The effectiveness of nutritional supplements in the management of Attention Deficit Hyperactivity Disorder (ADHD)

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2012

Acknowledgments

I would like to acknowledge my scholarly project advisor, Professor Gentry, for all her support and guidance through this writing and researching process.

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Introduction

Attention deficit hyperactivity disorder (ADHD) is a behavioral disorder occurring in children and adolescents and may continue into adulthood. The Center for Disease Control (CDC) reports approximately 5.4 million children in the United States from the age of 4-17 are affected by ADHD in comparison to 4.4 million in 2003. It also reports 2.7 million of those children with ADHD use medication (Visser, Bitsko, Danielson, Perou, & Blumberg, 2010). Effective management of ADHD is determined by the control of symptoms. The management of ADHD has to distinguish the risks from the potential benefits especially due to the young age of occurrence. The importance of considering all options is imperative to the health and well-being of the patient.

Although nearly half of the children with ADHD use medication, there are other therapies being used in the management of ADHD. A study from 2007 found approximately two and a half percent of children use Complementary and Alternative Medicine (CAM) to manage ADHD. Natural products were the most commonly used type of CAM including fish oil or omega-3 fatty acid nutritional supplements. The report also showed 30.5% of children used fish oil or omega-3 and 16.7% of children used flaxseed oil (Barnes, Bloom, & Nahin, 2007). Nutritional supplements are products such as vitamins, minerals, herbs, amino acids, or enzymes taken by oral administration to supplement the diet (U.S. Food and Drug Administration, 2009).

The purpose of this paper is to review the literature and determine the effectiveness of nutritional supplements in the management of ADHD. A discussion of the symptoms, etiologies, and current ADHD treatments are included for a thorough understanding of how nutritional supplements may play a role in the management of ADHD. The conclusions drawn from this literature review are relevant to the Physician Assistant (PA) profession and society. If

nutritional supplements are shown to be effective in the management of ADHD, then they can be provided as an option for management and more studies may be done to prove the effectiveness of nutritional supplements.

There are three different types of ADHD which are determined by the symptoms exhibited by patients. They are inattentive, hyperactive, or combined type. The patient with inattentive type is characterized by failing to pay close attention to details or tasks, difficulty paying attention, and forgetful at home and school. The patient with hyperactive type often cannot sit or play quietly and interrupts others and patient with combined type ADHD exhibits characteristics of both (4th ed., text rev.; DSM-IV-TR; American Psychiatric Association, 2000). For purpose of this literature review ADHD will refer to the combined type.

There is not a single diagnostic test to determine if a patient has ADHD; however, there are criteria established by the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (2000) to help determine if a child or adolescent has ADHD. According to the Diagnostic and Statistical Manual of Mental Disorders (2000), ADHD is a combination of inattentive and hyperactive symptoms present before the age of seven persisting for six months or more and occurring in two settings such as home and school. The signs and symptoms of ADHD are difficulty paying attention, not completing tasks, easily distracted, cannot sit still for long periods of time, and difficulty waiting for turn (4th ed., text rev.; DSM–IV–TR; American Psychiatric Association, 2000). ADHD is a chronic disease because it begins in childhood and may continue into adulthood. Other problems with mood, learning, or behavior may affect the child or adolescent with ADHD. The main goal is improving quality of life and daily functioning for the child or adolescent.

In most cases the etiology of ADHD is unknown, but there are some proposed causes. According to the Center for Disease Control (CDC), studies show the various causes of ADHD include genetic predisposition, low birth weight, premature birth, toxic agent exposure during pregnancy, and brain injury (Centers for Disease Control, 2010). Another proposed etiology is an imbalance of the catecholamines dopamine and norepinephrine in the fronto-subcortical pathways involved in alertness, attention, monitoring of actions, and inhibition (Biederman & Spencer, 1999). Individuals with ADHD have a decrease in dopamine transmission in the brain potentially due to genetic factors. Various environmental factors such as exposure to toxins during pregnancy, viral or bacterial infections, and nutrient imbalances during childhood may also play a role (Millichap, 2012). Deficiencies of essential fatty acids, iron, and zinc are proposed to be responsible for the etiology of ADHD. A study examining rats found a deficiency in iron decreases the neurotransmission of dopamine and norepinephrine (Burhans et al., 2005). Therefore, nutritional supplements of essential fatty acids, zinc, and iron may be beneficial in the management of ADHD.

