The Use and Misuse of Herbs and Dietary Supplements

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Learning Objectives

- Identify the current trends regarding use of herbs and dietary supplements in the US
- Describe regulations of the herbs and dietary supplement industry
- Evaluate current literature and information about commonly used herbs and dietary supplements including:
  - Common uses or conditions treated
  - Latest evidence regarding safety and efficacy
  - Major adverse effects
  - Major drug-herb interactions

Background

- Three-fourths of world relies on natural medicines
- JAMA study[1]
  - 1990 - 34% used > 1 alternative therapy
  - 1997 - 42% used > 1 alternative therapy
- Current use approximately 40-62%[2,3]
- $34 billion spent out of pocket annually on CAM[3]
  - Products, classes, visits to providers
- $15 billion spent on herbs and dietary supplements[3]

1.Eisenberg et al. *JAMA* 1998;280:1569-75.
2.Barnes PM et. CDC Advance Data from Vital and Health Statistics No 343; May 2004
3.Barnes PM et al. CDC National Health Statistics Report No 12; Dec 2008.
4.Clinical Toxicology Dec 2010, Vol. 48, No. 10: 979–1178.

Trends in Consumer Use of Herbs and Dietary Supplements

- 2010 NIH and AARP surveyed Americans over the age of 50 years old[1]
  - 37% used herbs and dietary supplements
  - 67% never discuss CAM use with a health care provider
- 2011 Harvard Opinion Research Program[2]
  - Conducted telephone survey of 1579 respondents
  - Approximately 4 out of 10 Americans reported using supplements in past 2 years

1. AARP/NCCAM Survey of U.S. Adults 50+, 2010. Available at URL http://nccam.nih.gov/news/camstats/2010/findings1.htm
2. Blendon RJ et al. Arch Intern Med. 2012; doi:10.1001/2013.jamainternmed.311

Trends in Consumer Use of Herbs and Dietary Supplements

- 2011 Harvard Opinion Research Program
  - 36% had not told physician about use of supplements
  - 5% had been told by physician or nurse to stop supplement
  - 25% reported that they would stop using supplement if public health authorities found it was ineffective

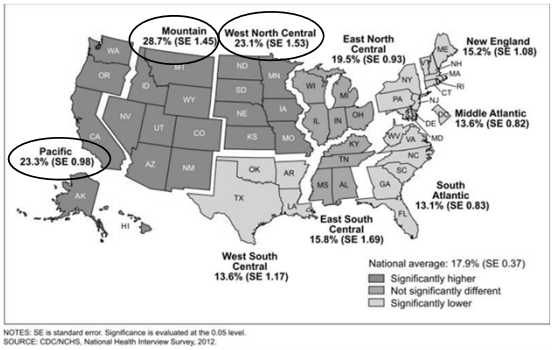
Blendon RJ et al. Arch Intern Med. 2012; doi:10.1001/2013.jamainternmed.311

2012 National Health Interview Survey

- Supplement to the Census Survey
- Asked about use of 18 non-conventional health care practices
- Results:
  - Found that use of non-vitamin/non-mineral dietary supplements was highest used CAM modality
  - Use of these dietary supplements highest in Pacific, Mountain, and West North Central Regions

Peregoy JA, Clarke TC, Jones LI, et al. Regional variation in use of complementary health approaches by U.S. adults. NCHS data brief, no 146. Hyattsville, MD: National Center for Health Statistics. 2014.

2012 National Health Interview Survey



NOTES: SE is standard error. Significance is evaluated at the 0.05 level.
SOURCE: CDC/NCHS, National Health Interview Survey, 2012.

Peregoy JA, Clarke TC, Jones LI, et al. Regional variation in use of complementary health approaches by U.S. adults. NCHS data brief, no 146. Hyattsville, MD: National Center for Health Statistics. 2014.

2012 National Health Interview Survey

- Fish oil
- Glucosamine or chondroitin
- Probiotics or prebiotics
- Melatonin
- Coenzyme Q10
- Echinacea
- Cranberry
- Garlic
- Ginseng
- Ginkgo
- Green tea
- MSM
- Milk thistle
- Saw palmetto
- Valerian

Clarke TC, Black LI, Stussman BJ, et al. Trends in the use of complementary health approaches among adults: United States, 2002–2012. National health statistics reports; no 79. Hyattsville, MD: National Center for Health Statistics. 2015.

NY Times Article on Liver Damage from Dietary Supplements

Spike in Harm to Liver Is Tied to Dietary Aids

O'Connor, Anahad. "*Spike in Harm to Liver Is Tied to Dietary Aids*." *New York Times*. New York Times, 22 Dec. 2013. Web. 21 Dec. 2013.

http://www.nytimes.com/2013/12/22/us/spike-in-harm-to-liver-is-tied-to-dietary-aids.html?pagewanted=all

Liver Injury Related to Dietary Supplements

- **Drug-Induced Liver Injury Network (DILIN) established in 2003 to track cases of liver injury**
  - **In 10 year period, 130 of 839 cases related to dietary supplements**
    - **First 2 years, dietary supplement injuries = 7%**
    - **10 years later, dietary supplement injuries = 20% (p=0.0007)**
- **Dietary supplements had significantly more severe cases vs. medications (p=0.002)**
- **Quality product selection is an important safety aspect**

1. Navarro VJ, et. al. *Hepatology*. 2014;60(4):1399 – 1408.
2. Seeff LB, et. al. *Gastroenterology*. 2015;148(3):517-532.e3.

