Safety of Dietary Supplements from a Clinical Pharmacology Perspective and What it Means to the U.S. Public

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Overview

- Definition of a dietary supplement and use of these agents by the American public.
- Dietary supplement regulation from a clinical pharmacology viewpoint.
- Safety of dietary supplements as clinical pharmacologists see it.
- Some suggestions as to how to improve supplement safety and efficacy.
Definition of a Dietary Supplement

- A product (other than tobacco) intended to supplement the diet.
- Contains one or more of the following ingredients.
  - Vitamin
  - Mineral
  - Herb or other botanical
  - An amino acid
  - Dietary substance that increases total dietary intake
Dietary Supplement Use in the United States

- At least 35% of adults utilize alternative and complementary medical approaches.
- Sales of dietary supplements in 2002 in excess of $18 billion.
- Widely used by potentially vulnerable populations including children, adolescents, and the elderly.
- Use has markedly increased since 1970’s.
Dietary Supplement Use in the United States

- Over 30,000 products currently available.
- Approximately 1000 new products introduced annually.
- It is the belief of consumers that dietary supplements are:
  - Subject to regulations similar to OTC drugs.
  - Have undergone extensive FDA review.
Regulation of Dietary Supplements

- Dietary Supplement Health and Education Act (DSHEA) of 1994.
  - Designed to protect the right of access of the consumer to dietary supplements to promote wellness.
  - Assumption is that a supplement is safe and is thus exempt from regulation as a food additive or drug.
    - Pre-marketing approval not required nor is a “generally recognized as safe” status.
    - Considered unsafe if it presents a significant risk of injury under conditions recommended or suggested for use.
Regulation of Dietary Supplements Under DSHEA

- FDA bears burden of proof to assert a supplement unsafe.
  - Supplements introduced after 1994 require a 75 day notification prior to marketing but FDA approval not required.
  - DSHEA assumes dietary supplements safe as claimed.

- These regulations severely limit regulation of supplement industry.

- Other countries have much more strict regulations.
Recent Concerns Regarding Supplement Safety Under DSHEA

- The ephedra episode and other concerns have led the FDA, various healthcare organizations, and Congress to propose changes to DSHEA to bolster supplement oversight.

- FDA strategies to enhance regulation regarding claims of safety and efficacy.
- Proposal for good manufacturing practices.
- IOM recommendations.
- Recommendations by other healthcare organizations.
- Congressional interest in tightening DSHEA.
Safety of Dietary Supplements

- Little definitive scientific evidence exists to prove safety of most agents.
- Many supplements contain active ingredients with the potential for serious adverse effects even at standard doses.
  - Ephedra-containing products contain ephedrine which is associated with significant cardiovascular effects that led to removal of these agents from the market. Associated with a number of deaths.
- Adverse events caused by dietary supplements can fall into three categories:
  - Toxicity-inherent side effects.
  - Interactions-dietary supplements with another supplement or drug.
  - Adulteration-contamination with other substances.
Clinical Pharmacology and Dietary Supplement Safety

- Most safety statements based on traditional experience which is generally not a scientifically reliable approach.
- Very little research has been undertaken regarding dietary supplement safety.
  - Not required.
  - No clear-cut funding sources.
  - View of the public is that agents are safe.
  - Inability to accurately gain information regarding adverse events related to supplements.
Role of the Clinical Pharmacologist in the Safety of Dietary Supplements

- Can play an important role with proper tools and support in evaluating the safety of dietary supplements.
  - Interpret adverse events.
  - Design clinical trials to assess safety and efficacy.
  - Evaluate data regarding evidence to assess risk/benefit of agents.
  - Provide education to other healthcare professionals regarding dietary supplements.
Selected Dietary Supplements Associated with Toxicities

- **Gingko**-headache, GI complaints, cerebral hemorrhage, seizures.
- **Ginseng**-hypertension, mania, sleep disorders.
- **St. John’s Wort**-dizziness, allergic skin reactions, sexual dysfunction, interference with drug metabolism.
- **Yohimbine**-anxiety, panic, mania, renal failure.
- **Kava kava**-liver failure, hepatitis, abnormal liver functions. Recently banned in some countries.
Some Recommendations Regarding Dietary Supplements to Improve Safety

◆ Improve detection of adverse events associated with dietary supplements.
  • Require reporting of adverse events by manufacturers and distributors.
  • Require safety and efficacy information pre-marketing.
  • Utilize the FDA to provide consumers with adverse event information.
Some Recommendations Regarding Dietary Supplements to Improve Safety

- Implement the FDA’s current good manufacturing practice for dietary supplements.
  - Conform to USP standards for active agent content.
  - Many studies have found great inconsistencies in amount of active ingredients in supplements despite claims.
  - Contaminants not uncommon.
Some Recommendations Regarding Dietary Supplements to Improve Safety

- Improve labeling templates for dietary supplements.
  - Are frequently inaccurate and misleading.
  - Include information regarding intended uses, safety, directions for use, and manufacturing information.
  - Contact information for manufacturer and distributor.
  - Adverse event reporting information.
Some Recommendations Regarding Dietary Supplements to Improve Safety

◆ Provide enhanced educational opportunities on dietary supplements to healthcare professionals and consumers.

• Safety of supplements assumed by public.
• Education in medical/pharmacy schools.
• Governmental websites containing information on supplements.
• Consumer information from healthcare professionals and the public.
• Regulation of advertising.
Some Recommendations Regarding Dietary Supplements to Improve Safety

◆ Enhance research opportunities on adverse effects and efficacy of dietary supplements.
  • Unlikely to occur via manufacturer.
  • NIH funds would be required.