American College of Medical Toxicology

ACMT Position Statement: Dietary Supplements

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Disclaimer

While individual practitioners may differ, this is the position of the College at the time written, after a review of the issue and pertinent literature.

Introduction

In 2004 the Practice Committee of American College of medical Toxicology (ACMT) composed a Position Statement on Dietary Supplements which was posted for member comment, edited, and published in the Journal of Medical Toxicology in 2006. This original Position Statement arose out of increased poison center calls about dietary supplements, a greater number of case reports of herbal toxicity and herb-drug interactions and surveys showing rapid growth of dietary supplement use among the lay public after passage of the Dietary Supplement and Health Education Act (DSHEA) in 1994. As well, the Eisenberg report in the American Medical Association (1998) stated that 42% of those surveyed used some alternative forms of medical therapy, increased from 34% in his 1991 survey. While the percentage of herbals was relatively low at 12% in 1998, this was dramatically increased from 2.5% in 1991.

Historically passage of the Food Drug & Cosmetics Act in 1938 “grandfathered” pre-existing plant-based drugs, such as atropine, codeine and morphine into approved use along with everything listed in the United States Pharmacopoeia-National Formulary. Herbals were exempted from registration as drugs following a review commissioned by the FDA (authorized by the Kefauver-Harris amendments in 1962) and by the National Academy of Sciences. In 1994 DSHEA designated the US Food and Drug Administration’s (FDA’s) Center for Food Safety and Applied Nutrition (CFSAN) with responsibility for developing regulations for dietary supplements, which include amino acids, biological extracts, herbals, minerals and vitamins. In 1995, a National Center for Complementary and Alternative Medicine was established at the US National institute of Health with a growing budget for sponsored research. Then in May, 1998, the dietary supplement branch of CFSAN published a container-labeling requirement; and, a 10-year plan was issued in January, 2000, for the total regulation of dietary supplements.

Demonstrating enforcement powers, since the original position statement, the FDA later in 2004 took dramatic action to remove ephedra-containing dietary supplements from the market in response to reports of cardiovascular risks of cardiac arrhythmias. And, in May, 2006, based on reports of hepatotoxicity in Europe, a warning was issued on kava. More recently in 2007, FDA has issued guidance directives on filing serious adverse event reports for both dietary

supplements and over-the-counter products as well as Good Manufacturing Practices for dietary supplements; and, a pathway has been established in the Center for Drug Evaluation and Research for bringing botanical substances to market as drugs with approval of a green tea extract for the treatment of genital warts. There are also three trade organizations, including the American Herbal Products Association and the Council for Responsible Nutrition, which self-regulate members according to established codes of ethics.

Applying principles of evidence-based medical practice to dietary supplements, as well as educating health professionals and the lay public concerning hazards associated with their use is vitally important. Among the concerns of the American College of Medical Toxicology is that patients may choose dietary supplements rather than pharmaceutical agents that are established to be safe and effective. Although there may be case-control study data that demonstrates varying degrees of therapeutic effectiveness of single agents such as ginger, St. John's wort, saw palmetto and ginkgo biloba, there are also multi-ingredient herbal preparations such as those from Traditional Chinese Medicine and of Ayurvedic (Indian subcontinent) origin that can introduce significant confounding issues into this type of risk to benefit analysis. In this regard, medical toxicology is primarily focused on the risk of harm to human health related to recommended use as well as overdose of these preparations and adverse interactions with other agents including pharmaceuticals, rather than their therapeutic effectiveness.

Direct Harm

Aside from single agent toxicity of the marketed preparation, toxicity from contamination/ adulteration of the source product with heavy metals, such as lead and arsenic, has been, as well as misidentified plant material being substituted for the botanical agent that is, thus, falsely identified as present in that product. In addition, the inclusion of pharmaceuticals such as butazolidine in antiarthritics and benzodiazepines in calmatives has occurred in preparations purported to be nonpharmaceutical dietary supplements.

There were certain naturally-occurring substances withdrawn due to hepatotoxicity by the time of the original position statement, such as comfrey tea, chaparral and pennyroyal. There have also been reports that some ingredients in supplements are potential central nervous system toxicants. These include henbane, imson weed and mandrake. In addition, there have also been reports that chan su, foxglove, oleander and squill may be cardiovascular toxicants. Commercially available dietary supplements can also be abused with adverse effects, such as the gastrointestinal use of aloe, buckthorn, cascara, pokeweed and senna for dyspepsia and constipation, where systemic electrolyte deficits and other problems can occur. This can result in secondary complications from concurrent use of prescription medications, such as cardiac drugs and diuretics.

Potentially Harmful Interactions

Reports of herb-drug interactions with the 6 isomers in ephedra-containing Ma huang have led to the FDA s withdrawal of herbal ephedra from the market, with the exception of their use in

traditional Chinese medicines. Other herbal supplements with adverse interaction potential include St. John's wort through its induction of CYP 3A4-mediated metabolism of antiretroviral drugs and oral contraceptives, as well as its associated risk of serotonin syndrome if combined with drugs that inhibit postsynaptic serotonin reuptake (e.g., sertraline, trazodone, nefazodone). Ongoing collection of reports from the FDA's MedWatch system at www.fda.gov/medwatch and the American Association of Poison Control Centers surveillance system helps update this information.

Conclusions

Dietary supplement use has become increasingly common with the implementation of the DSHEA in 1994. The National Center for Complementary and Alternative Medicine at NIH is sponsoring clinical trials which have prompted as well as answered questions. Clinicians not only need to specifically ask for dietary supplement histories, but be aware of the potential for product contamination and misidentification of the ingredients therein, as well as herb-drug interactions. The American College of Medical Toxicology strongly recommends consultation with a medical toxicologist in cases of suspected or confirmed toxicity, adverse effects or interactions from dietary supplements, and other issues relating to product safety. In addition to establishing requirements for "Supplement Facts" label information on dietary supplement bottles marketed in the US, FDA has taken regulatory action to withdraw ephedra-containing supplements and is instituting Good Manufacturing Practices. The ACMT strongly supports further review and regulation, as well as augmentation of clinical education and scientific information and enhanced awareness of potential harm from dietary supplement use.

Disclosure

This statement has been developed by members of the ACMT with principal contribution in writing by Tom Kurt, MD, reviewed and approved by the ACMT Practice Committee and Board of Directors, and opened to comment by all members of the College. Disclosure statements for participating members of the ACMT Practice Committee and ACMT Board of Directors will be available soon.

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Weblinks

The Federal Drug Administration at www.fda.gov