of treatment, one of which includes supplementation with natural fatty acids. Finding a safe adjunct therapy that lessens adverse side effects and improves overall well-being by allowing for lower doses of stimulant medication would have a profound effect on the treatment of ADHD. Fatty acids are a promising candidate for this purpose.

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-V), ADHD is defined as a "persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development" characterized by 6 or more inattentive and/or 6 or more hyperactive/impulsive symptoms for at least 6 months.[2] Symptoms must be inconsistent with the patient's developmental level and should negatively impact social, academic, and/or occupational activities. In addition, the DSM requires several symptoms to be present by age 12 in at least 2 settings. After determining the type and extent of a patient's symptoms, the following subtypes of ADHD can be diagnosed: Combined, Predominately Inattentive, or Predominately Hyperactive/Impulsive.[2] See Table 1 for an ADHD symptom list by subtype.

Table 1. ADHD symptoms by subtype.

Inattention	**Hyperactivity/Impulsivity**
- Failing to pay attention to detail, making careless mistakes	- Fidgeting or squirming
- Difficulty sustaining attention	- Leaving one's seat when expected to stay in it
- Not listening when spoken to directly	- Running or climbing when inappropriate
- Not following through on instructions, failing to finish tasks	- Inability to quietly participate in leisure activities
- Difficulty organizing	- Described as "on the go" or "driven by a motor"
- Avoiding/disliking tasks that require sustained mental effort	- Talking excessively

- Losing things needed for tasks - Easily distracted - Forgetful	- Blurting out answers before the question is finished - Difficulty waiting his or her turn - Interrupting/intruding on others

Adapted from the DSM-V.[2]

Traditional treatment for ADHD includes stimulant medications such as dextroamphetamine/amphetamine (Adderall®), methylphenidate (Ritalin®, Concerta®), and lisdexamfetamine (Vyvanse®). These medications have potentially serious side effects including but not limited to anxiety, insomnia, irritability, hypertension, tachycardia, weight loss, and in children with heart disease, sudden death. Given the negative side effects of stimulants, frequent monitoring of weight, heart rate, and blood pressure are recommended in all patients. Stimulant medications also pose risks of misuse and diversion. In people without ADHD, stimulant medications provide highly sought effects like increased focus, energy boosts, and weight loss. For these reasons, stimulant medications are classified by the Drug Enforcement Administration (DEA) as "controlled substances." In many states, this designation mandates practitioners to see patients more frequently and check government databases to monitor where and when prescriptions are picked up. Nonetheless, stimulants are considered vital for patients with ADHD, as they help focus attention and control symptoms of hyperactivity/impulsivity so that children may function at an appropriate level.

The combination of health risks and potential for misuse and diversion has led researchers to seek alternative treatment options. In researching biochemical baselines in ADHD patients, polyunsaturated fatty acids (PUFA) became of interest. PUFAs include both omega-3s [alpha linolenic acid (ALA), eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA)] and omega-6s [linoleic acid (LA), arachidonic acid (AA)]. These fatty acids are classified as essential fats because the body cannot produce them; they must be obtained through diet. Omega-3 fatty acids are found in fish, walnuts, and various seeds while omega-6 fatty acids are found in

safflower, sunflower, corn, and soybean oils. The body utilizes omega-3s in brain development and function whereas excessive intake of omega-6s is associated with detrimental inflammation. Research shows that children with ADHD have lower levels of EPA and DHA and a higher ratio of omega-6/omega-3 compared to their peers. These findings correlate significantly with the severity of their ADHD symptoms.[3] On the basis of this discovery, randomized controlled studies have been conducted to determine the effect of omega-3 fatty acid supplementation in children with ADHD.

The outcomes of combination omega-3 fatty acid supplementation compared to traditional stimulant treatment alone, on symptoms of inattention and hyperactivity/impulsivity will be examined. If adjunct therapy with fatty acids reduces ADHD symptoms, clinicians may be able to decrease traditional stimulant doses which would, in theory, reduce the negative side effects associated with that drug class and improve the patient's quality of life.

Discussion

Several studies answered the question of whether fatty acid supplementation would allow for decreased dosing of stimulant medications in ADHD.

A prospective observational Italian study revealed that 51 children ages 7-14 with ADHD had lower baseline fatty acid levels, poorer well-being, difficulty with emotional regulation, conduct issues, trouble with reading, and decreased focused and sustained attention when compared to healthy controls. Higher levels of DHA and EPA were associated with less parent-rated symptoms of ADHD and lower symptom severity as well as a better quality of life. Moreover, as expected, a higher AA/DHA ratio correlated with more severe symptoms.[4] These findings identified the need for blinded, randomized, controlled studies.

