Date: October 15, 2003

RE: Review of Adverse Events Associated with Dietary Supplements


Adverse events associated with the use of dietary supplements are not well monitored in the United States. As of January 2002, there were 29,000 dietary supplements on the U.S. market. Dietary supplements are defined in the 1994 U.S. Dietary Supplement Health and Education Act as "orally ingested foods that include botanical products (such as herbal remedies), and non-botanical substances (such as glands, minerals, metalloids, amino acids, vitamins, and microbial products), and traditional cultural remedies, including Asian herbal prescription medicines." The objective of this study was to collect information on adverse events associated with dietary supplement use and to qualitatively assess the assumption that foods that are safe and free from adulteration are not associated with moderate to severe outcomes, including death.

The authors conducted a one-year multicenter, observational study (from January 1 to December 31, 1998) of dietary supplement exposures reported to 14 poison control centers in the United States. Non-botanical and botanical ingredients were included in the analysis, as were ß-hydroxybutyrate (GHB) precursor products. The dietary supplements identified in the calls were identified by using specific names from two herbalist sources. The poison control specialists at these centers obtained information for the Toxic Exposure Surveillance System (TESS), which has a predefined hierarchy for organ systems. The authors used five reference sources (a commercial database used by the U.S. poison control centers, a European monograph series [i.e. ABC's The Complete German Commission E Monographs], and three industry sources [including the American Herbal Products Association's Botanical Safety Handbook]) to search for the most frequently recorded dietary supplements in the reports. Categories of symptom severity and outcome based on the TESS database were used to describe the exposure to the dietary supplements as mild,
moderate, or severe. Deaths were included only if they were directly caused by the exposure. The authors used a multtiered review process to assign probable cause scores to the exposures. The Mantel-Haenszel test for trend was used to calculate p-values (i.e. statistical significance) for outcome categories (mild, moderate, severe exposure, or death), short-versus long-term ingestion, and single-ingredient versus multiple-ingredient doses. Mean numbers of ingredients or symptoms were compared with student's t test. (Student's t-test, often known simply as the t-test, is one of the most commonly used of all statistical tests. It comes in two versions: the paired t-test and the unpaired t-test. Both types are used to test the hypothesis that some variable differs between two groups, but the paired test is specifically used when each data point in one group corresponds to a matching data point in the other group.)

Eleven poison control centers completed the study; three centers withdrew, but their data were retained. Of the 2,991 calls to the poison control centers, 2,332 were about dietary supplements. Of these 2,332 calls, 1,466 were about the ingestion of dietary supplements (725 asymptomatic and 741 symptomatic). The botanical substances most frequently associated with adverse events were ephedra (a.k.a. ma huang; Ephedra sinica), guarana (Paullinia cupana), "ginseng" (presumably Panax spp.) and St. John's wort (Hypericum perforatum); the respective non-botanical supplements were chromium, melatonin, and zinc. Thirty-one percent of the adverse events were of moderate or worse severity. Compared with short-term use, long-term use was associated with outcomes of greater severity and with a higher frequency of moderate and severe outcomes (p < 0.0001). Dietary supplements composed of multiple ingredients appeared to be associated with a larger number of symptoms and with more severe symptoms. The symptoms reported included chest pain, dyspnea (shortness of breath), coma, seizures, liver failure, and myocardial infarction. The severity of the reported adverse effects increased with age.

The reliability of the results was limited by many factors. For example, recording practices varied between the poison control centers; selection bias and under-reporting were suspected as well. The absence of a comprehensive register of dietary supplements, product labeling regulations, and mandatory reporting regulations limited the reliability of the data also. However, it was concluded that some dietary supplements have the potential to be substantially hazardous. The findings suggest "the need for a comprehensive register of dietary supplements, strengthened surveillance (particularly mandatory reporting of adverse events), enforceable definitions of what constitutes a risk to safety, and what circumstances warrant product recall." In addition, research into the safety of dietary supplements to identify possible risks should be a priority, according to the authors.

—Brenda Milot, ELS

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