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for children with special health care needs
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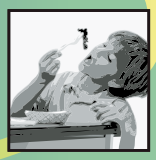

Supplements for Children with Special Health Care Needs

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INTRODUCTION

The focus of this article is micronutrient (vitamin and mineral) supplements for children, particularly children with special health care needs. The article explores current trends in dietary supplementation, oversight of supplement quality, estimates of children's nutritional intake from foods, and assessment of need for micronutrient supplementation. In addition, supplements for children with special health care needs, and vulnerability for excessive or unnecessary supplementation are discussed. The last section uses attention-deficit/hyperactivity disorder (ADHD) as an example.

DEFINITION AND REGULATION OF DIETARY SUPPLEMENTS

Definition

Dietary supplements include micronutrients (vitamins and minerals), macronutrients (protein, carbohydrate and fat), as well as herbal and other botanical supplements. Micronutrient supplements are a subcategory of dietary supplements, and are regulated by the Food and Drug Administration (FDA) Center for Food Safety and Applied Nutrition as a subcategory of food.[1] The FDA defines nutritional supplements in general as "a supplement to the diet that contains a vitamin; a mineral; an herb or other botanical; an amino acid; a dietary substance used by man to supplement the diet by increasing total dietary intake; or a concentrate, metabolite or constituent, extract or combination of any ingredient mentioned above." These may come in pills, powders, liquids or other forms and must be labeled as a "dietary supplement." The Dietary Supplement Health and Education Act (DSHEA) of 1994 amended the Food, Drug and Cosmetic Act of 1938, giving the FDA more oversight of all dietary supplements. It defines and sets safety and labeling requirements for supplements.[1,2]

Regulation and oversight

Label claims

The FDA regulates label claims, such as high potency, or claims related to structure or function. Examples of allowed claims include "calcium builds strong bones," and "fish oil improves cardiovascular health." Labels cannot claim that a supplement heals or cures a specific disease. Claims must be approved by the FDA within 30 days of a supplement being marketed. The FDA does not pre-approve any claims before they hit the market.

Safety

Manufacturers are responsible for making sure their products are safe and that they contain what they say they do. The FDA does not do any pre-market safety or quality review. If a person feels they have been harmed by a supplement they can report it to the FDA via MedWatch, the FDA's Safety and Adverse Event Reporting Program. Manufacturers or distributors of supplements must submit any serious adverse event reports that they get to the FDA within 15 days of getting a report. Adverse events are considered serious if they result in "death, a life-threatening experience, inpatient hospitalization, a persistent or significant disability or incapacity, or a congenital anomaly or birth defect, or requires, based on reasonable medical judgment, a medical or surgical intervention to prevent an outcome listed above." The FDA can remove any product that is deemed unsafe or dangerous.[1]

There are FDA-established good manufacturing practices for supplements to ensure proper identity, purity, strength and composition. Again, they do not do any premarketing review or inspection of supplements; it is the manufacturers' responsibility to follow these practices. Independent organizations test supplements for manufacturers to assure safety, accurate labeling, and that they are free of contaminants: NSF International,[3] Consumer Lab,[4] and the US Pharmacopeia Convention.[5] Manufacturers of supplements can contract with one of these organizations to test their products. Products which meet the organization's quality specifications bear the organization's seal of approval. It is not required that a manufacturer use one of these organizations; it is assumed that manufacturers will follow the FDA's guidelines and create quality products.[1]

Regulation

Regulation of supplements is extremely challenging and varies from country to country. There is not international agreement regarding what is a supplement. For example, in the US, melatonin is considered a dietary supplement that can be purchased over the counter; in Australia, it is a prescription medication. The sheer number of supplements on the market just in the US makes regulation and oversight difficult. In 1994, when the DSHEA first became law, there were about 600 supplement manufacturers producing about 4000 supplement products. Six years later, in 2000 there were approximately 29,000 products on the US market, with few documented analytical methods or reference materials available for most products. At this time, it is estimated that there are more than 85,000 supplement products in the US marketplace. There has been a similar explosion in supplements sold in other countries. In Canada, there have been reports that over 100,000 product license applications have been approved since the Canadian Natural Health Products Regulations came into force in 2005.[6]

Safety of supplements is a major concern. It is quite possible for supplements to contain harmful ingredients when they come to market, since manufacturers have 30 days from that time to submit safety, quality, and efficacy information for a product. Given the explosion of supplements coming to market in the last 25 years, a supplement that contains unsafe ingredients could be on the market for quite a while before coming to FDA attention. The FDA maintains a list of potentially harmful ingredients.[7]

During manufacturing, ingredients may be added at higher amounts than stated on the label. There is no standard practice for overages used. The Dietary Supplement Ingredient Database (DSID) analyzed supplements reported to be used by participants in the National Health and Nutrition Examination Survey (NHANES) 2001-2008. Many multivitamin mineral supplements for both children and adults contained 10% to more than 20% above the labeled amount for some nutrients or other ingredients. Some adult products contained less than the labeled amount for some nutrients.[2]

To learn more about the research evaluating supplements, go to https://dietarysupplementdatabase.usda.nih.gov/.