Effective management of ADHD allows improvement in symptoms, patient and parent satisfaction, decreased use of medications, and parent and/or teacher improved assessments. The American Academy of Pediatrics (AAP) recommends appropriate combination of medications and behavior therapy to manage ADHD. Current treatments include stimulants (methylphenidate), selective norepinephrine reuptake inhibitor, tricyclic antidepressants, and alpha-2-adrenergic agonists (Subcommittee on Attention-Deficit/Hyperactivity Disorder, Steering Committee on Quality Improvement and Management, 2011). While these medications are helpful in management of ADHD, a concern arises for the side effects.

Stimulants increase the release of dopamine and norepinephrine transmission thus improving the imbalance and activity of the catecholamines in the brain on neurotransmission (Solanto, 1998). The most common side effects of stimulants include appetite suppression or anorexia, sleep disturbances, and weight loss. Less common side effects include increased heart rate, rebound irritability, and headache (Elia, Ambrosini, & Rapoport, 1999).

Atomoxetine is a selective norepinephrine reuptake inhibitor. The side effects include appetite suppression, vomiting, nausea, and sleep disturbances (Pliszka & American Academy of Child and Adolescent Psychiatry Work Group on Quality Issues, 2007). Antidepressants such as tricyclic antidepressants inhibit the reuptake of norepinephrine and serotonin. Adverse reactions include cardiovascular and anticholinergic effects and lowers seizure thresholds. Alpha-2 adrenergic agonists such as clonidine are used in the management of ADHD more commonly along with stimulants. Alpha-2 adrenergic agonists inhibit norepinephrine release. The side effects of alpha-2 adrenergic agonists have been associated with stimulants (Elia et al., 1999). The side effects of stimulants and other medications have made parents reluctant to use them, encouraging trials with other therapies. This has lead to the incorporation of nutritional supplements into the management of ADHD.

Although nutritional supplements are not included in the current treatment guidelines, various studies have been conducted to determine their effectiveness in the management of ADHD. Nutritional supplements studied include essential fatty acids, omega-3 fatty acids, zinc, iron, magnesium, Vitamin B_6, flax oil, antioxidants, and Vitamin C. Many studies report these nutritional supplements may be significant in the management of ADHD but also in normal brain development and function. This literature review will determine the effectiveness of nutritional supplements in the management of ADHD.

Methods

A clinical literature review was conducted to determine the effectiveness of nutritional supplements in the management of ADHD. The literature involved published studies pertaining to nutritional supplements in the management of ADHD. Articles included followed strict inclusion criteria. All articles were from peer reviewed journals. Articles published from 1998-2012 were acceptable. All articles were in English. The pediatric population under study was from the ages of four to 18. PubMed, American Academy of Pediatrics, and National Institutes of Health National Center for Complementary and Alternative Medicine were searched for the following terms: “Attention-Deficit Hyperactivity Disorder”, “ADHD”, “nutritional supplements”, and “dietary supplements”. PubMed was searched using the following search terms: (("Attention Deficit Disorder with Hyperactivity"[Majr])) AND ("Dietary Supplements"[Mesh:noexp]) and (treatment of AD/HD) AND (nutritional supplements).

Discussion

Nutritional Supplements and Effect on ADHD

Nutritional supplements are products taken orally to potentially increase the essential fatty acids, vitamins, or minerals deficient in the diet. By providing beneficial nutrients to the body and portions of the neuronal membranes, neurotransmission of dopamine and norepinephrine can be restored and normal cognitive function and behavior can be resumed. Nutritional supplements which include essential fatty acids, zinc, iron, magnesium, Vitamin $B_{6,}$ flax oil, antioxidants, and Vitamin C are effective in the management of ADHD because they improve symptoms, patient and parent satisfaction, and decrease the use of medications.

