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SHORT REPORT

Artificial Sweetener Use and One-Year Weight Change among Women

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Weight change over a 1-year period was examined in a highly homogeneous group of 78,694 women ages 50–69 enrolled in a prospective mortality study. Artificial sweetener usage increased with relative weight and decreased with age. Users were significantly more likely than nonusers to gain weight, regardless of initial weight. Average weight gains or losses by artificial sweetener users differed by less than 2 pounds from gains or losses among nonusers. These results were not explicable by differences in food consumption patterns. The data do not support the hypothesis that long-term artificial sweetener use either helps weight loss or prevents weight gain.

INTRODUCTION

Artificial sweeteners (AS) rank among the most controversial of food additives. Saccharin, the most widespread AS in current use, is an acknowledged bladder carcinogen in multigenerational feeding studies of rats (1, 6, 23), and is permitted in foods in the United States only through a specific law. Aspartame, a sweetener that has recently replaced saccharin in a number of consumer products, is not known to be hazardous to most persons but may pose a problem to those with phenylketonuria, as phenylalanine is one of its decomposition products (7, 24). A committee of the National Research Council has recently found that cyclamate, which was banned by the Food and Drug Administration in 1969, is not a carcinogen by itself, but may possess tumor-promoting activity in the urinary bladder of rodents (5).

Epidemiologic studies of the relationship between artificial sweeteners and bladder cancer have been largely negative (8, 10, 14, 15, 17, 18, 22, 25, 26), with two exceptions (9, 13, 16). However, the widespread use of AS, particularly in diet beverages, is a relatively recent event, compared with the latency period of most cancers. Furthermore, most case–control studies were designed to examine bladder cancer only, so that little information is available about cancer risk at sites other than the bladder (5).

It has been argued that the possible risks of AS may be outweighed by potential health benefits, such as weight control, diabetes management, and prevention of dental caries. Excessive weight is a risk factor for heart disease, cancer, and other diseases (11); safe and effective methods of weight loss would obviously be of value, but the possible role of AS in such methods is uncertain. A National Academy of Sciences report asserted that "it has not yet been established whether saccharin leads to measurable health benefits" (4). In particular, efficacy

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of AS either in promoting weight loss in the obese or in preventing weight gain in others has not been established (20).

Very few clinical studies of AS efficacy have been conducted. A 1956 study by McCann of 147 obesity clinic patients found no significant difference in AS use between those who lost weight and those who gained weight or stayed the same over a 3-year period (12). Recently, Porikos and Van Itallie studied 13 obese and 11 nonobese volunteers housed on a metabolic ward for 15–30 days, with close monitoring of food consumption, weight, and energy output. When aspartame was covertly substituted for sucrose, the subjects stabilized their energy intake at 85% of baseline after about 12 days. It was concluded that "low-calorie food analogs can offer an effective new approach to dieting" (19). It can be seen, however, that both studies involved small numbers of subjects; the former provided no information on nonobese individuals, and the latter covered an extremely short period of intense observation.

While it would be highly desirable to perform more extensive studies of this type, their great cost makes future large-scale clinical efficacy studies unlikely. However, observational studies may provide useful information, particularly when they contain sufficient numbers of subjects and variables to control important sources of bias and confounding. We present here data from a recently begun cohort mortality study in which information gathered at baseline made it possible to analyze the relationship between past AS use and weight change over the 1-year period prior to enrollment.

METHODS AND MATERIALS

In September 1982, 77,437 American Cancer Society volunteers enrolled 1.2 million men and women from all 50 states, the District of Columbia, and Puerto Rico in a prospective mortality study. The subjects were not selected at random, but were persons over 30 years of age whom the volunteers knew well enough to keep track of for at least the 6-year study period. Follow-up is to be done biennially through 1988. Subjects filled out the questionnaires by themselves and returned them to the volunteers in sealed, confidential envelopes.

Among the questions asked at baseline were age, current weight, weight 1 year ago, height, whether a major change in diet took place within the past 10 years, and the following question: "Do you now or have you ever added artificial sweeteners (saccharin or cyclamates) to coffee, tea, or other drinks or food?" Choices were: yes, currently; formerly; never. The next question was "If ever used artificial sweeteners, indicate amount per day and for how long," with separate space to record packets, drops, and tablets. Also asked were quantity and duration of both current and former use of diet soda and diet iced tea.