It is important for registered dietitian nutritionists (RDNs) and other healthcare professionals to understand the challenges in assuring supplement safety before recommending a supplement and to evaluate the supplements that patients are using to make sure they are safe and labeled accurately. Families of children with special health care needs are vulnerable to unscrupulous marketing practices in their quest to find whatever treatment may improve their child's health, wellbeing, and functioning. Just the financial burden of many supplements can affect a child's wellbeing, especially if other proven treatments are not being done due to limited resources.

SUPPLEMENT INTAKE BY CHILDREN IN THE US

Several studies show that approximately one-third of all children in the US take one or more dietary supplements; most of these are multivitamin-mineral supplements.[8] Supplement use is highest among children from families with high education levels and high incomes, and lowest among families with low incomes and food insecurity and those using Supplemental Nutrition Assistance Program (SNAP) benefits.[8] Reasons for using supplements include: "improve overall health" (41%), "maintain health" (37%), "supplement the diet" (23%), "prevent health problems" (14%), and "boost immunity" (14%). For children under 2 years of age 14% of parents cited "tooth health and cavity prevention" as a major reason for using a supplement. For 16- to 19-year old adolescents, 10% used supplements to "get more energy." Only 18% of supplement use in children was based on the advice of a healthcare provider. [1,9]

Abbreviations and Definitions

Term	Definition
FDA	Food and Drug Administration
DSHEA	Dietary Supplement Health and Education Act of 1994
RDN	Registered Dietitian Nutritionist
NHANES	National Health and Nutrition Examination Survey
DSID	Dietary Supplement Ingredient Database
ADHD	Attention deficit-hyperactivity disorder
PUFA	Poly-unsaturated fatty acid
LCPUFA	Long chain poly-unsaturated fatty acid
DHA	Docosahexaenoic acid (an omega-3 PUFA)
EPA	Eicosapentaenoic acid (an omega-3 PUFA)
GLA	Gamma Linolenic acid (an omega-3 PUFA)
DPA	Docosapentaeinoic acid (an omega-3 PUFA)

MICRONUTRIENT STATUS OF CHILDREN IN THE US

Nutrient Intake

Studies that examine the nutrient intake of children have found many areas of concern. An extensive review of the literature in 2011 by Victoria Drake of the Linus Pauling Institute (Oregon State University, Corvallis, OR) looked at intake of children, 4 to 13 years of age. It suggests that many children were not meeting recommended daily allowance for calcium and vitamin D. Among 4- to 8-year-old children, 17% of boys and 33% of girls had calcium intakes below the Estimated Average Requirement (EAR) and Recommended Dietary Allowance (RDA). (The EAR for calcium is 800 mg/day, and the RDA is 1000 mg/day). Calcium intake decreased as children got older. Between 9 and 13 years of age, only 23% of boys and 15% of girls met the RDA for 1300 mg calcium with diet and supplements; 20% of boys and 24% of girls took supplemental calcium.

A 2009 study by Frei, et al looked at the macro- and micronutrient intakes of 175 5- to 11-year old children in four elementary schools in Corvallis, Oregon. All children in the study were from families who had the necessary resources to access healthful and nutrient-dense foods. Findings showed that 60% of the 5 to 8-year old children and 78% of 9 to 11-year old children did not meet recommendations for fiber. Most of the children had diets high in saturated fats and sodium. None met recommendations for potassium. Sixteen percent of the younger children and 45% of the older ones did not meet calcium recommendations.

Biochemical Indicators

A study by Bird, et al examined data from 15,030 NHANES pediatric (>9 years of age) and adult participants in the 2003-2004 and 2005-2006 data cycles. Biochemical analyses of selected vitamins and measures of anemia examined and compared to nutrient intake and supplement use. Approximately 31% of the US population is at risk for deficiency of at least one vitamin or has anemia. Those at highest risk of anemia were pregnant or breastfeeding females, females aged 19-50 years, and adolescent females aged 14-18 years. Individuals who took a multivitamin supplement or who met the Estimated Average Requirement for nutrients evaluated had the lowest incidence of biochemical nutrient deficiencies (14% and 16% respectively).[10]

Biochemical deficiencies in children and adolescents for many nutrients were unacceptably high. For vitamins B6, B12, C, D and measures of anemia, 14- to 18-year-old adolescents, especially girls, had a higher rate of biochemical deficiency than did 9- to 13-year-old children. Vitamin D is a good example: 4 % of 9- to -13-year-old children, 7.1% of 14- to 18-year-old boys, and 10.6% of 14- to 18-year-old girls showed biochemical deficiencies of vitamin D. Of note, deficiency was defined as a vitamin D level of less than 12 ng/mL; many researchers use less than 20 ng/mL as diagnostic of vitamin D deficiency. Over 1% of children showed deficiencies in pyridoxine, vitamin B12, vitamin C, and vitamin E.[10]

The 2009 Frei study also measured vitamin D status of 71 (of the 175 subjects). Sixty-one percent of the 71 children tested had insufficient vitamin D levels (<30 ng/mL), and 8% were considered deficient (<20 ng/mL).[11] Several other studies show that low vitamin D status is a concern for children and adults.[12-15]

MODIFYING INTAKE – WHEN IS A SUPPLEMENT NEEDED?