A study published in 2003 by Harding, Judah, and Gant supports management of ADHD with nutritional supplements. A total of 20 children between the ages of seven to 12 were included in the study. 10 subjects were given Ritalin and the remaining 10 subjects were given dietary supplements consisting of a multiple mineral, phytonutrients, essential fatty acids, probiotics, and amino acids. The treatment of the children was chosen by their parents. The authors used the Intermediate Visual and Auditory/Continuous Performance Test (IVA/CPT) to measure the results of treatment. The IVA/CPT is a very effective and accurate assessment of management of ADHD. The Full scale response control quotient (FSRCQ) measures impulsivity and the full scale attention control quotient (FSACQ) measures inattention which comes from the IVA/CPT assessment. The FSRCQ and FSACQ were significantly increased for both subject groups respectively, ($p \leq 0.01$) and ($p \leq 0.001$). Despite the small sample size, this study examined effects of nutritional supplements against Ritalin and found nutritional supplements are as effective in the management of ADHD (Harding et al., 2003).

Bloch and Qawasmi (2011) found omega-3 fatty acids to be effective in the management of ADHD. In their systematic review and meta-analysis studies using omega-3 fatty acid supplementation to manage ADHD were searched and reviewed to determine the effectiveness of management and improvement in symptoms. The studies included were randomized placebo-controlled trials using omega-3 supplementation in individuals with ADHD and a validated rating scale to measure ADHD. The result of their study shows omega-3 fatty acids to be effective in the management of ADHD. Omega-3 fatty acids act to improve processes of neurotransmitters in ADHD. This article found 10 studies with 699 participants of omega-3 fatty acid supplementation in ADHD showing effectiveness in management of ADHD ($p< 0.0001$). Omega-3 fatty acid supplementation was also found to be effective in the treatment of inattentive and hyperactive symptoms, respectively ($p=0.009$) and ($p=0.005$). There was no difference between omega-3 fatty acid supplementation as monotherapy or in addition to ADHD medications ($p=0.5$). The study recommends using omega-3 fatty acids for management of mild symptoms and for those who are interested in alternative therapies (Bloch & Qawasmi, 2011). Despite the small amount of articles found to conduct this article's research, it includes 699 participants from the studies and shows omega-3 fatty acids can be used in the management of ADHD. Another study supports the use of nutritional supplements especially omega-3 fatty acids in the management of ADHD. In this open-label study, Sorgi, Hallowell, Hutchins, and Sears (2007) gave nine children from the ages of eight to 16 eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) which provided omega-3 fatty acids supplements and measured the arachidonic aicd (AA) to EPA ratio and assessments of ADHD symptoms over eight weeks. The children discontinued their stimulant medication and were given 10.8 grams of EPA and 5.4 grams of DHA and met with a psychiatrist initially, at four weeks, and at eight weeks. An

ADHD Symptom Checklist-4 (ADHD SC-4) and The Clinical Global Impression Scale were used to assess ADHD symptoms and severity, respectively by the psychiatrist. The parents of the children also completed an assessment of ADHD called the Conner's Parent Rating Scale (CPRS). The results of the study show the EPA/DHA (omega-3 fatty acids) supplement may be effective in managing ADHD. The ADHD SC-4 showed significant improvement after eight weeks ($p<0.01$). The CPRS also showed significant improvements ($p<0.05$). Sorgi et al. (2007) found a decreased AA to EPA ratio showed a significant positive change in ADHD severity ($p=0.027$) (Sorgi et al., 2007). Although the sample size is small, it is important to know this was the first study done to determine the effects of EPA/DHA supplement on the AA to EPA ratio and symptoms of ADHD. It is an option for Physician Assistants to consider and to counsel the pediatric patient and their family about the use of nutritional supplements, especially omega-3 fatty acids.