Patterns of food consumption were assessed by asking consumption frequency (days per week) of each of 28 food items, including beef, poultry, specific fruits and vegetables, breads, and potatoes, among others. Self-administered food-frequency questionnaires are generally deemed useful and valid for broad epidemiological classification purposes (3). They have been shown, for example, to give distributions of vitamin A similar to 24-hr food recalls administered by certified

nutritionists (21). Foods specifically containing AS were not included on the list, but these are minor sources of AS (10).

As previously reported by Wynder and Stellman (26), AS use was associated with numerous potentially confounding variables, such as sex, age, socioeconomic status, cigarette smoking, history of chronic diseases (such as diabetes and heart disease), and current weight. Rather than attempt to adjust for a multitude of factors, the large study population made it feasible to restrict the analysis to a homogeneous subgroup representing the majority having each trait. Analysis has therefore been confined to white women, ages 50–69, with at least a high school education, and with no history of diabetes, heart disease, or cancer, conditions that may affect both weight and dietary behavior (including AS usage). We further excluded those who said their diet had undergone a major change in the past 10 years, which in itself might have led to weight change. Since smoking cessation is associated with weight gain (2), we included only lifelong nonsmokers, and current and former smokers whose smoking status had not changed for at least 5 years. Finally, because the strongest correlate of AS consumption is weight itself, all analyses are stratified by initial relative weight, computed as the quetelet index (QI = weight/height^2), and data are reported separately for five strata of QI.[1]

The study was also restricted to those either who had never used AS or who were long-term current users, defined as those who answered "yes, currently" to the usage question and who had used packets, tablets, drops, and diet beverages for at least 10 years. Former AS users were excluded.

RESULTS

A total of 78,694 women out of the original cohort of 685,748 women met these restrictions. There were 17,016 long-term AS users (21.6%) and 61,678 nonusers. Subjects were classified according to approximate quintiles of QI in this subsample.

Age-specific AS usage is plotted against relative weight in Fig. 1. The overall proportion of AS users increased with QI from 12.9% in the lowest quintile to 29.8% in the highest. In each age group, AS usage increased monotonically with relative weight; it decreased monotonically with increasing age at each relative weight level.

There were no significant differences between the age-adjusted percentages of AS users and nonusers who lost weight at any initial relative weight level, as shown in Fig. 2. However, the rate of weight gain in AS users was significantly greater than in nonusers irrespective of initial relative weight, the difference ranging from 2.7% in the leanest quintile ($P = 0.008$) to 9.1% in the next to most obese ($P < 0.0001$). Furthermore, the proportion of AS users who gained 10 pounds or more was significantly greater than the proportion of nonusers who gained 10 pounds or more at each weight level. The same effect was observed

[1] QI in British units of lb/in.^{2} can be converted to metric units of kg/m^2 by multiplying by 703.07.

