The effect of aspartame as part of a multidisciplinary weight-control program on short- and long-term control of body weight\textsuperscript{1-3}

George L Blackburn, Beatrice S Kanders, Philip T Lavin, Susan D Keller, and Janet Whatley

ABSTRACT This study investigated whether the addition of the high-intensity sweetener aspartame to a multidisciplinary weight-control program would improve weight loss and long-term control of body weight. One hundred sixty-three obese women were randomly assigned to consume or to abstain from aspartame-sweetened foods and beverages during 16 wk of a 19-wk weight-reduction program (active weight loss), a 1-y maintenance program, and a 2-y follow-up period. Women in both treatment groups lost \textasciitilde{}10\% of initial body weight (10 kg) during active weight loss. Among women assigned to the aspartame-treatment group, aspartame intake was positively correlated with percentage weight loss during active weight loss ($r = 0.32, P < 0.01$). During maintenance and follow-up, participants in the aspartame group experienced a 2.6\% (2.6 kg) and 4.6\% (4.6 kg) regain of initial body weight after 71 and 175 wk, respectively, whereas those in the no-aspartame group gained an average of 5.4\% (5.4 kg) and 9.4\% (9.4 kg), respectively. The aspartame group lost significantly more weight overall ($P = 0.028$) and regained significantly less weight during maintenance and follow-up ($P = 0.046$) than did the no-aspartame group. Percentage weight losses at 71 and 175 wk were also positively correlated with exercise ($r = 0.32, P < 0.001$; and $r = 0.34, P < 0.01$, respectively) and self-reported eating control ($r = 0.37, P < 0.001$; and $r = 0.33, P < 0.01$, respectively). These data suggest that participation in a multidisciplinary weight-control program that includes aspartame may facilitate the long-term maintenance of reduced body weight. \textit{Am J Clin Nutr} 1997:65:409–18.

KEY WORDS Aspartame, obesity, weight loss, body weight control, high-intensity sweetener, exercise

INTRODUCTION

Currently, 33\% of all adults in the United States aged \textasciitilde{}20 y are overweight (1). Overweight is associated with several chronic diseases, including hypertension, diabetes, heart disease, certain types of cancer, and gallbladder disease (2). The direct cost of disease attributable to obesity was \textasciitilde{}$30 billion in 1995, or 3.4\% of the total national health expenditure, whereas the indirect cost was estimated to be \$49 billion (3). Obesity continues to represent a major avoidable contribution to the cost of illness in the United States.

Indeed, weight loss is associated with an amelioration of disease associated with obesity, and even modest weight loss can improve health status (4–6). A 10\% reduction in body weight would result in 280 fewer deaths and 400 fewer morbidities per million (7, 8).

Consuming high-intensity, low-energy sweeteners as part of a multidisciplinary program for safe, gradual weight loss may be one strategy to promote compliance with weight-control regimens by improving the palatability of the diet. Americans currently consume \textasciitilde{}80 g (1338 kJ) sugar/d (excluding lactose), about half of which comes from sugars added to foods (9). Replacing even half of the added sugars with a low-energy, high-intensity sweetener could theoretically save \textasciitilde{}120 200 kJ/y. Indeed, \textasciitilde{}100 million adults consume low-energy, sugar-free foods and beverages (10), about half of whom claim to use these products to reduce or to maintain body weight. Despite the widespread use of low-energy sweeteners, their effect on the long-term control of body weight has not been systematically studied in a free-living obese population.

To date, only four published prospective studies in humans have investigated the effect of low-energy sweeteners on body weight. Porikos et al (11, 12) found that lean and obese participants living in a metabolic ward consumed less energy during a 6- or 12-d period when investigators covertly replaced all sucrose with aspartame in an ad libitum diet compared with when they provided them with a high-sucrose diet. Tordoff and Alleva (13) reported that consumption of aspartame-sweetened soda significantly reduced energy intake in both males (1183 kJ/d) and females (987 kJ/d) eating their normal diet, and significantly decreased the body weight of males over a 3-wk period when compared with a no-drink condition. These studies suggested that the use of aspartame-sweetened foods and beverages might facilitate the control of energy intake and body weight. None of these studies, however, specifically investigated a dieting population.

