Safe Use of Dietary Supplements

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Objectives

• Discuss facts and fiction regarding supplements
• Appropriate sources of information
• Considerations when searching the internet
Basic Definitions

• Dietary supplements
  ▪ “… a product taken by mouth that contains a dietary ingredient intended to supplement the diet…”¹

• Dietary ingredients may include:
  ▪ Vitamins
  ▪ Minerals
  ▪ Herbs or botanicals
  ▪ Amino acids
  ▪ Other substances

¹http://cfsan.fda.gov/~dms/ds-oview.html
Epidemiology of Use

- National Center for Health Statistics
  - Data from NHANES (2003 to 2006)
  - 72 million; 44% - males 53% - females
  - Multivitamin/multimineral supplements most used – 33%
  - Botanicals – 14%
  - Amino acids – 4%

- Council for Responsible Nutrition, Natural Marketing Institute, Nutrition Business Journal have other statistics
  - CRN: 66% of US adults use supplements
  - NMI: 47%
  - NBJ: $26.1 billion/year industry ($93 billion by 2015 in global market)
Reasons for Use

• Baby boomers
• Interested not only in longevity but “wellness”
• Certain products used
  ▪ Supplements
  ▪ Multivitamins, multiminerals
  ▪ Probiotics
  ▪ Turmeric
• Disease modulation
  ▪ Omega 3 fatty acids ($5 billion/year)
    • Fish oil, krill, algae
    • Flax, chia
Why Be Cautious? Facts and Fiction

- Facts – Supplements contain active chemical constituents
  - Fiction: Supplements are “natural”
- Fact – Supplements may have disease interactions
  - Fiction: Supplements may be taken in any disease
- Fact – Supplements may cause adverse effects
  - Fiction: Unlike drugs, supplements do not cause side effects
- Fact – Supplements may interact with drugs or other supplements
  - Fiction: Supplements do not have drug interactions
Why Be Cautious? Facts and Fiction

• Facts – Study design for supplement trials often “flawed” and with low numbers; Surrogate markers often used
  - Fiction: Supplements are well studied

• Facts – Supplements are considered foods; few dose-ranging studies; impurities/undeclared ingredients
  - Fiction: Supplements are FDA-approved

• Facts – Takes time to remove DS from market
  - Fiction: FDA must remove DS from market immediately; report to *MedWatch (www.fda.gov/medwatch)
Supplements

• Does natural mean safe?
• Natural products contain pharmacologically active ingredients and thus one may see not only a pharmacologic effect but possibly side effects and drug interactions\(^1\)

\(^1\) http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/UCM420449.pdf
Reasons for Caution

- Product variability
- Adverse Effects\(^1,2\)
- Drug interactions\(^3,4\)
- Surgery precautions\(^5,6\)

1 Drug Safety 1997;17:342-56  
3 JAMA 1998;280:1569-75  
5 www.asahq.org/PublicEducation/herbal.html  
6 AORN J 1999;69:173-5,177-8,180-3
Other Reasons for Caution

• Recalls¹

• Illegally sold treatments²
  “Lowers your blood sugar naturally”
  “Replaces your diabetes medicine”

• Confusing labeling (mislabeled) and information³,⁴

² http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/UCM361807.pdf
⁴ Consumer Reports September 2012 “10 surprising dangers of vitamins and supplements”
Other Reasons for Caution

• Quality issues
  Ocean sources may be contaminated\(^1\)
  Animal origin products may be contaminated\(^2\)

Animal sources may transmit disease\(^2\)
Misidentification, mislabeling, adding other substances\(^3\)

\(^1\) JAMA 2000;284:1425-9
\(^2\) http://www.centerforfoodsafety.org/page285.cfm
Problematic Supplements?

- Weight loss products
- Body building products
- Men’s health products

- JAMA study: supplements recalled by FDA for containing banned substances (sibutramine, steroids, sildenafil, fluoxetine) back on the shelf 6 mo later

http://time.com/3554782/dietary-supplement-safety/
Supplements + Medications?

- Fish oil
  - In combination with antihypertensives = ↓↓ BP
  - OCPs attenuate TG lowering effect of fish oil
  - High doses of fish oil + ginkgo = possible bleeding
  - High doses of fish oil + high dose Vit E = possible bleeding

- Echinacea + prednisone
  - Interferes with drugs that suppress the immune system

- Melatonin
  - May ↓ clotting; so in combination with blood thinners = possible bruising
  - May ↑ BP; offsets possible benefits of antihypertensives
  - ↑↑ sedation with other sedating products (valerian, SJW)
Evaluating Internet Information

- How to evaluate information on the internet –
  http://www.fda.gov/Food/DietarySupplements/UsingDietarySupplements/ucm110567.htm#tips