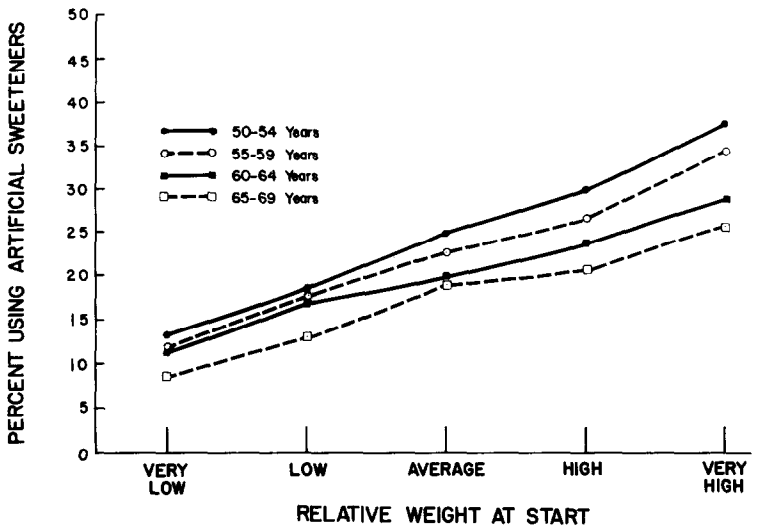

FIG. 1. Variation of artificial sweetener use with age and relative weight (defined in Table 1), among 78,694 white women ages 50–69 years. All women had at least a high school education, had no history of heart disease, cancer, or diabetes, and did not experience a major change in either diet or smoking habit during the preceding 10 years. Use of artificial sweeteners means current use of at least 10 years' duration in any form, including tabletop sweeteners and diet beverages.

when percentage of, instead of absolute, weight change was used: the proportion of AS users whose weight increased by at least 16% (highest quintile of relative weight change) was significantly greater than the corresponding proportion of nonusers at every level of initial QI.

The proportion of AS users who lost 10 pounds or more was not significantly different from that of nonusers, except among the most obese, where 2.0% more users than nonusers lost at least 10 pounds ($P < 0.001$).

Among those women who gained weight, AS users, on average, gained significantly more weight than did nonusers, regardless of initial QI ($P < 0.001$); differences in gains between users and nonusers ranged from 0.6 to 1.5 pounds (Table 1). Among women who lost weight, there were no differences in weight loss between AS users and nonusers of average QI or less. However, AS users in the two heaviest groups lost an average of 0.7 to 1.4 pounds more than did nonusers in the same categories ($P < 0.001$). These differences in average weight gains and losses, though statistically significant because of the very large sample size, are minor and may be of little biological or health importance.

To investigate whether AS users and nonusers had markedly different patterns of food consumption which might explain the observed weight changes, we compared the frequency of consumption of a number of food items by AS users with that by nonusers. There were no differences in the mean number of times per week AS users reported eating beef, pork, liver, ham, smoked meats, franks or sausages, carrots, squash, citrus fruits or juices, cereal or oatmeal, ice cream, or chocolate. Differences in food consumption were confined to a small number of items. AS users consumed green leafy vegetables, tomatoes, cabbage, chicken,

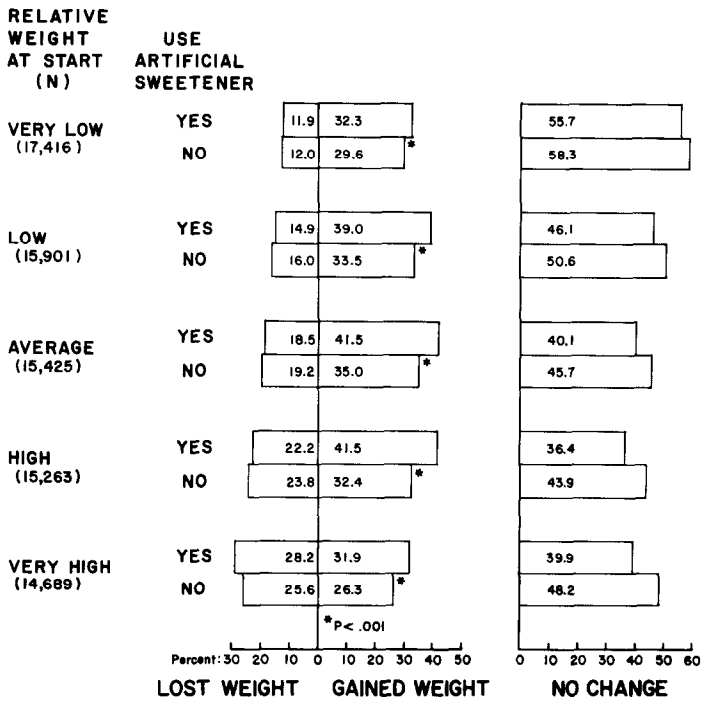

FIG. 2. Percentage of women who gained or lost weight or whose weight did not change during the 1-year period prior to enrollment in the study, according to artificial sweetener use. Percentages are adjusted for age in 5-year intervals.

and fish significantly more often than did nonusers. They consumed butter, white bread, and potatoes significantly fewer times per week than did nonusers. These observations suggest that differences in weight gain between users and nonusers of AS cannot be explained solely in terms of patterns of food consumption. We emphasize that this conclusion is based on average frequency of consumption of food items, and not on actual quantity per serving. Therefore, we cannot test the hypothesis that AS users increase their total food consumption, thereby leading them to gain more weight than nonusers.

