Complementary and Alternative Therapies in Developmental Disabilities

Teresa Bailey, PharmD

teresabailey@ferris.edu

Objective:

Identify advances in clinical assessment and management of selected healthcare issues related to persons with developmental disabilities

Notes:
Complementary and Alternative Therapies
Developmental Disabilities
Teresa Bailey, PharmD, BCACP, BCPS
Professor
Ferris State University College of Pharmacy
2016

Objectives
• Explain the steps that should be taken when counseling a patient about a dietary supplements
• Understand the general guidelines regarding dietary supplements
• Recognize dietary supplements that are considered unsafe

News Media

Dietary Supplements

Pros

Cons

Advantages Regarding Dietary Supplements
• Patient autonomy
• Patient use
• Cheaper than prescription medication
• Profit to be made?
2012 National Health Interview Survey
National Institutes of Health National Center for Complementary and Alternative Medicine Report
• 33.2% adults reported using CAM in previous year

• 83 million adults spent $33.9 billion out-of-pocket on CAM (1.5% of total)
  – Conventional out-of-pocket = $268.6 billion
  – Total health care spending = $2.2 trillion

$14.8 billion on natural products vs $47.6 billion on Rx drugs

Children with Autism Spectrum Disorder
• 30-95% of children have been provided with CAM

Limitations to Dietary Supplement
• Fear of legal liability
• Lack of reputable manufacturers
• Absence of FDA approval
• Difficulty identifying product content
• Reviewing hundreds of products and indications
• Health care provider concerns

Unsafe Dietary Supplements
Food and Drug Administration
• Carcinogens
  – Borage*
  – Calamus
  – Coltsfoot
  – Comfrey*
  – Life root
  – Sassafras

Unsafe Dietary Supplements
Food and Drug Administration
• Hepatotoxicity
  – Butterbur*
  – Chaparral
  – Germander
  – Life root
  – Pennyroyal oil → renal/ hepatic
  – Heliotrope
  – Comfrey
  – Kava*
Unsafe Dietary Supplements

Food and Drug Administration

- Miscellaneous
  - Licorice* → pseudoaldosteronism
  - Ma Huang (ephedra) → death
  - Pokeroat (Children)
  - Willow bark
  - Jin Bu Huan → paralysis
  - Stephania and Magnolia → kidney failure

- Germanium → acute renal failure
- Lobelia → respiratory depression and death
- L-tryptophan or Phenylalanine → eosinophilia-myalgia syndrome
- Yohimbe* → seizures and death

Miscellaneous

12 Dangerous Dietary Supplements Named by Consumer Reports
http://www.drugdanger.com/Others/4-04-01consumerreports.htm

- Androstenedione
- Aristolochic Acid (cancer)
- Bitter orange
- Chaparral
- Comfrey
- Germander
- Kava
- Lobelia (tachycardia)
- Organ/glandular products
- Pennyroyal (liver/kidney)
- Skullcap (liver damage)
- Yohimbe

- Brands of dietary supplement products not equivalent
- Lack of active ingredient consistency
- Difficulty in identifying reputable manufacturers

Quality of Dietary Supplement
Pediatrics 2008;121:775-781

Standardization

ConsumerLab.com
USP Verified

National Science Foundation
http://www.nsf.org/consumer/

Top Dietary Supplements Used in Developmental Disabilities

Best Researched and Safest

• According to Autism Speaks
  – Vitamins
  – Melatonin
  – Omega 3 fatty acids
  – Probiotics
  – Casein and Gluten free diets
**Vitamins/Minerals**

- Autism Speaks Autism Treatment Network
  - Found that supplements and special diets for children with autism
  - Unsafe levels of Vitamin A, folic acid and Zn
  - Low levels of Calcium and Vitamin D

**Melatonin**

- Orphan drug status
  - Treatment of circadian rhythm sleep disorders in blind people with no light perception
- Non-approved indications
  - Jet lag, insomnia, depression, and cancer

**Melatonin**

- Mechanism of action
  - Hormone made from serotonin and secreted by the pineal gland
  - Melatonin controls the periods of sleepiness and wakefulness
  - May possess antioxidant properties

**MENDS**

Melatonin or placebo capsules in doses of 0.5mg, 2mg, 6mg and 12mg for 12 weeks

- Time to sleep onset 45.34 minutes sooner*
- Total sleep time 22.43 minutes longer*
- Total sleep time 9.5 hours*

**Melatonin Dose Escalation**

<table>
<thead>
<tr>
<th>Dose (mg)</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>15%</td>
</tr>
<tr>
<td>2</td>
<td>20%</td>
</tr>
<tr>
<td>6</td>
<td>26%</td>
</tr>
<tr>
<td>12</td>
<td>39%</td>
</tr>
</tbody>
</table>
Melatonin

Contraindications/precautions
- Avoid in pregnancy
- Melatonin may aggravate depressive symptoms
- Melatonin may increase the incidence of seizures
- Hypertension (exacerbated)
- Diabetes (hyperglycemia)