It is important that public health efforts focus on improving nutrient intake from foods. Increasing vegetables, fruits, whole grains, legumes, and low/non-fat dairy products would go a long way toward improving nutrient intake of our population as a whole. However, due to a variety of factors, many individuals, especially children, need supplementation of one or more micronutrients to maintain adequate nutrition status. Children with special health care needs are often at very high risk for nutrient deficiencies. Many chronic diseases or conditions alter nutrient needs, making it difficult to meet 100% of micronutrient needs with food alone. For example:

- A child with cystic fibrosis may have fat malabsorption fats and may need fat-soluble vitamins in a water-miscible form in order to meet needs.
- Children with sensory deficits may have a difficult time with taste and texture of many foods, thus limiting the variety of foods accepted; these children may need a multivitamin-mineral supplement to meet needs.
- A child with meningomyelocele (spina bifida), who is non-ambulatory has decreased energy needs, making it difficult to meet all micronutrient needs without exceeding energy needs; supplements of one or more nutrients may be necessary.
- Children who have had a solid organ transplant and are treated with some anti-rejection medications may need to limit potassium intake, which in turn limits intake of many fruits and vegetables and thus many vitamins, necessitating supplementation.

In order to determine whether or not a child needs one or more supplements, the RDN needs to do a thorough assessment of the child's nutrient intake from foods. It is important to note intake of fortified foods (e.g., breakfast cereals, meal replacement drinks), as intake of fortified foods AND a supplement may result in excessive intake of some nutrients. A study of the NHANES data from 2007-2010 showed

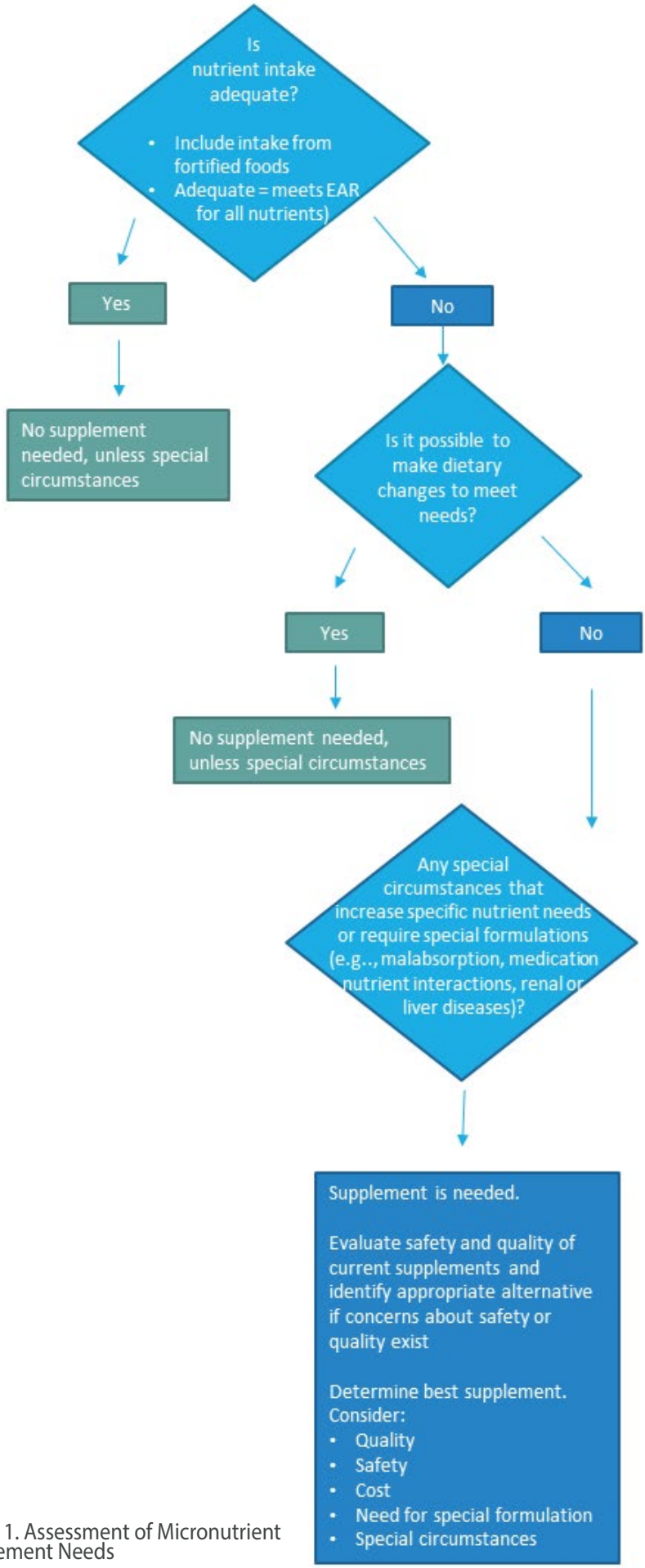

Figure 1. Assessment of Micronutrient Supplement Needs

that some children who used dietary supplements had excess intake of folic acid (49%), zinc (52%) and vitamin A (45%). This is likely due to the consumption of fortified foods along with natural foods that contain these nutrients and the addition of a supplement.[9]

Once the RDN has evaluated current nutrient intake, she or he must look at any special circumstances that alter nutrient needs, such as specific disease states, or medications that have medication-nutrient interactions.[16]