In our own pilot study of obese outpatients (14), women ($n = 46$) lost slightly more weight (7.4 kg compared with 5.8

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Received September 6, 1996.

Accepted for publication September 16, 1996.
kg) when they supplemented a hypoenergetic diet with aspartame-containing foods and beverages; however, men (n = 13) showed the opposite trend (10.4 kg compared with 12.2 kg). At the 1-y follow-up evaluation (15), factors associated with maintenance of weight loss were increased physical activity levels, increased aspartame consumption, and decreased desire for sweets. A negative correlation between aspartame consumption and weight regain was found for the males but not for the females. However, there were too few subjects in the weight-loss and follow-up studies to conclude whether the addition of the low-energy sweetener aspartame aided body weight control. Building on these results, the present study (16) was designed to assess in a prospective, randomized fashion whether the high-intensity sweetener aspartame could facilitate weight loss and aid in the long-term control of body weight in an outpatient population of obese women.

SUBJECTS AND METHODS

Subjects

Between July 1988 and August 1989, obese women were recruited to participate in a 17-mo weight-control program. Participants were recruited by advertisement, physician-referral, and word-of-mouth. Obese [140–225% of ideal body weight based on the 1959 Metropolitan Life Insurance Tables (17)], sedentary, but otherwise healthy women aged 20–60 y whose alcohol intake was < 15% of total energy, who expected to reside in the Boston area for ≥ 18 mo, who were willing to abstain from or to use aspartame-sweetened products for the duration of the study, who had not dieted within the last 90 d, and who were not pregnant or planning to become pregnant over the next 18 mo were invited to be screened.

This study was approved by the New England Deaconess Hospital Institutional Review Board, and informed consent was obtained from each prospective subject in writing at their first clinic visit. Subjects then completed a detailed medical and dieting-weight history and underwent clinical and laboratory evaluation. Subjects were also given the 40-question eating attitudes test (EAT-40) (18), Beck’s depression inventory (19), and other questionnaires to assess food preferences and cravings. At this first screening visit, prospective participants were taught how to keep a 3-d food record by a research nutritionist. Three-day food records were brought in and reviewed for accuracy and completeness at the second screening visit.

Subjects were excluded if they were depressed or revealed a tendency toward disordered eating as determined by scores on the Beck’s depression inventory and EAT-40 (> 20 and ≤ 20, respectively). Other medical exclusion criteria included phenylketonuria, hypothyroidism, active psychiatric treatment (including frank eating disorders), significant hepatic insufficiency, respiratory insufficiency, insulin-dependent diabetes, and certain cardiac problems that would contraindicate the use of a low-energy diet.

Study design

The study—a prospective, randomized, stratified, two-arm parallel design—tested the hypothesis that the addition of aspartame to a multidisciplinary weight-loss program improves weight loss and control of body weight for up to 3 y after weight loss. The primary outcome measures were aspartame consumption and body weight change. Secondary measures included level of physical activity and subjective reports of hunger, desire for sweets, and eating control. Intercurrent health events were also evaluated.

After they completed the baseline evaluation, eligible subjects were stratified on the basis of percentage of ideal body weight (140–179% and 180–225%) and clinic assignment (Brookline, Quincy, Wellesley, Winchester, Boston) and were randomly assigned to one of two dietary treatment programs by use of a computer-generated identification number. Participants were told that the purpose of the study was to evaluate two research diets for their ability to promote weight-loss and long-term control of body weight. Participants were not blinded to their treatment assignments to permit intensive group-appropriate counseling.