According to a recent randomized controlled study by Milte et al. (2012), DHA may improve symptoms of ADHD. The study consisted of 90 children supplemented with either the omega-3 fatty acids EPA and DHA or the omega-6 fatty acid linoleic acid (LA) for four months. 70 out of the proposed 90 children from the ages of six to 13 finished the study. The primary and secondary outcomes were assessed using the Wechsler Individual Achievement Test III, Test of Everyday for Attention for Children, CPRS, and fatty acid analysis. Milte et al. concluded there was no significant difference in the treatment groups between the omega-3 fatty acids and the omega-6 fatty acid supplementation due to a small study population; however, omega-3 fatty acids supplementation showed improvement in ADHD symptoms and behavior (Milte et al., 2012).

Colter, Cutler, and Meckling (2008) conducted a study in Canada on adolescent children from the ages of ten to 16 with ADHD to assess essential fatty acids intake and determine abnormalities in red blood cell fatty acids. The ADHD group consisted of 11 children and the control group consisted of 12 children. The authors collected blood samples and Conners' Parent Rating Scale long version (CPRS-R:L) scores which is an ADHD behavior assessment at the beginning of the study. The subjects had to write down their diet intake for seven days. Then the subjects were assessed in a month and blood samples were taken to conclude the study. The results of the study show the ADHD group had higher scores on CPRS-R:L than the control group which did not have ADHD ($p<0.05$). The intake of omega-3 and omega-6 fatty acids was not significant between the ADHD group and control group; however, the red blood cell fatty acid analysis indicates significant difference between ADHD and control groups level of omega-3 fatty acid ($p=0.018$). The ADHD group had lower omega-3 fatty acids than the control group (Colter et al., 2008).

According to a recent article by Millichap and Yee (2012), omega-3 fatty acids and omega-6 fatty acids supplements are recommended based on a review of the literature using PubMed. The authors found improvement in symptoms and parents wanting to try the nutritional supplements and recommend 300-600 milligrams per day of omega-3 and 30-60 milligrams per day of omega-6 fatty acids for two to three months. Essential fatty acids such as omega-3 and omega-6 fatty acids have benefits in management of ADHD shown by the authors' review of the literature. The authors conclude nutritional supplements may be used when patient is deficient in nutrients and as an alternative to medications (Millichap & Yee, 2012).

Zinc acts to promote synthesis of neurotransmitters and fatty acids involved in ADHD (Millichap & Yee, 2012). Millichap and Yee (2012) did not find clear evidence zinc

supplements may be effective in managing ADHD after reviewing studies. The authors state zinc deficiency is found in Middle Eastern countries and zinc supplements may show improvement with ADHD but may not be applicable in the United States because zinc may not be a deficient nutrient (Millichap & Yee, 2012). Lepping and Huber (2010) found zinc deficiency may be involved in ADHD due to zinc's effects on dopamine neurotransmission. Not only does zinc play a role in ADHD, but it also plays a role in normal brain function and synthesis of fatty acids. Therefore, the authors indicate zinc supplements may be effective in managing ADHD patients with zinc deficiency and propose continuing research (Lepping & Huber, 2010).

Konofal et al. (2011) conducted a randomized, double blind with placebo study to determine the effectiveness of iron supplements on children affected by ADHD from the ages of five to eight with iron deficiency. In their study, 17 children were given 80 milligrams per day of an iron supplement and five were given placebo for duration of 12 weeks. The primary outcome measurement of the study was the Conners' Parent Rating Scale (CPRS). The results show the CPRS improved in the iron treatment group than the placebo ($p=0.055$). Not only did the subjects improve their iron deficiency state with the iron supplement ($p=0.000$), there was also significant improvement determined by one of the secondary outcome measures which was the Attention-Deficit Hyperactivity Disorder Rating Scale ($p=0.008$). Patients taking either the iron supplement or placebo tolerated it well with a minimal side effect of abdominal pain. There were no exacerbations of ADHD symptoms and improvement of inattentive and hyperactive symptoms was concluded (Konofal et al., 2011).