Nutrients from Food

In all cases we take the stance that meeting needs from food is preferable to giving a supplement. There are many instances when changes to diet are reasonable and achievable and thus, preferable to giving a supplement. For example, increasing dietary calcium would be preferable to giving a calcium supplement. Four- to eight-year-old children can meet the RDA for calcium with 3.3 cups of milk or servings of dairy products per day; 9- to 13-year-olds can meet the RDA with 4.3 cups of milk or servings of dairy products per day. There is some calcium in certain vegetables and grains, but it is less bioavailable than the calcium in milk.[17]

Once the nutrition assessment has shown that one or more micronutrient supplements are needed, it is important to find a supplement that has been shown to be high quality and meets the child's needs. If it is decided that a multivitamin-mineral supplement is needed, then one must make sure that the supplement chosen is complete. A common problem is the use of "gummy" supplements. They are easy to chew and kids like them, however, they are not as complete as a regular chewable multivitamin-mineral supplement. Table 1 compares two chewable and two gummy type children's supplements. Note that the nutrient composition varies widely by brand, and neither of the gummy forms contain iron, thiamin, riboflavin, niacin, calcium, copper or magnesium (the Flintstones Complete Chewable also does not contain magnesium). It is incumbent on the RDN to evaluate any multivitamin/mineral supplement a child is taking to make sure it is meeting the required nutrient supplements, as well as to make informed recommendations to parents when advising a nutrient supplement.

DOWN SYNDROME

Families of children with Down syndrome have been shown to be particularly vulnerable to suggestions that a supplement might improve their children's functioning. A 2018 study by Lewanda, et al looked at supplement use by children with Down syndrome. Approximately half of the children they studied were being given or had been given at least one supplement (average of 3 supplements). Most parents had heard of the supplement via a parent group or a friend. Supplements included vitamins and minerals as well non-vitamin-mineral antioxidants, a variety of plant concentrations, alternative foods (e.g., bee pollen) and combination supplements. Supplements were started as early as 4-6 months of age. Only 19.5% of the families got their supplement information from their child's physician, and many did not inform their healthcare providers about the supplements their children were being given. Families spent from $15 to $400 per month, with one outlier family spending $3000 per month; the average cost for supplements was $90.53 per month. Parents of 87% of these children believed that there was improvement in speech, immunity and attention. Seventeen percent noted side effects, such as gastrointestinal distress, and many of these discontinued the supplements. Many of the supplements used had potentially dangerous levels of some vitamins, and most had not been studied for safety and effectiveness for children with Down syndrome.[18]

A 1981 study published in the Proceedings of the National Academy of Science showed that a mega-vitamin-mineral supplement resulted in significant increases in IQ.[19] However, this study was not peer reviewed and was not well-controlled. The lead author, Ruth Harrell, was interviewed by many media sources, including popular talk shows, discussing the amazing results of the study. Parents of children with Down syndrome were clamoring to get this supplement for their children. Developmental pediatricians at the University of Washington Center on Human Development and Disability (at the time called the "Child Development and Mental Retardation Center") and at least 3 other university child development centers repeated the study, using a double blind, placebo-controlled format. Both the supplement and the placebo were made by Bronson Pharmaceuticals, the same company which produced the supplement and placebo for the Harrell study. All of the controlled studies came up with negative results. There were absolutely no improvements in children on the supplement versus those on the placebo.[20] This is an example of how vulnerable parents can be swayed by information in the media, even when it is not accurate. Similar products are periodically promoted as ways to improve function in children with Down syndrome and other developmental disabilities. The RDN or other healthcare provider has a responsibility to evaluate such products for safety and effectiveness and to give families objective information to use in deciding whether or not to give the product to their children.

ATTENTION DEFICIT HYPERACTIVITY DISORDER

A lot of attention has been given to nutritional supplements as a way to improve symptoms of attention deficit hyperactivity disorder (ADHD). Research has looked at supplements by themselves, as well as supplements as an adjunct therapy to medication, especially methylphenidate.

Table 1. Comparison of Multivitamin-mineral Supplements - Chewable and Gummy Forms				
Supplement name	**Flintstones Complete Children's Chewable Multivitamin Supplement, 1 tablet**	**Flintstones Gummy Complete 2 gummies, dose for child <4 years**	**Centrum Kids Multivitamin/ Multimineral Chewable ,1 tablet**	**L'il Critters Gummy Vites Complete Multivitamin, 2 Gummy Bears**
Vitamin A (mcg RAE)	750 (33% as beta carotene)	400	450 (53% as beta carotene)	450
Vitamin C (mg)	60	30	60	20
Vitamin D (IU)	600	600	400	800
Vitamin E (IU)	30	18	10	12 mg
Vitamin K (mcg)	55	--	10	--
Thiamin (mg)	1.5	--	1.5	--
Riboflavin (mg)	1.7	--	1.7	--
Niacin (mg)	15	--	20	--
Vitamin B6 (mg)	2	1	2	1.8
Folic Acid (mcg)	400	200	400	200
Vitamin B12 (mcg)	6	3	6	2.4
Biotin (mcg)	40	75	45	16
Pantothenic Acid (mg)	10	5	10	3
Calcium (mg)	100	--	108	--
Iron (mg)	18	--	8	--
Iodine (mcg)	150	30	150	42
Zinc (mg)	12	2.5	15	2.8
Copper (mg)	2	--	2	--
Magnesium (mg)	--	--	40	--

