Life-Span Exposure to Low Doses of Aspartame Beginning during Prenatal

Life Increases Cancer Effects in Rats

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FROM ABSTRACT:

BACKGROUND: In a previous study conducted at the Cesare Maltoni Cancer Research Center of the European Ramazzini Foundation (CMCRC/ERF), we demonstrated for the first time that aspartame (APM) is a multipotent carcinogenic agent when various doses are administered with feed to rats from 8 weeks of age throughout the life span.

OBJECTIVE: The aim of this second study is to better quantify the carcinogenic risk of APM, beginning treatment during fetal life.

METHODS: We studied groups of 70□95 male and female rats administered APM

(2,000, 400, or 0 ppm) with feed from the 12th day of fetal life until natural death.

RESULTS: Our results show

a) a significant dose-related increase of malignant tumor□bearing animals in males, particularly in the group treated with 2,000 ppm aspartame

b) a significant increase in incidence of lymphomas/leukemias in males treated with 2,000 ppm and a significant dose-related increase in incidence of lymphomas/leukemias in females, particularly in the 2,000-ppm group

c) a significant dose-related increase in incidence of mammary cancer in females, particularly in the 2,000-ppm group

CONCLUSIONS: The results of this carcinogenicity bioassay confirm and reinforce the first experimental demonstration of aspartame□s multipotential carcinogenicity at a dose level close to the acceptable daily intake for humans.

Furthermore, the study demonstrates that when life-span exposure to aspartame begins during fetal life, its carcinogenic effects are increased.

THESE AUTHORS ALSO NOTE:

□Aspartame is one of the most widely used artificial sweeteners in the world.□

Aspartame was approved by the U.S. Food and Drug Administration in 1981.

□Aspartame is now present in more than 6,000 consumer packaged goods and in nearly 500 pharmaceutical products, including children□s medicines.□

In the US, more than 70% of aspartame sales are attributed to soft drinks.

□The acceptable daily intake (ADI) of aspartame is currently 50 mg/kg body weight (bw) in the United States and 40 mg/kg bw in the European Union for both children and adults.□

Daily consumption of artificial sweeteners by women of childbearing age and by children is about 2.5□5.0 mg/kg bw.

Aspartame is metabolized in the gastric tract to its three constituents:

1) aspartic acid

2) phenylalanine

3) methanol

The methanol is transformed into formaldehyde and then to formic acid.
[Important]

Studies that demonstrate that aspartame is not genotoxic or carcinogenic in animals are flawed because:

□In our opinion, the small number of animals used per sex and per group and the termination of these experiments after 110 weeks of age, rather than observing animals over their life span, represent limiting factors when evaluating the carcinogenic risk or safety of artificial sweeteners such as aspartame.□

These authors designed and performed a mega-experiment using seven groups of rats (100□150 per sex per group) treated with aspartame in feed at various dose levels (including one very close to the ADI for humans), from 8 weeks of age until natural death.

□The study demonstrated for the first time that aspartame is a multipotential carcinogenic agent, capable of inducing, in our experimental conditions

a) a significant, dose-related increased incidence of malignant tumor□bearing animals in males and in females, particularly in females treated at 50,000 ppm

b) a significant dose-related increase in lymphomas/leukemias in both males and females, particularly in females treated at doses of 100,000, 50,000, 10,000, 2,000, or 400 ppm

c) a significant, dose-related increased incidence of transitional cell carcinomas of the renal pelvis and ureter and their precursors (dysplasias) in females treated at 100,000, 50,000, 10,000, 2,000, or 400 ppm

d) a significant, dose-related increased incidence of malignant schwannomas of peripheral nerves in males .☐

In this study, the rats were exposed to aspartame during fetal life in the feed of their mothers from the 12th day of pregnancy. Control animals received the same feed without aspartame. All animals were kept under observation until natural death. Upon death, all animals underwent complete necropsy.