Dietary Supplement Use in Chronic Kidney Disease

- **The National Kidney Foundation webpage for herbal supplement use and kidney disease:**
  - **https://www.kidney.org/atoz/content/herbalsupp**
  - **Recommendation to avoid all dietary supplements for patients with kidney disease**
  - **Lists specific ones to avoid contain potassium or phosphorus and can contribute to hyperphosphatemia**
- **Consider those that can affect renal function or worsen other disease states**
- **Refer to a nephrologist if patient wants to use**

Hume AL. *Pharmacy Today* [Feb. 1, 2015]. Available at: http://www.pharmacist.com/chronic-kidney-disease-and-the-use-of-dietary-supplements. Accessed February 3, 2015.

New York Attorney General and Supplements

- **February 2015 New York Attorney General accused 4 retailers of selling fraudulant and dangerous supplements**
  - **GNC**
  - **Target**
  - **Walgreens**
  - **Walmart**
- **Testing showed 4 out of 5 products didn't have labeled ingredients but instead had fillers**

New York Attorney General and Supplements

- Walgreens
  - Ginseng contained powdered garlic and rice
- Walmart
  - Ginkgo biloba contained powdered radish, houseplants and wheat (labeled as wheat and gluten free)
- Target
  - 3 out of 6 products didn't have ginkgo, SJW or valerian but instead powdered rice, beans, peas and wild carrots
- GNC
  - Unlisted ingredients including class of plants that includes peanuts and soybeans

Regulations

- 1951: 2 classes of drugs were established (prescription and non-prescription (OTC))
- 1962: Kefauver-Harris Amendment
- 1994: Dietary Supplement Health and Education Act (DSHEA)
- 2006: Dietary Supplement and Nonprescription Drug Consumer Protection Act
- June 22, 2007: New Dietary Supplement Current Good Manufacturing Practices (cGMPs) Final Rule Issued by FDA

DSHEA

- Signed into law on October 25, 1994
- Herbal supplements, vitamins and minerals considered dietary supplements not drugs
- Dietary ingredients in supplements no longer subject to pre-marketing safety evaluations
- Labeling criteria
  - Body structure and function claims
  - Cannot make therapeutic claims
  - Must state not approved by FDA
  - Must have manufacturer's name and address
  - Not required to have lot numbers, expiration dates or contraindications

Dietary Supplement and Nonprescription Drug Consumer Act

- Passed by Congress on 12/26/06; effective 12/26/07
- Known as the Adverse Event Reports Bill (S. 3546)
- Amends the Federal Food Drug and Cosmetic Act and requires manufacturers to report serious adverse events for OTC drugs and dietary supplements
- Requires manufacturers to submit report of adverse event within 15 business days of receipt
- Requires labels to have address or phone number so that patients can report serious adverse events

Herbs and Dietary Supplements

Fish Oils

- Can consume in diet through cold water fish that are high in omega-3 fatty acids or through other natural products like avocado or almonds (alpha-linolenic acid)
- Uses include treatment of high triglycerides, reduction in risk of death from heart disease, cognitive function
- Look for EPA and DHA as active ingredients
- FDA approved products: Lovaza, Vascepa, and Epanova

Fish Oils

- Summary of clinical studies:
  - Appears to reduce triglycerides by 20-50%
  - May decrease risk of coronary heart disease death by 25% in healthy patients
  - May decrease overall cardiac mortality and MI risk in secondary prevention 16-20%
  - No apparent benefits in patients with atrial fibrillation
  - Controversial study related to prostate cancer

Fish Oils

- Side effects include fish aftertaste, burping/belching, flatulence
- Important Drug Interactions
  - Contraceptives may decrease the triglyceride lowering effect of fish oils
  - May increase risk of bleeding with antiplatelets and anticoagulants with high dose fish oils
  - Orlistat decreases absorption of fish oils

Probiotics

- Available as bacteria:
  - Lactobacillis species (L. acidophilus, L. rhamnosus, L. bulgaricus, L. reuteri, L. casei)
  - Bifidobacterium species (B. infantis, B. breve, B. longum, B. lactus)
- Available as yeast: Saccharomyces boulardii
- Benefits of probiotics are strain specific

Probiotics

- Summary of clinical studies:
  - Acute infectious diarrhea
    - S. boulardii (Florastor®), Lactobacillus GG (Culturelle®), L. reuteri and some mixtures are most beneficial
  - May reduce risk of antibiotic associated diarrhea by ~50%
    - L. rhamnosus GG (Culturelle®), L. acidophilus and S. boulardii (Florastor®)
  - Irritable bowel syndrome (IBS)
    - B. infantis (Align®), B. animalis (Activia®) and a combination product (VSL#3) may reduce symptoms of IBS