Drug Interactions

Selective serotonin reuptake inhibitors
- May increase melatonin serum concentrations
Other sedatives may exacerbate the sedative effects of melatonin
- Alcohol
- Benzodiazepines
Caffeine
- Theoretically, efficacy of melatonin may be decreased

Drug Interactions

Immunosuppressants
- Melatonin may interfere
Antidiabetic agents
- May be less effective
Anticoagulants
- Increased effect
Contraceptives
- Theoretically efficacy of melatonin may be increased
Verapamil
- Increased melatonin excretion

Melatonin

Side effects
- Drowsiness
- Daytime fatigue
- Headache
- Dizziness
- Transient depression
- Alertness decreased (Caution use of machinery)
- Long-term side effects are unknown

Melatonin

Dosage 0.3–5 mg at bedtime
Rozerem™ (ramelteon)
- Selective agonist of melatonin receptors
- FDA indication: insomnia
Circadin (melatonin)
- As a prescription drug in Canada and Europe

Omega-3 Fatty Acids

Omega 3 fatty acids
- Eicosapentaenoic acid (EPA)
- Docosahexaenoic acid (DHA) important for brain development
- Alpha linolenic acid (ALA)
- Human body cannot produce omega-3 fatty acids
- Nor can it convert omega-6 fatty acids

Omega-3 Fatty Acids

http://www.circadin.com/
Omega-3 Fatty Acids for ADHD

- Conflicting data on the effectiveness of omega-3 fatty acids in ADHD
  - Necessary for proper brain development and function
  - When supplemented, results are clinically insignificant
  - No studies prove that fatty acids alone are an effective treatment for ADHD

Omega-3 Fatty Acids

- Likely safe in children when taken orally and appropriately
- Dose for pediatric patients for ADHD has not been established however there are many different sources
  - Breast milk, flaxseed oil, Docosahexanoeic Acid (DHA), Alpha linolenic acid (ALA)

Omega-3 Fatty Acids

- For Autism
- Small studies suggest omega-3 fatty acids
  - reduces symptoms of repetitive behavior, hyperactivity
  - improves socialization
- Studied dose of 1.3 grams of omega-3 fatty acids/day for 12 weeks

Contraindications and Precautions

- Seafood allergy
- Bipolar disorder (possible hypomania)
- Bleeding
- Cardiac disease
- Depression (possible hypomania)
- Diabetes mellitus (possible BG worsens)
- Immunodeficiency (possible suppression)
- Hypertension

Drug Interactions

- Anticoagulants/Antiplatelets/Thrombolytics
  - Increase bleeding
- Anthypertensives
  - Additive blood pressure reduction
- Xenical, Alli, Orlistat
  - Decreased fish oil absorption
  - Separate by 2 hours

Adverse Reactions

- Bleeding
- Ecchymosis (bruising)
- Epistaxis (nosebleeds)
- Hypervitaminosis A
- Hypervitaminosis D
- Rash
- Dyspepsia
- Eructation (burping)
- Nausea/Vomiting
- Diarrhea
- Halitosis
- Dysgeusia (taste perversion)

- Freeze capsules???
- Enteric coated capsules
Dosing
Natural Medicine Comprehensive Database

- Fish oil
  - 1 capsule provides daily:
    - Eicosapentaenoic acid (EPA) 300 mg
    - Docosahexaenoic acid (DHA) 200 mg

Lovaza/generics
- 1000 mg
  - Each capsule:
    - Eicosapentaenoic acid (EPA) 465 mg
    - Docosahexaenoic acid (DHA) 375 mg

Probiotics in Autism

- Only animal research
  - Improves behaviors as improves dysbiosis
- Lactobacilli and bifidobacteria most research

Probiotics

- Little or no quality control
- Low/no levels of “live” probiotics
- Recommend probiotic yogurt with billions of viable microorganisms listed on label

Consumers Health Report
Top 5 Probiotics of 2016

- Based on:
  - Price
  - Potency
  - Colony Forming Units (CFU)
  - Strains
  - Strain purity

Vitamin B6

- Essential cofactor for neurotransmitter systems
  - Serotonin, GABA, dopamine, epinephrine, norepinephrine
- 1968 Bonisch reported vitamin B6 100-600 mg per day
  - Improved behavior in 12 of 16 autistic children
- Other doses studied:
  - 100-200 mg/day
  - 200mg/70 kg
  - 30mg/kg; max 1 gram/day
**Vitamin B6**

- **Drug Interactions:**
  - Isoniazid, cycloserine, hydralazine antagonize pyridoxine.
  - Levodopa is antagonized
- **Side effects:** neuropathy

**Dietary Sources**

- ****Protein rich foods---extra-lean meat, chicken, fish, soybeans, cooked dried beans and peas, wheat germ, brewer’s yeast, and peanuts
- Avocados, bananas, cabbage, cauliflower, potatoes, whole grain breads and cereals

