Beverage Science Update

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National Cancer Institute Finds Aspartame-sweetened Beverages Do Not Raise Leukemia, Lymphoma or Brain Cancer Risk in Humans

Large Human Study Reaffirms Aspartame Safety

A new epidemiology study from the National Cancer Institute confirms previous study conclusions that there is no link between the consumption of aspartame-containing beverages and leukemias, lymphomas or brain tumors. The study, which appears in the September 2006 issue of *Cancer Epidemiology Biomarkers Prevention*, evaluated nearly 500,000 men and women between the ages of 50 and 71 over a five-year period.

According to the NCI researchers, the study was designed to specifically determine whether humans who consumed diet soft drinks and other beverages sweetened with aspartame were at greater risk of developing brain cancers, lymphomas or leukemias. Although a few animal studies have found an increase in the risk of these or other cancers with aspartame consumption, most have not. However, concern has lingered because data on humans has been sparse.

The study found no evidence of an increased risk of leukemia, lymphomas or brain tumors among the study participants who reported drinking aspartame-containing beverages at the start of the study when compared with those who reported never drinking these beverages. The researchers report, "Our prospective epidemiologic study suggests that aspartame consumption derived from its main source, aspartame-containing beverages, does not raise the risk of hematopoietic or brain malignancies."

The study findings confirm the findings of a recent 2005 report, *Review of Lymphatic and Hematopoietic Cancer Incidence Trends & Consumption of Aspartame,* in which researchers concluded, upon examining cancer trends from the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) program there is no consistent pattern (of leukemias or lymphomas) that parallels the rise in aspartame consumption. Further, the findings also support those of three recent animal studies conducted by the National Toxicology Program (NTP) designed to evaluate whether aspartame is capable of causing cancer. These U.S. government-funded and managed studies were conducted using Good Laboratory Practices (GLP). The results of these cancer studies, in which aspartame was fed to mice bred to be especially sensitive to cancer-causing agents, unequivocally indicated that "there was no evidence of carcinogenic activity [cancer] of aspartame."

About the Study

The NCI researchers asked 285,079 men and 188,905 women ages 50 to 71 participating in an NIH-AAPR Diet and Health study to report the amount of diet beverages they drank, including sodas, fruit drinks and iced teas, and whether they added aspartame to their coffee or tea. Their responses were used to calculate how much aspartame consumed on a daily basis.

Later, during the study's 5-year follow-up, the researchers collected cancer data from the group and found 1888 had developed leukemia and 315 had developed brain cancer. These rates were comparable to the incidence of these cancers in the general US population. They then looked at the daily aspartame consumption data collected at the start of the study for those who developed these cancers versus those who remained cancer-free.

The researchers found that participants who had reported consuming aspartame-containing beverages at the beginning of the study were no more likely to have developed these cancers five years later than were their aspartame-abstaining counterparts. The researchers also noted that a more detailed categorization of aspartame intake showed no increase in cancer risk at even the higher level of reported intake. As a result, the researchers state, "Our prospective epidemiologic study suggests that aspartame consumption derived from its main source, aspartame-containing beverages, does not raise the risk of hematopoietic or brain malignancies."

An abstract of the study appears at the end of this article.

Assessment

- This NCI study was a long-term case-controlled observational epidemiologic study that collected pairs of data -- aspartame intake at the start of the study and cancer incidence 5 years later -- from a large number of individuals.
    - This study compared the aspartame-containing beverage consumption and cancer incidence of each individual in the study. As a result, the researchers were able to determine that those who consumed up to 600 milligrams of aspartame a day through beverages did not develop hematopoietic or brain malignancies at a higher rate than those who did not drink aspartame-sweetened beverages. 600 milligrams of aspartame is about the amount found in 3 cans of a diet soft drink.
    - The study's large size allowed the researchers to look for associations between aspartame-containing beverage consumption and several rare forms of cancer, including non-Hodgkins lymphoma. No association was found.
    - The NCI researchers also commented that the study relied on individuals to accurately recall their aspartame-containing beverage consumption habits for the previous year, making the data subject to 'recall bias.' However, the researchers noted that the questionnaire used was validated against two

24-hour recalls, indicating that it is of similar high quality to other questionnaires used in prospective cohort studies in the U.S. The researchers also note that very few participants consumed high amounts of aspartame (1200 mg/day), which made assessment regarding cancer risk and high consumption rates not possible.

- The authors also noted the relevant published scientific studies that either raised or refuted the aspartame - cancer link hypothesis, including:
  - An ecological study published in 1996 that first raised concerns over aspartame and brain cancer risk. According to the NCI researchers, that study made an association between an observed rise in brain tumors in the U.S. from 1975 to 1991 and the introduction of aspartame into the U.S. food supply in 1981 and was subsequently criticized in the scientific literature for committing 'ecological fallacy', "wherein the temporal coincidence of two events observed at an ecological level without examination of individual data can lead to faulty conclusions regarding risk association." That study did not collect data on the aspartame intake of those who developed tumors.
  - Three recent extensive animal trials that failed to show an association between cancer and aspartame.
  - A case-controlled epidemiological study that found no association between childhood brain tumors and aspartame intake of children or of their mothers during pregnancy and lactation.
  - A recent large rat study conducted by the Ramazzini Institute in Italy. According to the NCI researcher, that study's results, which found female rats fed aspartame at levels lower than the acceptable intake levels established by the FDA developed more leukemias and lymphomas than controls, were subsequently dismissed by the European Food Safety Authority for several reasons, including an unusually high incidence of chronic inflammatory in the rat population studied and no indication that there was a dose-dependent response.

ABSTRACT:

Consumption of aspartame-containing beverages and incidence of hematopoietic and brain malignancies. Lim U, Subar AF, Mouw T, Hartge P, Morton LM, Stolzenberg-Solomon R, Campbell D, Hollenbeck AR, Schatzkin A.

Cancer Epidemiol Biomarkers Prev. 2006 Sep;15(9):1654-9

BACKGROUND: In a few animal experiments, aspartame has been linked to hematopoietic and brain cancers. Most animal studies have found no increase in the risk of these or other cancers. Data on humans are sparse for either cancer. Concern lingers regarding this widely used artificial sweetener. OBJECTIVE: We investigated prospectively whether aspartame consumption is associated with the risk of hematopoietic cancers or gliomas (malignant brain cancer). METHODS: We examined 285,079 men and 188,905 women ages 50 to 71 years in the NIH-AARP Diet and Health Study cohort. Daily aspartame intake was derived from responses to a baseline self-administered food frequency questionnaire that queried consumption of four aspartame-containing beverages (soda, fruit drinks, sweetened iced tea, and aspartame added to hot coffee and tea) during the past year. Histologically confirmed incident cancers were identified from eight state cancer registries. Multivariable-adjusted relative risks (RR) and 95% confidence intervals (CI) were estimated using Cox proportional hazards regression that adjusted for age, sex, ethnicity, body mass index, and history of diabetes. RESULTS: During over 5 years of follow-up (1995-2000), 1,888 hematopoietic cancers and 315 malignant gliomas were ascertained. Higher levels of aspartame intake were not associated with the risk of overall hematopoietic cancer (RR for >/=600 mg/d, 0.98; 95% CI, 0.76-1.27), glioma (RR for >/=400 mg/d, 0.73; 95% CI, 0.46-1.15; P for inverse linear trend = 0.05), or their subtypes in men and women. CONCLUSIONS: Our findings do not support the hypothesis that aspartame increases hematopoietic or brain cancer risk.