Source: Manufacturers' websites:

- https://www.flintstonesvitamins.com/ accessed 9/16/19
- https://www.centrum.com/products accessed (and company contacted 9/13/19)
- http://www.gummyvites.com/en/Lil-Critters/Products/Lil-Critters-Gummy-Vites/ accessed 9/13/19

Vitamins and minerals

Vitamin D + methylphenidate improved serum vitamin D levels and seemed to improve evening symptoms, compared to methylphenidate alone. A double-blind, placebo-controlled study by Mohammadpour, et al (2018) looked at the effect of 2000 IU vitamin D/day in addition to the drug methylphenidate. None of the children had been on any type psychostimulant drug for the previous month, or on any supplement containing vitamin D for at least three months prior to the study. All of the children received methylphenidate, half were randomized to receive vitamin D and half to receive placebo for 8 weeks. Symptoms improved in both groups, but evening symptoms, presumably when medication was wearing off, improved significantly more in the vitamin D group. Of note, none of the children had optimal levels of vitamin D prior to the study (average level 15.7 +/- 5.26 for the vitamin D group and 12.979 +/- 5.9 for the placebo group); the vitamin D levels of the group given vitamin D increased significantly to an average of 34.6 +/- 9.5 by the end of the study, while levels for the placebo group fell to 11.2 +/-5.1.21

A multivitamin-mineral supplement improved aggression and emotional regulation, but vitamin A intakes were at or above the tolerable upper limit (UL). A study by Rucklidge et al showed improvement in aggression and emotional regulation, but not in all symptoms in children with ADHD given a multivitamin-mineral supplement (Daily Essential Nutrients). The supplement was given in 3 doses each day, the children started with 3 capsules/day and increased to 12 capsules/day. The ending dose had doses of vitamin A that were concerning: 5760 IU as retinyl palmitate = 1728 mcg pre-formed vitamin A; the tolerable upper limit preformed vitamin A is 900 mcg for 4-8 year olds and 1700 mcg for 9-13 year olds. If a child took this supplement and was eating foods naturally high in pre-formed vitamin A, they could possibly be getting a

toxic amount of vitamin A. [22,23] Another study by the same authors showed that blood levels of vitamins and minerals did not make a significant difference in whether or not a child with ADHD responded to the multivitamin-mineral treatment. [24]

Omega-3 fatty acids

Many studies can be found on the use of omega-3 fatty acids in children with ADHD. Several studies show that plasma concentrations of omega-3 fatty acids are lower in children with ADHD than in the general population.[25-28]

Studies looking at omega-3 fatty acid supplementation in children with ADHD have mixed results. A 2012 Cochrane review looked at 366 references and found 13 research trials with a total of 1011 participants that met inclusion criteria. The results showed some improvement in symptoms, but no significant improvement in parent-rated ADHD symptoms, inattention, or hyperactivity/impulsivity when the subjects from all the studies were combined and evaluated. There were also no differences between groups in behavior, side effects or loss to follow-up. [29]

Heterogeneity among study methods makes it difficult to reach firm conclusions about the efficacy of omega-3 fatty acids for treatment of ADHD. A 2017 systematic review by Agostoni et al looked at the use of omega-3 fatty acids in early psychosis, autism and ADHD. They reviewed 25 randomized, controlled studies on treatment of ADHD with omega-3 fatty acids. Thirteen out of 25 studies showed some beneficial effects of omega-3s; the other 12 studies had negative results. The negative studies more often had short study duration (<15 weeks), variations in supplement (either DHA or EPA alone), lack of a placebo arm and small sample sizes (<50). Of the 8 studies reviewed that looked at omega-3 PUFAs in combination with medication (methylphenidate [Ritalin or Concerta] or atomoxetine [Straterra]), 6 showed no improvement with omega-3 PUFAs and 2 showed significant improvement. Many of the studies showed greater improvement of symptoms in the study groups over the placebo groups, but the differences did not reach significance. The authors conclude that longer studies with more subjects and homogenous study protocols are needed to determine whether or not there is reduction of symptoms with treatment with omega-3 PUFAs.[30]

Ongoing studies continue to have mixed results. Some studies show no benefit of omega-3 supplements on ADHD symptoms. A 2018 controlled study by Cornu et al, not included in the above systematic reviews, did not show a beneficial effect of an omega-3 supplement in children with mild ADHD symptoms. This study looked at 162 children from 6 to 15 years of age with an established diagnosis of ADHD. The children were randomized to receive docosahexaenoic (DHA) and eicosapentaenoic acid (EPA) or placebo for 3 months; none were treated with ADHD medications during that time. The primary outcome was the change in Attention-Deficit Hyperactivity Disorder Rating Scale version 4 (ADHD-RS-IV), other outcomes included safety, lexical level, attention, anxiety and depression. The ADHD-RS-IV score reduction was actually greater in the placebo group than the DHA-EPA group. The authors note that it is possible that certain children will respond to omega-3 PUFA treatment. They note that two large studies with 220 and 438 patients are ongoing; their results will add evidence and may even "close the debate" (neither study is published as of writing of this article).[31]