Run-in period

All participants were prescribed the same 3-wk run-in diet and were instructed on its use by a research nutritionist. This phase allowed for water diuresis associated with hypoenergetic diets and weaned all participants off low-energy sweeteners. The run-in diet was based on the American Dietetic Association exchange list (20) and provided 4180 ± 836 kcal/d (1000 ± 200 kcal/d): 27% of energy as protein, 49% as carbohydrate, and 24% as fat. Participants were encouraged to take a daily vitamin-mineral supplement as well. Participants were told not to consume any low-energy sweeteners (eg, aspartame, saccharin) during this time. Participants met weekly with the nutritionist for instruction on the diet and for reinforcement of behavioral strategies. Participants were also told to begin walking 15 min/d, 3 d/wk.

Intervention period

The intervention period lasted 16 wk and the run-in period diet was consumed during this time. All participants underwent the same program delivered by a multidisciplinary team. The dietary intervention was highly structured: a research nutritionist gave participants sample menus, recipes, and personalized menu plans and explained the diet plan in detail. Subjects in the aspartame group were given their milk exchanges as aspartame-sweetened pudding or milk shakes. In addition, they were given an aspartame-sweetened noncarbonated beverage mix and packets of a tabletop sweetener containing aspartame and were encouraged to use other products sweetened with aspartame. The no-aspartame group was told to avoid products sweetened with any low-energy sweetener and to use instead up to 50 g (3 tsp) sugar or honey daily as a sweetener; participants in this group were also given a nonenergy-containing flavored seltzer water to drink instead of diet soda, and their menus and recipes for low-fat, low-energy foods and beverages did not include high-intensity sweeteners.

Participants were seen weekly for 60–90 min in closed groups of 10–15 persons. Group sessions were led by registered dietitians who instructed participants in nutrition, exercise, and behavior modification. All group leaders followed the same detailed group manual (21). Although separate groups were held for the aspartame and no-aspartame participants, at each site the same group leader led both groups to ensure uniform treatment.

Participants were instructed to complete 200 min of aerobic exercise per week (walking); the prescribed program increased
exercise levels gradually over a period of 6–8 wk. Participants were also encouraged to increase their daily activity (eg, use stairs instead of an escalator).

Maintenance period

During the 12-mo maintenance phase, energy intake was adjusted on an individual basis to maintain each participant’s reduced body weight. The diets provided ~6270 ± 1254 kcal/d (1500 ± 300 kcal/d): 24% of energy as fat, 56% as carbohydrate, and 20% as protein, with an emphasis on restricted fat intake. Participants were either encouraged or discouraged from using aspartame-sweetened products according to their original assignment. Each participant also received a personalized exercise program developed by an exercise physiologist. Prescriptions were based on each woman’s level of fitness and preferences.

Finally, participants attended hour-long monthly group sessions. Groups were led by a research nutritionist who focused on relapse prevention and strategies for maintaining weight loss. Group leaders all followed the same detailed instruction manual. Separate maintenance groups were held for the two treatment groups.

Follow-up period

During the period after maintenance, subjects were contacted annually for 2 y to determine body weight, aspartame intake, exercise level, subjective measures of eating control, and intercurrent health events.

Data collection

Aspartame intake

Aspartame intake was measured by use of a form that listed by food group all foods containing aspartame at the time of the study. Participants were asked to record their use of these products over 7 d. Average values for the particular food groups were used to determine mean intake of aspartame. The form was administered at baseline and weeks 19, 71, and 175.

Body weight

Body weight was measured on the same digital, spring scale (model no. 8850; Detecto Scale Co, Webb City, MO) to the nearest pound. Weight was measured weekly during active weight loss, monthly during maintenance, and annually thereafter.

Exercise

Minutes of purposeful exercise per week were calculated from a daily exercise log kept by all participants during the week immediately before data collection (baseline and weeks 19, 71, and 175).