Indeed, an unblinded, randomized Mexican study of 90 treatment naïve children ages 6-12 with ADHD – comparing methylphenidate (MPH), omega 3/6 supplementation, and MPH + omega 3/6 therapy – showed that MPH was surprisingly only slightly more effective than fatty acid supplementation alone. Although combination therapy was not superior compared to MPH for ADHD symptoms over the course of 1 year, the combination did allow for lower doses of MPH, resulting in fewer side effects and better treatment compliance.[5]

Confirming the findings of previous research, a double-blind, randomized, placebo-controlled study from the Netherlands following 40 boys ages 8-14 with ADHD, compared with 39 matched controls without ADHD, demonstrated that problems with inattention negatively correlated with baseline omega-3 levels over 4 months. Supplementation with omega-3s was shown to reduce symptoms of inattention in boys without ADHD, those with treatment naïve ADHD, and those taking MPH. Researchers noted, however, that omega-3s had no effect on rule-breaking or aggressive behavior. Overall, this evidence substantiates the importance of omega-3 intake during the development of all children. It should be noted that a few boys had increases in their MPH dosage during the trial. Importantly, exclusion of this group from reanalysis did not alter the results, proving that the positive effects of omega-3s on inattention were not confounded by increased stimulant dosing. This evidence further supports the advantage of utilizing omega-3s as adjunct therapy to traditional treatment of ADHD.[6]

Unlike previous research that showed no correlation between fatty acid supplementation and symptoms of rule breaking and aggressive behavior, data from a blinded, randomized Australian study of 90 non-medicated children ages 6-13 with ADHD symptoms had different outcomes. Significantly, researchers only included children with reported literacy problems at school who scored above the 90th percentile on validated parent-rated ADHD scales. Although

the power necessary to assess the effect of fatty acid treatment was not met, an increase in erythrocyte DHA correlated with improvements in reading and defiant behavior, while an increase in erythrocyte EPA and decrease in omega-6s correlated with improvements in anxiety and shyness over 4 months. Interestingly, children with ADHD and learning disabilities benefited the most from higher levels of DHA with regards to oppositional behavior, hyperactivity, restlessness, attention, spelling, and reading. These findings anecdotally support omega-3 supplementation in children with ADHD and learning disabilities, especially those with more severe symptom profiles.[7]

Contrary to previous findings, a small double-blind, randomized Canadian study of 26 children ages 6-11 did not confirm that patients with ADHD had lower baseline levels of omega-3 fatty acids compared to age and sex-matched controls. Nor was a correlation found between concentrations of omega-3s and severity of ADHD symptoms. Despite these initial data, researchers concluded that over the 4-month study, about half of participants experienced mild improvement and about a third of participants had statistically significant improvement in behavior and academic outcomes after receiving omega-3 supplementation. Furthermore, researchers observed that parents of participants chose to continue supplementation rather than start stimulant medications because defiant behaviors decreased without the implementation of traditional therapy. Importantly, children with other mental health symptoms and learning disabilities were excluded from this study.[8]

Similar to the findings of the Canadian study, a double blind, randomized, placebo-controlled clinical trial in 50 drug naïve Italian children ages 7-14 with ADHD concluded that DHA supplementation had no significant impact on the frequency of parent-reported ADHD symptoms over 6 months. As with multiple other studies, all patients with ADHD were found to

have lower levels of DHA compared to controls. However, positive outcomes were found; the group receiving DHA supplementation experienced small but significant improvements in focused attention, emotional problems, and quality of life with regards to psychosocial functioning.[9]

Whereas many studies exhibited small but positive effects of omega-3 fatty acid supplementation in ADHD, other research findings were not as promising. For example, a double-blind, randomized, controlled French study of 148 children diagnosed with ADHD concluded that placebo had a greater effect on symptoms of hyperactivity/impulsivity and inattention than omega-3 supplementation over 3 months. Researchers found no biological explanation for this outcome, commenting that it was either incidental or due to lack of blood samples, short duration of therapy, or inclusion of patients with only "mild to moderate ADHD." In previous studies, participants with severe ADHD symptom profiles seem to benefit most from fatty acid supplementation.[7,10] Similar to the French trial, a German blinded, randomized, placebo-controlled study of 95 children ages 6-12 diagnosed with ADHD reported no statistical difference in parent or teacher ratings of symptoms for children receiving placebo versus omega-3s and also found that an increase in DHA correlated with more frequently reported social issues. However, an increase in omega-3s and decrease in omega-6s did correlate with improvements in working memory. Researchers commented that utilizing a reporting system based on the number of ADHD symptoms rather than the severity of symptoms may have contributed to these findings.[11]