Huss, Volp, and Stauss-Grabo (2010) conducted an observational, longitudinal study in Germany showing omega-3 and omega-6 fatty acids, magnesium, and zinc supplements may be

effective in managing ADHD. The study consisted of 810 children from the ages of five to 12 who took a food supplement called ESPRICO containing 440 milligrams of omega-3 fatty acids, 60 milligrams of omega-6 fatty acids, 80 milligrams of magnesium, and five milligrams of zinc for 12 weeks. The authors' purpose was to evaluate improvement of ADHD symptoms. The measures for effectiveness of management were assessed by two questionnaires called SNAP-IV named by the creators Swanson, Nolan, and Pelham (SNAP-IV) and the Strengths and Difficulties Questionnaire (SDQ). The results of the study show significant reduction in attention-deficit symptoms ($p<0.001$) and hyperactivity symptoms ($p<0.001$). The average point scores (APS) decreased on the SNAP-IV questionnaire by 5.36 points for attention deficit and 3.65 points for hyperactivity (Huss et al., 2010). The authors demonstrate a reduction in symptoms of inattention and hyperactivity after taking a nutritional supplement containing omega-3 and omega-6 fatty acids, magnesium, and zinc. There should be more studies done like this to determine the effectiveness of nutritional supplements.

Mousain-Bosc et al. (2006) compared magnesium and vitamin B_6 supplements effect on symptoms in children with ADHD against children not affected by ADHD. Magnesium is needed for normal brain function and deficiency may be seen in patients with ADHD. There were 40 children with ADHD and 36 children with no diagnosis of ADHD given six milligrams per kilogram per day of magnesium and 0.6 milligrams per kilogram per day of vitamin B_6 supplement for six months. Their study measured serum magnesium, intra-erythrocyte magnesium, and ionized calcium blood levels of the children to correlate improvement of ADHD symptoms. Hyperactivity, aggressiveness, and inattentive symptoms of ADHD were scored zero for absence of symptom and four for very hyperactive, aggressive, or poorly attentive. The results of the study found increased blood levels of magnesium in children with ADHD

($p=0.004$) and reduced symptoms of hyperactivity, aggressiveness, and inattention ($p<0.0001$) with magnesium and vitamin B_6 (Mousain-Bosc et al., 2006). This study supports the effectiveness of nutritional supplements in the management of ADHD because it shows improvement in symptoms and behavior after supplementation with magnesium and vitamin B_6.

Flax oil, antioxidants, and Vitamin C were studied by Joshi et al. (2006) in a pre- and post-supplementation study design with normal control group and an ADHD group. Joshi et al.'s (2006) study involved 60 children in India with an average age of seven and a half years for the normal control group and eight years for the ADHD group. The Parent Rating Scale was used to assess pre- and post-supplementation hyperactivity symptoms based on DSM-IV criteria and six categories including restlessness, inattention, impulsivity, self-control, social problems, and learning problem. The subjects were given 200 milligrams of flax oil supplement and 25 milligrams of Vitamin C two times a day for three months. A fatty acid analysis was also obtained to determine any changes in the red blood cell components. Flax oil contains essential fatty acids. The results of the study show flax oil and Vitamin C post-supplementation significantly increase in eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) ($p<0.001$). The results of the scores in the assessment of symptoms and behavior significantly decreased after supplementation with flax oil and Vitamin C ($p<0.05$) (Joshi et al., 2006). Although the study does not have a placebo group, all the subjects completed the study without complications and side effects. This study shows improvement in hyperactive and inattentive symptoms of ADHD after administration of a supplement.

Hurt, Arnold, and Lofthouse (2011) reviewed literature on studies with nutritional supplements to determine effectiveness in management of ADHD. The authors concluded a multivitamin, multimineral, and omega-3 fatty acids can be used to manage patients with ADHD.

Iron supplementation can be used in patients affected by ADHD with iron deficiency (Hurt et al., 2011). Therefore, Physician Assistants should consider nutritional supplements when managing pediatric patients with ADHD. The authors did not include studies of vitamin B_6. The authors conclude more research studies need to be conducted especially in regards to zinc and magnesium supplementation (Hurt et al., 2011).