Some studies have shown positive effects of omega-3 supplementation on plasma EPA and DHA levels and on some (but not all) cognitive and behavioral markers. Several studies do show positive outcomes in children with ADHD supplemented with omega-3 PUFAs. A 2014 study by Widenhorn-Muller found that supplementation with a daily dose of 720 mg omega-3 fatty acids (600 mg EPA and 120 mg DHA) improved EPA and DHA concentrations in erythrocyte membranes and improved working memory function. However, there were no effects on other cognitive measures and parent- and teacher-rated behavior in the study population.[32]

Supplementation did not improve ADHD symptoms, but may have had small, positive effects on other behavioral and cognitive difficulties. Crippa et al studied the effect of just DHA supplementation on behavior and cognition in school-aged, drug-naïve children with ADHD. Fifty children aged 7 to 14 years were randomized to receive either DHA or placebo. The primary outcome measure was the change in the ADHD-RS-IV after 4 and 6 months. Secondary outcomes measures were the Conners Parent Rating Scale-revised, as well as scales looking at quality of life, global functioning and computerized cognitive tasks. Blood test looking at fatty acid profile was done a baseline. There was no benefit found in the ADHD-RS-IV, but there were small, significant effects on children's psychosocial functioning, emotional problems and focused attention. The conclusions are that DHA supplementation has no beneficial effect on ADHD symptoms in school-aged, drug naïve children with ADHD. However there appear to be small positive effects on other behavioral and cognitive difficulties. Given no side effects found in this study, and small, positive effects in some areas, the authors concluded that it would be reasonable to follow-up with future intervention studies.[33]

Likewise, use of a marine oil did not improve ADHD symptoms, but was associated with improved working memory, cognitive, and hyperactivity scores using tests other than the Connors Parent Rating Scale. A study by Kean, et al looked a very specific marine oil, PCSO-524®, a standardized lipid extract of the New Zealand green-lipped mussel in 112 6- to 14-year-old children with confirmed ADHD. They found no improvement on the Conners Parent

Rating Scale (the primary outcome measured) between the placebo or treatment groups. However, they did find significant improvement in working memory, cognition as well as hyperactivity and attention in other tests in the treatment group over the placebo group.[34]

Thirteen of sixteen studies reviewed reported benefit of LCPUFA supplements on ADHD symptoms. A 2017 systematic review of 16 randomized, controlled studies included a total of 1514 children and young people with ADHD who were randomized to omega-3/6 supplementation or placebo. Four studies used supplements containing a 9:3:1 ratio of eicasapentanoic acid:docosahexaenoic acid: gamma linolenic acid; this combination appeared to be effective at improving erythrocyte levels of long chain poly-unsaturated fatty acids. Thirteen of the studies reported favorable benefits on ADHD symptoms, including improvements in hyperactivity, impulsivity, attention, visual learning, word reading and working/short term memory. In some studies, LCPUFAs were given as the only treatment for ADHD and in others, they were given as an adjunct to stimulant medications. The author concludes that while medications play an important role in the treatment of ADHD, omega-3/6 supplementation can provide a promising adjunctive therapy, possibly decreasing the dose of psychopharmacologic medications needed.[35]

PUFA + methylphenidate reduced ADHD symptoms more than methylphenidate + placebo in a short study of 33 children. An eight-week study by Moghaddam et al evaluated the effectiveness of methylphenidate plus poly-unsaturated fatty acids (180 mg EPA and 120 mg DHA) for the treatment of ADHD. They looked at 33 children, mean age 9.5 years. The children were randomized to receive methylphenidate plus PUFA or placebo. The methylphenidate + PUFA group had a significantly greater reduction in symptoms than the methylphenidate + placebo group, suggesting that poly-unsaturated fatty acids are a reasonable treatment for ADHD. The authors recommend repeating the study with a larger sample size and longer study period. [36]

Long-term use of a high-dose supplement found improvements in behavioral and cognitive measures. One, 2019 study by Rodriguez et al looked at highly concentrated docosahexaenoic acid (DHA) and showed improved symptoms of ADHD. This 6-month, prospective study randomized 66 patients, 6 to 18 years old into experimental or placebo groups. The participants were either medication naïve or using a stimulant medication (75% of the experimental group and 70.6% of the placebo group were taking medications) The experimental group received an omega-3 fatty acid supplement consisting of 1000 mg DHA, 90 mg EPA and 150 mg DPA (docosapentaenoic acid, not used in other studies). This study found improvements in behavioral and cognitive measures.[37] This study was the only one in this review which used a much higher amount of DHA than EPA.

Summary

Research into the use of long chain fatty acids, omega-3 or a combination of omega-3 and 6 as treatment for ADHD is promising, but not conclusive. There is not one long chain fatty acid formulation that stands out as the most effective for improving ADHD symptoms. Some studies give just omega-3 fatty acids, others give omega-3 and omega-6 fatty acids. Most studies give a larger proportion of EPA than DHA, but the study by Rodriguez gave far more DHA than EPA and included a different omega-3 FA, DPA. Many studies saw some significant improvement in memory and cognitive skill; none saw big improvements in parent or teacher ratings of ADHD symptoms. Omega-3 fatty acids given as adjunct therapy with traditional ADHD medications seemed to result in greater improvement in symptoms than the medication alone. Given the low levels of side effects noted in studies, it would be quite reasonable to consider omega-3/6 supplements in addition to traditional medications to children with ADHD. However, before omega-3/6 supplements can be widely recommended for ADHD, there needs to be more large scale research and a standardized dose available. A large, multi-center double blind study evaluating the same long chain poly-unsaturated fatty acid supplement would be extremely helpful in settling this question.