RESULTS

☐The incidence of malignant tumor☐bearing animals occurred with a significant, dose-related increase in males.☐

☐The incidence of malignant tumors was significantly increased in males treated with 2,000 ppm aspartame compared with controls.☐

☐A numeric increase of the incidence of animals bearing malignant tumors was also observed among females exposed to 2,000 ppm aspartame compared with controls.☐

DISCUSSION

☐In our first mega-experiment, we demonstrated for the first time that aspartame is a multipotential carcinogenic agent inducing, among other cancers, a dose-related, significant increase in lymphomas/leukemias in females.☐

In the present study, ☐we again confirmed that aspartame induces carcinogenic effects.☐

□When comparing life-span exposure beginning during prenatal and postnatal life, we have shown that prenatal exposure to aspartame clearly increases the incidence of lymphomas/ leukemias in females.□

□When comparing the cumulative prevalence by age of death of animals with

hemolymphoreticular neoplasias, it is clear that prenatal exposure to aspartame also accelerates the insurgence of these lesions in females.□

The two epidemiologic studies that found no relationship to aspartame and incident cancers are flawed because:

□Both studies consider the eating habits of a large population of males and females 50□70 years of age in the 1990s. Given the time frame of these surveys and the commercialization of aspartame in the 1980s, the subjects□ potential use of the sweetener could not have exceeded 10□15 years. It is difficult to believe that this limited adult period of exposure to aspartame could confirm or exclude a potential carcinogenic risk. The design of these studies underlines the importance of conducting an epidemiologic study in which exposure to aspartame is monitored beginning in fetal life, particularly given the use of products containing aspartame by children and women of child-bearing age.□

CONCLUSIONS

□The results of this study, our second longterm carcinogenicity bioassay on aspartame, not only confirm but also reinforce our first experimental demonstration of aspartame□s multipotental carcinogenicity at a dose level close to the human acceptable daily intake.□

□Furthermore, the study demonstrates that when life-span exposure to aspartame begins during fetal life, its carcinogenic effects are increased.□

□On the basis of the present findings, we believe that a review of the current

regulations governing the use of aspartame cannot be delayed. This review is particularly urgent with regard to aspartame-containing beverages, which are heavily consumed by children.☐

KEY POINTS

1) In a previous study, these authors demonstrated that aspartame is a multipotent carcinogenic agent when fed to rats from 8 weeks of age throughout the life span.

2) This study shows that when exposure to aspartame begins in fetal life, there is a significant dose-related increase of malignant tumors, in incidence of lymphomas/leukemias, and in the incidence of mammary cancer.

3) ☐The results of this carcinogenicity bioassay confirm and reinforce the first experimental demonstration of aspartame☐s multipotential carcinogenicity at a dose level close to the acceptable daily intake for humans.☐

4) ☐When life-span exposure to aspartame begins during fetal life, its carcinogenic effects are increased.☐

5) ☐Aspartame (APM) is one of the most widely used artificial sweeteners in the world.☐

6) ☐Aspartame is now present in more than 6,000 consumer packaged goods and in nearly 500 pharmaceutical products, including children☐s medicines.☐

7) In the US, more than 70% of aspartame sales are attributed to soft drinks.

8) Aspartame is metabolized in the gastric tract to its three constituents:

aspartic acid, phenylalanine, and methanol, which is transformed into formaldehyde and then to formic acid.

9) ☐The results of this study, our second long-term carcinogenicity bioassay on aspartame, not only confirm but also reinforce our first experimental demonstration of aspartame☐s multipotental carcinogenicity at a dose level close to the human acceptable daily intake.☐

10) ☐Furthermore, the study demonstrates that when life-span exposure to aspartame begins during fetal life, its carcinogenic effects are increased.☐

11) ☐On the basis of the present findings, we believe that a review of the current regulations governing the use of aspartame cannot be delayed. This review is particularly urgent with regard to aspartame-containing beverages, which are heavily consumed by children.☐

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