The advantages of using nutritional supplements are minimal side effects, facilitating brain function and growth, and improvement in hyperactive and inattentive symptoms of ADHD. Nutrients may be found naturally in a healthy diet rich in fruits and vegetables as well as provided by a nutritional supplement. The disadvantages are insufficient studies available and lack of strict regulation of nutritional supplements. Nutritional supplements are regulated by the Dietary Supplement Health and Education Act of 1994. According to the Dietary Supplement Health and Education Act (1994), nutritional or dietary supplements may prevent chronic diseases with a healthy diet low in fat, sodium, and cholesterol. Good manufacturing practices are in effect to guarantee the packaging and preparation of a nutritional supplement. A nutritional supplement label may indicate it benefits nutritional deficiencies and overall health and well being but it must include the phrase, "This statement has not been evaluated by the Federal Drug and Administration. This product is not intended to diagnose, treat, cure, or prevent any disease" (Dietary Supplement Health and Education Act, 1994). The use of nutritional supplements to aid in the management of ADHD should be discussed with your patient to make sure he/she understands the benefits and risks. The patient and patient's parents can monitor symptoms for improvement and make necessary adjustments to manage ADHD effectively.

Conclusion

The evidence indicates nutritional supplements may be useful as an adjunct to other therapies and proven effective alone in managing ADHD. The nutritional supplements omega-3 and omega-6 fatty acids, iron, zinc, Vitamin B_6, flax oil, antioxidants, and Vitamin C aid in physiologic processes and neurotransmission. At present time, nutritional supplements are not included in the AAP treatment guidelines for ADHD; however, individuals use them. The most commonly reported nutritional supplements used were omega-3 and omega-6 fatty acids. It was also concluded in most studies nutritional supplements improved symptoms and were as effective as pharmacologic therapy.

Although there is literature and information regarding the efficacy of nutritional supplements in ADHD, one must take into account small study population, no standard method of studying nutritional supplements, severity of the symptoms, co-morbid conditions, and combination of pharmacotherapy and behavior therapy. The literature review focused mainly on essential fatty acids such as omega-3 and omega-6 fatty acids because benefits are associated with their use in the management of ADHD. There was also literature found to support the effectiveness of zinc, iron, Vitamin B_6, flax oil, and Vitamin C on management of ADHD with deficiencies. More studies should be done to determine efficacy, amount, and type of nutritional supplements in the management of ADHD.

Nutritional supplements should be considered first line therapy in the management of ADHD. If nutritional supplements alone are not effective, other drugs and therapies may be started. Nutritional supplements may also be used as an adjunct with pharmacotherapy and behavioral therapy.

This literature review may be beneficial to Physician Assistants and other health care professionals because it offers evidence to support the use of nutritional supplements in the management of ADHD. Communication between provider and patient is imperative. The role of nutritional supplements in the management of ADHD should be discussed. The management of ADHD should focus on the improvement of patient's symptoms, patient's satisfaction, and decreasing the use of medications with side effects. Further research should continue to investigate nutritional supplements role in management of ADHD.

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Abstract

Objective

The purpose of this literature review was to determine the effectiveness of nutritional supplements such as omega-3 and omega-6 fatty acids, zinc, iron, magnesium, and Vitamin B_6 in the management of attention deficit hyperactivity disorder (ADHD).

Method

Articles were searched using PubMed, American Academy of Pediatrics, and National Institutes of Health National Center for Complementary and Alternative Medicine for the following terms “ADHD”, “nutritional supplements”, and “dietary supplements”.

Results

There were 24 references obtained and reviewed including case studies, original research articles, and literature reviews.

Conclusion

Nutritional supplements may be effective in the management of ADHD and as adjunct with other therapies. Several nutrients especially essential fatty acids have been shown to improve symptoms. Further research is warranted. Physician Assistants should discuss the role of supplements with patients. The management of ADHD must focus on improving symptoms, quality of life, and daily function while decreasing medication use.