Dietary intake

Nutrient intake was determined by the use of 3-d food records. A research nutritionist instructed each subject on how to complete food records with the use of food models and household measures (22). The importance of keeping timely and accurate records was emphasized. Particular attention was paid to the consumption of any low-energy foods, beverages, or sweeteners. Completed food records were reviewed with each participant by the research nutritionist and sent to the Nutritional Coding Center at the University of Minnesota (Minneapolis) for coding and analysis. Food records were kept at baseline and weeks 19, 71, and 175.

Subjective measures

Level of hunger and desire for sweets were assessed by a self-administered questionnaire. The subject was asked to rate her level of hunger and desire for sweets over the past 7 d by use of a 10-point category scale described previously (14). Ratings for hunger and desire for sweets were anchored with “none” and “severe.” Subjective levels of eating control were also assessed by use of a 10-point category scale that was anchored with “binging” and “restricting.” This questionnaire was administered at baseline and weeks 19, 71, and 175. Self-assessment of eating control was compared with more direct measures of food intake from dietary records.

Intercurrent health events

Intercurrent health events were documented in the patient’s chart at each clinic visit by a research nurse according to the following classification schedule: mild (no medical intervention), moderate (medical intervention and/or follow-up), and severe (hospitalization or life-threatening).

Validation of aspartame intake and exercise-assessment forms

Ten obese subjects meeting study entry criteria were selected to participate in a validation study of the exercise and aspartame intake forms. These two forms were checked by recall against a 7-d food and activity diary for these subjects. Diary-reported exercise levels ranged from a total of 30 to 430 min/wk whereas the total number of diary-reported aspartame servings ranged from 0 to 46 servings/wk. For exercise, the study form underreported total minutes of exercise by a mean of 6.7%. The bulk of this difference was due to two subjects who forgot to report exercise sessions. Overall, 70% of the subjects reported the total minutes of exercise on the form within 20% of the total reported in the diary. For aspartame intake, the study form underreported total aspartame servings by 0.4%; 100% of subjects reported total aspartame servings within 5% of the total reported in the diary. Recall within specific exercise- and food-group categories was also acceptable.

Statistical analysis

The study was designed to test the null hypothesis that mean weight loss would be comparable between the two groups according to a two-sided test with 5% Type I error and 80% power versus the alternative hypothesis, which was adequate to detect a 3% difference in mean weight loss between the two treatment groups during active weight loss and was adequate to detect a 3% difference in weight regain during maintenance between the two treatment groups (14, 15). Subjects were stratified according to the degree of obesity at study entry and by participating clinic site.

Baseline characteristics for the two treatment groups were compared by use of unpaired t tests for continuous measures and by use of Fisher’s exact test for categorical measures. Within each treatment group, the characteristics of subjects
RESULTS

Patient population

Three hundred ninety obese women were screened. Of these, 222 subjects were not enrolled either because they were not eligible or because they decided that they would be unable to make a commitment to the study protocol. The remaining 168 subjects gave written consent and entered the run-in phase; 5 subjects dropped out during these 3 wk. After stratification by initial body weight and clinic site, a total of 163 subjects were randomly assigned to a treatment group at the end of run-in: 82 to the aspartame group and 81 to the no-aspartame group.

Sixteen percent (11 aspartame, 16 no-aspartame) of participants dropped out during the active weight-loss phase. Reasons cited for dropping out included relocation or conflict with job schedule (n = 3), inability to comply with the program (n = 10), auto accident (n = 1), family or personal problems (n = 3), and loss of interest (n = 10); 136 women successfully completed the week-19 visit.

One hundred twenty-five (61 aspartame, 64 no-aspartame) women, or 77% of the original population, participated in maintenance and completed the week-71 visit. With the exception of being taller (164.6 ± 6.6 cm compared with 162.1 ± 5.1 cm), these participants did not differ significantly on any other baseline variables from the women who did not participate in maintenance. However, they did differ with respect to weight loss during active treatment. Those who participated in maintenance lost significantly (P = 0.0001) more weight than did those who did not participate (9.8 ± 6.3% compared with 5.5 ± 4.2%).