DISCUSSION

It is worthwhile emphasizing some of the unusual features of this study that may strengthen or weaken our conclusion regarding lack of efficacy of AS in this cohort. Of prime importance is the large sample size (N = 78,694), which provides ample statistical power for all comparisons of interest, and the fact that these subjects are all alike on 10 important variables, which eliminates confounding as a likely source of bias. Although exclusive use of internal comparisons reinforces the study's validity within this subpopulation, further analysis would be required to extend these findings to women not meeting the inclusion criteria.

Another potential source of bias is use of self-reported rather than clinically

TABLE 1

MEAN WEIGHT (POUNDS) LOST OR GAINED OVER A 1-YEAR PERIOD BY CURRENT USERS AND NONUSERS OF ARTIFICIAL SWEETENERS (AS), BY APPROXIMATE QUINTILE OF INITIAL RELATIVE WEIGHT

Initial relative weight[a]	Lost weight		Gained weight	
	Non-AS users (*N*)	AS users (*N*)	Non-AS users (*N*)	AS users (*N*)
Very low	−3.72 ± 0.06 (1850)	−3.70 ± 0.18 (241)	4.17 ± 0.05 (4544)	4.79 ± 0.25* (674)
Low	−4.34 ± 0.07 (2099)	−4.09 ± 0.15 (412)	4.35 ± 0.05 (4393)	4.80 ± 0.10** (1074)
Average	−5.22 ± 0.08 (2308)	−5.50 ± 0.16 (636)	4.94 ± 0.06 (4190)	5.61 ± 0.11** (1438)
High	−6.64 ± 0.10 (2687)	−7.32 ± 0.18** (878)	5.37 ± 0.07 (3649)	6.27 ± 0.12** (1658)
Very high	−10.15 ± 0.18 (2531)	−11.50 ± 0.28** (1352)	6.71 ± 0.10 (2583)	8.19 ± 0.16** (1552)

Note. Categories of relative weight are very low, <299; low, 299–321.99; average, 322–346.99; high, 347–387.99; very high, ≥388. Values are means ± SE. Student's *t* test was used to evaluate the significance of observed differences in weight lost by AS users compared with nonusers and in weight gained by AS users compared with nonusers at each level of initial relative weight.

[a] Expressed as quetelet index = $10^4 \times$ weight (lbs)/height^2 (in.^{2}).

* $P < 0.01$.

** $P < 0.001$.

measured weights. However, since changes in weight between two points in time are used in our analyses, rather than the absolute values of the weights themselves, any bias due to systematic under- or overestimation by individuals will tend to be minimized. Errors in self-estimation of weight may somewhat affect the location of the QI strata boundaries, but otherwise they probably have little influence either on the mean weight changes indicated in Table 1 or on the estimated proportions of persons gaining and losing weight over the 1-year period, as presented in Fig. 2.

We did not determine which specific AS were consumed by subjects. Since cyclamate was banned in 1969, and aspartame did not become widely available until after 1982, saccharin was the predominant artificial sweetener used by this cohort during the 1-year period prior to enrollment. Therefore, our results pertain largely, though not exclusively, to saccharin.

These data do not support the hypothesis that long-term AS use either helps in losing weight or prevents weight gain. It is possible that a beneficial effect, if one exists, could best be demonstrated among recent (i.e., short-term) AS users or among persons whose AS consumption is coupled with major changes in dietary behavior, groups deliberately excluded from our analysis. However, given the upsurge in AS use in foods and beverages (4), and the pervasive notion in our society that dietary calories are to be minimized, it seems appropriate to examine

long-term users. Clearly there are some subgroups of women who lost weight while consuming AS and for whom additional correlates of weight loss should be sought in an effort to explain how they differed from the greater numbers of AS users who gained weight.

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