CONCLUSION

It is very important for the RDN to do a thorough nutrition evaluation before recommending a supplement. Primary healthcare providers and RDNs need to make sure to review supplement intake at each appointment, as most people taking supplements are not doing so on the advice of a healthcare provider. Whenever improvement in diet is possible, that should be the first line choice for meeting a child's nutrient needs. All supplements are not created equally. When recommending a vitamin/mineral supplement, the RDN must look at the ingredients in the supplement and whenever possible use one that has been evaluated for quality by an outside organization such as NSF international.

Given that vitamin D is obtained mainly from direct sunlight exposure and many children do not get enough to meet their vitamin D needs, either due to living where direct sunlight is limited or from wearing sunscreen. Vitamin D supplements are likely important for most children. Indeed, several studies cited in this paper showed that significant numbers of children had low blood vitamin D levels.

Parents of children with special health care needs want to do whatever is going to help their children function best. They are vulnerable to unsubstantiated reports that a specific treatment or supplement might improve their child's function. This can result in a lot of time and money spent on things that have no or little proven effect while not

doing the things for which there is a lot of good research. Healthcare providers need to help families determine what treatments and supplements will likely help their children, and be aware of any potentially harmful treatments or supplements. The use of supplements, especially omega-3 fatty acids has been suggested as a possible treatment for ADHD. The research evaluated here suggests that there might be a small effect of omega 3-6 poly-unsaturated fatty acids in functioning of children and adolescents with ADHD, especially when used in conjunction with traditional medications. However, none of the studies showed a major effect of these supplements alone. More research is needed before one could widely recommend omega 3-6 fatty acids for children and adolescents with ADHD.

CASE STUDIES

Type 1 diabetes and celiac disease

JT is an 11-year-old who was diagnosed with type 1 diabetes 1 year ago, and celiac disease 1 month ago. He was seen by an RDN 3 weeks after his diagnosis of celiac disease. He had been advised to start a gluten-free diet at the time of diagnosis, and his family conferred with the dietitian over the phone to help get started. Biochemical analysis at time of celiac disease diagnosis showed marginal vitamin D levels (30 ng/mL – optimal level is considered to be 30 to 100 ng/mL; deficiency is <20 ng/mL). No other biochemical assessments of nutrients were available. Diabetes is managed using an insulin pump, a continuous blood glucose monitor, and a "do it yourself" closed loop system that automatically alters basal insulin rate as needed. In spite of state-of-the-art diabetes care, JT was continuing to have frequent high and low blood glucose levels; this may have been due to nutritional absorption issues and poor eating due to undiagnosed celiac disease.

Review of typical eating habits showed that JT has always been a rather picky eater and has always had a low body mass index. He lost 12 pounds between time of diagnosis of type 1 diabetes and diagnosis of celiac disease, suggesting that overall nutritional intake was low and/or he had significant nutrient malabsorption. Current eating showed low intake of dairy products, vegetables, fruits and whole grains of any kind. JT is a very active and talented athlete, playing select soccer all year round.

Children with celiac disease often show biochemical deficiencies in iron (ferritin levels), vitamin D, and zinc at the time of diagnosis due to malabsorption of nutrients prior to instituting a gluten-free diet. All but vitamin D typically normalize within 6 months.[38] A gluten free diet can be deficient in several nutrients that are commonly in natural, whole grain or fortified gluten containing foods: vitamin D, vitamin B12, Folate, iron, zinc, magnesium and calcium.[39]

Review of typical eating habits and common deficiencies with celiac disease suggest that JT would benefit from a complete multi-vitamin-mineral supplement with iron that contains at least 1000 IU vitamin D. The plan is to work on improving food intake to better meet JT's needs while treating both type 1 diabetes and celiac disease. The team will use the angle that improved nutrition will help JT's sports performance since that is a major goal of his. Once nutritional intake has improved, he should be able to meet all needs except for vitamin D without a multivitamin-mineral supplement. He can then take a single vitamin D supplement. Follow-up biochemical levels of iron stores, indices of anemia and vitamin D and possibly zinc, folate, and vitamin B12 will be checked in about 6 months to make sure that JT does not have nutrient deficiencies.

Atypical Food Protein Induced Enterocolitis Syndrome (FPIES)

SG is a 10-month old breast-fed infant who has tolerated very few solid foods. He was first referred for nutrition evaluation at 9 ½ months of age. He typically has a delayed reaction to any new food that is introduced – he wakes screaming and crying, drawing up his legs and has extreme tenderness in his belly. He has diarrhea a few hours later. His working diagnosis is atypical FPIES. With typical FPIES there is a delayed reaction to foods, similar to SG's but reaction is also accompanied by extreme vomiting to the point of causing shock.