Probiotics

- Side effects include mild abdominal discomfort, flutulence
- Important Drug Interactions:
  - Separate antibiotics by 2 hours with bacteria-based probiotics
  - Avoid yeast-based probiotics with antifungals
- Use caution with immunocompromised patients

Melatonin

- FDA approved products for use in blind children to reset circadian rhythm for sleep
- Often used for treating jet lag
- New studies showing benefits with young children and difficulty sleeping

Melatonin

- Summary of clinical studies:
  - Orphan drug status for circadian rhythm sleep disorders in blind patients
  - May be beneficial for sleep wake cycle disturbances
  - May be beneficial for jet lag
    - 0.3-5mg at bedtime
  - Possibly effective for insomnia, nicotine withdrawal and preoperative anxiety and sedation
  - May be helpful with benzodiazepine withdrawal
  - Limited studies with cluster headaches
    - 10mg daily

Melatonin

- Side effects include daytime drowsiness
- Important Drug Interactions:
  - Anticoagulants/antiplatelets
  - Hypoglycemic agents
  - Calcium channel blockers
  - Fluvoxamine

Coenzyme Q10

- Used widely in Japan and on some hospital formularies in US
- FDA approval for mitochondrial encephalopathy and Huntington's Disease
- Used in patients with congestive heart failure
  - May improve exercise tolerance
  - May improve symptoms and/or classification of heart failure severity

Coenzyme Q10

- Summary of clinical studies:
  - FDA approved products:
    - UbiQGel® - Orphan Drug Status for Mitochondrial encephalomyopathies
    - Ubiquinol ® – Orphan Drug Status for Huntington's disease
  - May have additive effects with conventional therapy on QOL and NYHA classification and symptoms of CHF
  - May have additive effects with antihypertensive agents
  - May help with migraine control
  - Unclear if beneficial in diabetes

Coenzyme Q10

- Generally a well tolerated medication
- Important Drug Interactions:
  - May have additive effects with anti-hypertensive agents
  - HMG Co-A reductase inhibitors may reduce CoQ10 levels
  - May reduce effects of warfarin

Echinacea

- Native to North America; used to be treatment of choice for upper respiratory infections (URI)
- Uses include prevention and treatment of upper respiratory infections and fungal infections and dermatological conditions
- Comes in many forms – angustifolia, purpurea and pallida

Echinacea

- Summary of clinical studies
  - Majority of studies find no benefits in prevention of URI
  - May be useful for decreasing symptom severity and duration of URI
  - 2012 Jawad et al study in Evidence-Based Complementary and Alternative Medicine
    - 755 patients in a 4 month study looking at E. purpurea for safety, efficacy, and prevention of common cold
    - No difference in adverse effects
    - Echinacea reduced number of cold episodes and cumulated episodes
    - Echinacea showed some antiviral properties
  - May be useful in combination with antifungal drugs – decreased rate of recurrence of infection by 76% with Spectazole

Echinacea

- Side effects include allergic reaction which can range from mild to anaphylactic reaction, unpleasant taste
- Important Drug Interactions:
  - May counteract the effect of immunosuppressants
  - Inhibits metabolism through CYP450 3A4 and 1A2

Kava

- Consumed as social drink in South Pacific
- Uses include anxiety, stress, insomnia
- Withdrawn from market in some European countries and Canada
- Concern due to risk of liver-related adverse effects, not considered safe for use

Kava

- Summary of clinical studies
  - Thought to be effective for anxiety
    - Appears to be as effective as low dose benzodiazepines
    - May take 1-8 weeks for efficacy
  - May be beneficial with withdrawal of benzodiazepines
  - Increase dose of kava over 1 week while withdrawing dose of benzodiazepine over 2 weeks
  - Not considered safe enough to recommend for any use currently

Kava

- Side effects include hepatotoxicity, unclear effect on cognitive function and concerns with long term, high dose, chronic use
  - Over 100 cases of liver damage including hepatitis, cirrhosis, fulminant liver failure
  - Theory of genetic component to ADRs with kava: poor metabolizers of CYP450 2D6 develop hepatotoxicity
- Important Drug Interactions:
  - Inhibits CYP 450 2D6, 2C6, 3A4, 1A2, 2C19
  - Use with CNS Depressants may increase risk of drowsiness and motor reflex depression
  - Hepatotoxic drugs may increase risk of liver damage

Integration into Practice: Role of the Health Care Provider

- Provide unbiased and knowledgeable information
- Be informed of safety and efficacy literature
- Focus on being an educator, partner, and supporter for the patient
- Be a liaison between patient and other health care providers

Integration into Practice: Role of the Health Care Provider

- **Be a willing participant in integrative medicine**
- **Promote personalized health care for patients**
- **Involve the patient in their own health care**