- Ask these questions:
  - Who operates the website?
  - What is the purpose of the website? (Educate or sell products?)
  - What is the source of information? (Published studies/testimonials?)
  - Is the information current? (Date posted)
  - How reliable is the internet? (Easy way to spread myths, beware of overly emphatic language (ALL CAPS) or “This is not a hoax” or “Send this to everyone you know”)
• Examples of “suspect” statements:
  - “These are not medicines so taking these herbs in larger amounts or over a long period of time is not harmful”
  - “There are no ingredients available for this product”
  - To “determine dose for a child or pet, divide the weight by 150 and that determines the fraction of the adult dose”
Appropriate Patient References

• FDA websites
  ▪ Tips for the Dietary Supplement User
    http://www.fda.gov/Food/DietarySupplements/UsingDietarySupplements/ucm110567.htm
    - Do I need to think about my diet?
    - Should I check with my doctor?
    - Are there any interactions (supplements/meds)
    - What should I do if I am going to have surgery?
    - Who is responsible for safety of the products?
Appropriate Patient References

• FDA websites
  - Are there any risks because of my age?
  - Should I stop my regular medicines?
  - Should I check with my doctor?
  - Should I take the products in to checkups?
Appropriate Patient References

- FDA websites
  - MedWatch
    - www.fda.gov/medwatch
  - Problems with products listed
  - Reporting problems
Appropriate Patient References

• Read FDA 101: Dietary supplements
  http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/ucm050824.pdf
Appropriate References: Providers

- Natural Medicines Comprehensive Database (www.naturaldatabase.com)
  - Maintained by Pharmacist’s Letter/Prescriber’s Letter
  - Approximately 1100 ingredients reviewed in evidence-based monographs
  - Index containing over 38,000 brand names
  - Section on other alternative therapy modalities – acupuncture, balneotherapy, colonic irrigation, aromatherapy, shiatsu, reiki, etc.
  - USP-verified product names
  - References!!
Appropriate References:

Providers

• Natural Standard (www.naturalstandard.com)
  ■ Multidisciplinary research collaboration that uses evidence-based criteria to evaluate different products and enable decision-support
  ■ Excellent job of appraising original research on herbs/supplements
  ■ Monographs reviewed by Western-trained clinicians and CAM practitioners
  ■ Evidence grade
    • A – Strong positive scientific evidence
    • B – Positive scientific evidence
    • C – Unclear scientific evidence
    • D – Negative scientific evidence
    • F – Strong negative scientific evidence
Appropriate References:

Providers

• The Cochrane Collaboration – http://www.cochrane.org
  ▪ International organization providing up to date information about health care information interventions
  ▪ Cochrane Library has regularly updated databases and systematic reviews of different treatments
  ▪ Regularly updated evidence-based information

  ▪ Information for clinicians and the public
  ▪ Access information under “Research, Clinical Trials, Training, and Health Information”

• The Review of Natural Products
  ▪ Comprehensive chemistry, pharmacology, toxicology
Choosing an Appropriate Product

• Choose a reputable manufacturer – appropriate information on a label?
• Information about dietary supplements http://ods.od.nih.gov/
Choosing an Appropriate Product

• Ask yourself:
  § Is this too good to be true?
  § Think twice about chasing the latest headlines
  § Can you contact the manufacturer and what type of information is provided?

• Consider use of testing services
  § USP – http://www.usp.org
  § Consumer Lab – http://www.consumerlab.com
  § Natural Products Association – http://www.npainfo.org/
• A 48 y/o woman with type 2 DM and PCOS is on metformin and basal/bolus insulin, an ACEI/HCTZ and a calcium channel blocker for HTN, simvastatin for high cholesterol, warfarin post DVT, and sertraline for depression. She has high triglycerides, insulin resistance (↑ HOMA-IR), muscle aches, knee pain, ↓ energy.

• What supplements might be considered?
• Which supplements may interact with medications this person is taking?
• If the person decides to take any products, what should she be told?
Which Agents? Popular Products

- Cinnamon
- Ginseng
- Milk thistle
- St. John’s wort
- CoQ10
- Magnesium
- Turmeric
- Others
Cinnamon

- Active ingredient: Procyanidin type-A polymers (Cinnamaldehyde)
- Decreases fasting glucose and lipids
- May enhance insulin sensitivity
- May also delay gastric emptying; decrease PPG
- Side effects mostly benign
  - Hepatotoxicity?
- Contains coumarins
  - Caution with concomitant anticoagulants
- Most appropriate form: aqueous form?
Ginseng

- Side effects - ↑ BP, anxiety, insomnia
- Drug interactions – warfarin (↓ INR), attenuates effects of BP meds
- Other effects
  - Enhanced effects of polyvalent flu vaccine, ↓ colds/flu
  - Some benefits on “ED”
- Diabetes – modest benefit for PPG; only studied in type 2 DM
  - ↓ PPG, plasma insulin, improved insulin sensitivity
- Varying contents (Am J Clin Nutr 2001;73:1101-6)
  - Evaluation found quantities varied from less (12%) to more (137%) than indicated on the bottle
- American ginseng, no added benefit from > 3 g/day
- Take within 2 h of meal to avoid potential hypoglycemia
- Use: 2-week holiday q 2-3 weeks; others say limit use to 3 months (concerns about hormone-like effects)
Milk Thistle