The only foods that SG has tolerated so far are highly refined infant oat cereal and infant puffs that are made with refined oat and wheat flours, and apple puree. Trial of any of these foods in their whole form has resulted in severe symptoms. He has not tolerated any other food that has been tested to date (beef, pork, chicken, eggs, multiple vegetables and fruits).

SG tolerates a combination of his mother's breast milk and donor breast milk (from mother's cousin) very well. He has also tolerated Alimentum® infant formula, but will only drink a small amount of it when he is very hungry. He has gained weight and grown well with breastfeeding (common with FPIES). The concerns are that breast milk is not adequate in iron or vitamin D, and may not be meeting his needs for other nutrients at this stage of infancy. (See Table 2.) Indices of anemia showed marginal hematocrit and hemoglobin levels at 7 months of age. Recommendation is that he be started on an infant multi-vitamin with iron at this time.

Low Energy Needs

SA is an 18-month old with a history of hypoxic ischemic encephalopathy. He is significantly affected by this, and does not walk or crawl. He has seizures, which are managed with several medications including phenobarbital. SA is fed exclusively by g-tube, and his current pattern (which provides 600 calories per day, or 46 calories per kilogram) keeps his weight "in channel." Because increasing

Table 2. SG's intake compared to DRI for age recommendations (selected nutrients)		
Nutrient	**SG's intake (breastmilk)**	**Recommended intake**
Iron (mg)	0.8	11.0
Vitamin D (mcg)	1.1	10.0
Calcium (mg)	385	260
Thiamin (mg)	0.2	0.3
Riboflavin (mg)	55	0.4
Vitamin B6 (mg)	0.1	0.3
Vitamin B12 (mcg)	0	0.5
Vitamin K (mcg)	0	2.5

his tube feeding volume would result in excessive weight gain, supplements are used to meet needs for some micronutrients: calcium, vitamin D, niacin, sodium, potassium, and chloride.

Supplements and Autism Spectrum Disorder

LC is a 2 ½ year old boy with autism spectrum disorder. He is working with a feeding therapist to expand his food repertoire and was referred to an RDN to evaluate his nutrition status. LC takes a number of supplements; his mother explains that some are intended to help with autism symptoms and others to boost his immunity. Estimated intake of nutrients from food and supplements were compared to the DRI. The RDN made several recommendations to LC's family:

- Provide supplemental iron to meet iron needs (intake provides 2 mg; DRI is 7 mg)
- Discontinue or decrease zinc supplement (intake provides 60 mg/d; upper limit is 12 mg)
- Continue supplemental calcium and vitamin D

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To participate in this continuing education opportunity login to the Nutrition Focus website http://depts.washington.edu/nutrfoc/webapps/?page_id=1345 and select "Continuing Education" to access the quiz related to this issue. You must correctly answer 80% of the questions to pass. Cost is $20 (subscribers) or $40 (non-subscribers) for 2 CPEU.

1. True or false: Micronutrient supplements are a subcategory of dietary supplements are regulated by the USDA.
   a. True
   b. False. Only herbal and botanical supplements are regulated.
   c. False. Micronutrient supplements are regulated by the FDA.
   d. False. Dietary supplements are only regulated if insurance coverage is requested.

2. Which of the following is NOT an allowed claim on the label of a dietary supplement:
   a. Calcium builds strong bones
   b. Omega-3 fatty acids cures ADHD
   c. Fish oil improves cardiovascular health
   d. All of the above are allowed claims

3. Who is responsible for ensuring that FDA-established good manufacturing practices are followed?
   a. Manufacturers
   b. NSF International
   c. US Pharmacopeia Convention
   d. The Food and Drug Administration

4. According to the article, only 23% of boys and 15 % of girls ages 9 to 13 years were meeting the RDA for which nutrient:
   a. Iron
   b. Calcium
   c. Vitamin A
   d. Vitamin D

5. Which of the following was NOT identified by the article as a reason why a child with a special health care need might need a dietary supplement:
   a. Fat malabsorption
   b. Decreased energy needs
   c. Sensory deficits
   d. All of the above were identified by the article

6. What role does the RDN have in determining whether or not a dietary supplement is needed:
   a. Send supplements to labs to be tested for purity
   b. Order laboratory tests to evaluate individual need
   c. Conduct a nutrition assessment, including evaluation of nutrient intake from fortified foods and supplements
   d. None of the above

7. The article reviewed some vitamin/mineral supplements used as an adjunct for treatment of ADHD. Which of the following concerns was raised by the summaries:
   a. Rebound scurvy with high vitamin C intakes
   b. Potentially for vitamin A intakes above the tolerable upper limit (UL)
   c. Medication-nutrient interactions between methylphenidate and vitamin D
   d. None of the above; no potential risks were identified

8. Which of the following statements about fatty acid supplementation for ADHD is most accurate, according to the article:
   a. Research into the use of long chain fatty acids is promising but not conclusive.
   b. LCPUFA supplementation is more effective than treatment with ADHD medications.
   c. LCPUFA, either alone or as an adjunct to medication, have no effect on measures of ADHD symptoms.
   d. Omega-6 fatty acids given as adjunct therapy with ADHD medication results in greater improvement in symptoms than the medication alone.