**Magnesium**

- **Essential macromineral for enzyme-catalyzed metabolic reactions**
- When combined with vitamin B6, increased B6 efficacy
- **Doses studied:**
  - 100 mg/70 kg
  - 10 mg/kg; max 350 mg/day

**Side Effects**

- Diarrhea
- Abdominal cramping

**Toxicity increases with kidney impairment**

**Drug Interactions**

- Decrease effectiveness
  - Quinolones and tetracyclines
    - Separate by 2 hrs before or 6 hrs after the antibiotic
  - Levothyroxine
    - Separate by 4 hrs.
### Selected Food Sources of Magnesium

<table>
<thead>
<tr>
<th>FOOD</th>
<th>Milligrams (mg)</th>
<th>%DV*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Halibut, cooked, 3 ounces</td>
<td>90</td>
<td>20</td>
</tr>
<tr>
<td>Almonds, dry roasted, 1 ounce</td>
<td>80</td>
<td>20</td>
</tr>
<tr>
<td>Cashews, dry roasted, 1 ounce</td>
<td>75</td>
<td>20</td>
</tr>
<tr>
<td>Soybeans, mature, cooked, ½ cup</td>
<td>75</td>
<td>20</td>
</tr>
<tr>
<td>Spinach, frozen, cooked, ½ cup</td>
<td>75</td>
<td>20</td>
</tr>
<tr>
<td>Nuts, mixed, dry roasted, 1 ounce</td>
<td>65</td>
<td>15</td>
</tr>
<tr>
<td>Cereal, shredded wheat, 2 rectangular</td>
<td>55</td>
<td>15</td>
</tr>
<tr>
<td>Oatmeal, instant, fortified, prepared w/</td>
<td>55</td>
<td>15</td>
</tr>
<tr>
<td>water, 1 cup</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potato, baked w/ skin, 1 medium</td>
<td>50</td>
<td>15</td>
</tr>
<tr>
<td>Peanuts, dry roasted, 1 ounce</td>
<td>50</td>
<td>15</td>
</tr>
<tr>
<td>Peanut butter, smooth, 2 Tablespoons</td>
<td>50</td>
<td>15</td>
</tr>
</tbody>
</table>


### Carnitine

- Helps intracellular transport of long chain fatty acids and energy generation
- Improves expressive and receptive vocabulary
- Improves Gilliam Autism Rating Scale
- Dose 800 mg/day for 8 weeks

### Side Effects
- Nausea, vomiting, diarrhea
- Breath, urine may have a fishy odor
- Drug interactions: warfarin, levothyroxine
- Disease interactions: seizure disorder, hypothyroidism worsens

### Down Syndrome

- American College of Medical Genetics states no scientific evidence that supplements can improve mental functioning

### Cerebral Palsy

- WebMD
  - GABA (Insufficient evidence)
    - Might improve mental development, learning, vocabulary, and physical function
  - Magnesium (Possibly effective)
    - Given in utero may decrease risk of cerebral palsy in infant

### Valerian

**Valeriana officinalis**

- **Indications**
  - Restlessness
  - Nervous disturbance of sleep
- **Pharmacology**
  - Central depressant action
  - Inhibition of GABA enzyme
  - Spasmolytic effect
Valerian (Valeriana officinalis)

• Contraindications/Precautions
  – Similar: benzodiazepines, barbiturates, opiates
• Drug Interactions
  – Sedatives
  – Anxiolytics
  – Monoamine oxidase inhibitors
  – Alcohol
  – Antidepressants

• Side effects
  – Headache, hangover, insomnia, cardiac disturbances
  – Toxicity: Ataxia, hypothermia, hallucinations, increase muscle relaxation
  – No effect on reaction time, alertness, concentration in the morning
    – (Pharmacopsychiatry 1999;32(6):235-41.)

• Dosage: 2-3 grams QD-TID

General Guidelines Regarding Dietary Supplements

• “First do no harm.”
• Pregnancy, lactation
• Children
• Medications
  – Warfarin
  – Cytochrome P450
• Immunocompromised states
  – Cancer, HIV, transplant patients
• Anti-obesity herbs
  – Laxatives, diuretics, ma huang, thyroid herbs

Patient Counseling

• “What remedies are you using in addition to your medications?”
• Any OTC medications, any herbs, vitamins, or other dietary supplements?”
• Nonjudgmental

Patient Counseling

• Inform patients
  – FDA does not regulate
  » Standardization
  » Efficacy
  » Safety
  » Drug interactions
  – What is actually known of the product
  » Textbooks
  » Literature searches
  » Internet

• Document !!!!!!!!!!!!!!!!!!!!!!!!!!!!!
  – Potential liability
• Patient follow-up
  – Report Adverse Drug Reactions
    » FDA’s MedWatch hotline at 1-800-FDA-1088
    » Fax a report to 1-800-FDA-0178
    » http://www.fda.gov/medwatch/report/hcp.htm
  – Drug Interactions