• Background
  ▪ Aster family (daisies, thistles)
  ▪ Silymarin

• Mechanism
  ▪ Inhibits hepatotoxin binding
  ▪ Antioxidant
  ▪ Restores MDA levels (marker of oxidative stress)
  ▪ May benefit pts with insulin resistance secondary to hepatic damage

• Uses
  ▪ Hepatic disorders
  ▪ Hepatoprotectant
  ▪ Diabetes

• Side Effects
  ▪ GI, sweating, estrogenic effects

• Drug Interactions
  ▪ Beneficial interactions with hepatotoxins
  ▪ ↑ Cl of estrogens taken by mouth
  ▪ Inhibits CYP 2C9
Hippocrates/Galen: for “demonic possession”
Active ingredients: hyperforin, hypericin, quercetin
Inhibits neurotransmitter re-uptake
Preparations vary widely
Major/severe depression: inconsistent effects
Major drug interactions: Potent inducer of metabolism (CyA, HIV meds, warfarin, OCPs)
Pharmacodynamic interactions: Other antidepressants, SSRIs, sympathomimetics, narcotics
Turmeric

- *Curcuma longa* (curcumin)
  - Diferuloylmethane (polyphenol)
- GRAS status
- Arthritis, other inflammatory disorders
  - COX-2 inhibition
  - Inhibits PGs, leukotrienes, thromboxanes
- Cancer
  - Apoptosis of some cancer cell lines
  - Inhibits angiogenesis
- Diabetes (pre-diabetes)
- ADRs – GI, nephrolithiasis, ↓ BG
- Interactions: Antiplatelets
CoQ10

- Vitamin-like substance; ↑ ATP production; Scavenges OFRs; Membrane stabilizer
- Small studies have resulted in slight ↓ in FBG and A1C (NS)
- HF symptom improvement; may ↓ BP, improve angina, Parkinson’s, ↓ statin myopathy
- Long-term safety - 6 years
- Soybean oil formulation ↑ absorption

- Side effects
  - GI, rash, increased LFTs
- Drug interactions
  - Warfarin, statins, BP meds
  - Adriamycin® (less cardiac toxicity but less efficacy?)
- Some evidence for use in several diseases
- DM dose – 100-200 mg/day

Natural Medicines Comprehensive Database 13th ed.
Stockton, Calif., Therapeutic Research Faculty, 2013
Magnesium

• Highly used supplement
• DM pts consume fewer foods containing Mg – green, leafy vegetables, grains/nuts, meats, dairy products
• Many persons don’t meet RDA for Mg (320 mg/day for women, 420 mg/day for men)
• Many meds deplete Mg: diuretics, PPIs, beta-2 agonists
• May improve insulin resistance and ↓ fasting glucose in overweight, insulin resistant persons
• 15% risk reduction for T2DM with 100 mg/day of Mg
• May ↓ fasting glucose and ↑ HDL in T2DM
• Less neuropathy in T1DM
• Monitor renal function and potential drug interactions (may impair absorption of some antibiotics, Ca)
Turmeric

- *Curcuma longa* (curcumin)
  - Diferuloylmethane (polyphenol)
- GRAS status
- Arthritis, other inflammatory disorders
  - COX-2 inhibition
  - Inhibits PGs, leukotrienes, thromboxanes
- Cancer
  - Apoptosis of some cancer cell lines
  - Inhibits angiogenesis
- Diabetes
- Taken with fat or black pepper, easily absorbed, ↑ SDCs
- ADRs – GI, nephrolithiasis, ↓ BG
- Interactions: Antiplatelets
- 2000 mg/day in divided doses
A 48 y/o woman with type 2 DM and PCOS is on metformin and basal/bolus insulin, an ACEI/HCTZ and a calcium channel blocker for HTN, simvastatin for high cholesterol, warfarin post DVT, and sertraline for depression. She has high triglycerides, insulin resistance (↑ HOMA-IR), muscle aches, knee pain, ↓ energy.

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Supplement Use: Guiding Patients

- Determine why you want to use a supplement
- What are your goals for supplement – be specific
- Consider that products may cause side effects or drug interactions
- Select single-ingredient products
- Discuss use to determine appropriate length of treatment
  - Don’t stop or start without discussion since this may affect the other medications being taken
- Don’t stop taking your other medications
- Don’t share the products
- Consider that you must still eat healthy and exercise
Counseling Patients

- Providers must be respectful of patients beliefs
- Provide evidence-based information
- Discuss target goals, evidence (benefit or not?)
- Assess potential side effects; drug interactions
- Help evaluate whether brand is appropriate
- Emphasize role of conventional medications
- Be informed and supportive
QUESTIONS???