Overall, the evidence supporting the benefits of omega-3 fatty acid supplementation in ADHD is mixed. Several studies have shown the benefit of adjunct therapy with natural fatty acids while a few have not. In general, the limitations of these studies, like many of those

concerning children, are small sample sizes and suboptimal attrition rates. Other weakness included varying durations of studies as well as differing formulations of PUFA supplementation. The strengths of these studies include obtaining PUFA blood levels and using multiple validated questionnaires for symptom reporting. All researchers agree on the superior safety profile of fatty acid supplementation in children. The inclusion of studies from multiple countries reflects the prevalence of this disorder and provides external validity to this review – ADHD is a concerning neurodevelopmental disorder across the world, deserving of research to help understand its root cause and to explore possible safe, natural therapies.

Despite the differences in study designs and outcomes, most of the evidence supports the important role fatty acids play in ADHD. While the nuances of this role are not yet fully understood, these data suggest that the combination of PUFAs, particularly omega-3s, and traditional treatment allows for decreased stimulant dosing, resulting in fewer detrimental side effects. In the studies discussed, approximately 64% of all participants experienced positive effects of fatty acid supplementation with respect to symptoms of ADHD.[4,5,6,7,8,9,11] Omega-3 supplementation has been shown to decrease the severity of ADHD symptoms, social and emotional issues, defiant and oppositional behavior, anxiety, and shyness. It has also been linked to increased attention span, better working memory, and improved reading and spelling performance. Overall, supplementation with omega-3s is safe, natural, and despite some evidence to the contrary, significantly benefits children with ADHD by improving quality of life.

Many new and practical questions arise as a result of evidence discovered in this research. For example, why are baseline levels of fatty acids different in children with ADHD? How do we determine the optimal formulation and treatment duration for each patient? Without government regulation, how will consumers know if over-the-counter formulations have

adequate levels of fatty acids? Will insurance cover omega-3 supplementation? How long will it take to see a positive change in children receiving omega-3 supplementation? And, would supplementation help adults diagnosed with ADHD, whose brains are no longer developing?

Conclusion

Overall, omega-3 fatty acid supplementation has small but significant beneficial effects in children with ADHD. Combination therapy allows for decreased dosing of traditional stimulant medications, which in turn, decreases their side effects and increases patient compliance. The safety profile of adjunct omega-3 fatty acid supplementation is excellent and the decrease of ADHD symptoms in patients makes this a promising alternative to traditional treatment alone. Utilization of PUFA supplementation may also decrease the societal risks of stimulants, including misuse and diversion.

Future areas of investigation may center around the questions proposed in the above discussion. For example, head-to-head research with differing levels of ALA, EPA, and DHA supplementation would help to determine optimal dosing strategies. Researching the ideal time to initiate supplementation may also be of benefit. For instance, determining whether supplementation should start prenatally, at the time of symptom onset, or after traditional therapies have been initiated would benefit clinicians hoping to utilize this treatment plan. As evidenced by a large randomized, controlled study in Mexico that investigated the impact of prenatal DHA supplementation on 5 year-old cognition, behavior, and attention, it was unclear whether prenatal supplementation works as a "substitute of early stimulation for children with less-stimulating home environments" or "decreases the effect of early stimulation on development." Although researchers discovered a correlation between prenatal DHA

supplementation and improved attention and executive functioning in young children, the underlying mechanism must be understood before recommending it to expectant mothers.[12]

Despite somewhat mixed results, the safety profile and the evidence that omega-3 fatty acid supplementation positively effects patients with ADHD makes this research relevant. At this time, determining the most effective dosage of supplementation will need to occur on a child-to-child basis. At a minimum, it is the responsibility of the medical provider to educate all parents on the importance of a healthy, balanced, omega-3 rich diet for their children. Since the benefit of omega-3 fatty acid supplementation is an improved quality of life, and the risk of harm is approximately zero, it is within the best interest of ADHD patients for clinicians to recommend its use.

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