Finally, 86 women (41 aspartame, 45 no-aspartame), or 52% of the original population, attended the 2-y follow-up evaluation (week 175). Women who did not participate did not differ significantly from those who did participate in follow-up with regard to any baseline characteristics. However, they did differ with respect to weight loss from baseline. The participants in the follow-up lost significantly (P = 0.0001) more weight during the active weight-loss period than did those who did not participate (10.1 ± 6.0% compared with 7.3 ± 6.1%).

Baseline

Baseline sociodemographic characteristics, body weight, and nutrient intakes of the 163 women who entered the active weight-loss phase are shown in Table 1. The groups were nearly identical in age, body weight, aspartame intake, energy intake, number of years of high-intensity sweetener use, exercise level, education level, and marital status. Subjective measures of hunger, desire for sweets, and eating control were also similar between groups.

End of active weight loss

Aspartame intake

At the end of active weight loss, mean daily aspartame intake increased from 233 to 285 mg (P = 0.009) in the aspartame group and decreased from 239 to 16 mg (P = 0.001) in the no-aspartame group (Table 2). Subjects in the aspartame group consumed more puddings, gelatins, milk shakes, hot cocoa, tabletop sweeteners, and cereal to increase their aspartame intake. Among participants in the no-aspartame group, decreased aspartame intake resulted through reduced consumption of diet soda, tabletop sweeteners, chewing gum, and mints.

Body weight

The mean percentage weight loss for both groups was similar after 19 wk of dietary restriction (Figure 1). Women in the aspartame group lost 9.9 ± 6.1 kg whereas women in the

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Baseline characteristics of the patient population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Aspartame (n = 82)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>42.5 ± 9.3</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>101.1 ± 16.6</td>
</tr>
<tr>
<td>Percentage ideal body weight (%)</td>
<td>171 ± 23</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>37.4 ± 5.1</td>
</tr>
<tr>
<td>Aspartame intake (mg/d)</td>
<td>233 ± 223</td>
</tr>
<tr>
<td>Energy intake (kcal/d)</td>
<td>8506 ± 301</td>
</tr>
<tr>
<td>Exercise (min/wk)</td>
<td>3.5 ± 19.3</td>
</tr>
<tr>
<td>Married (%)</td>
<td>49</td>
</tr>
<tr>
<td>Employment (h/wk)</td>
<td>30.8 ± 19.2</td>
</tr>
<tr>
<td>Education (y)</td>
<td>16 ± 3</td>
</tr>
<tr>
<td>High-intensity sweetener use (y)</td>
<td>17.8 ± 8.2</td>
</tr>
<tr>
<td>Eating attitude score*</td>
<td>9.7 ± 7.0</td>
</tr>
</tbody>
</table>

* x ± SD.

A score >19 indicates disordered eating activities and behaviors.
Table 2
Comparison of daily aspartame intake, by treatment group assignment

<table>
<thead>
<tr>
<th></th>
<th>Aspartame</th>
<th>No aspartame</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>233 ± 223 [82]</td>
<td>239 ± 229 [81]</td>
</tr>
<tr>
<td>End of AWL (week-9)</td>
<td>285 ± 235 [81]</td>
<td>16 ± 46° [81]</td>
</tr>
<tr>
<td>Week 71</td>
<td>279 ± 178 [48]</td>
<td>172 ± 146° [38]</td>
</tr>
<tr>
<td>Week 175</td>
<td>293 ± 231 [42]</td>
<td>192 ± 164° [41]</td>
</tr>
</tbody>
</table>

1 ± SD; n in brackets. AWL, active weight loss.  
2-4 Significantly different from aspartame: ²P < 0.0001, ³P = 0.004, ⁴P = 0.02.

no-aspartame group lost 9.8 ± 6.5 kg. Mean body mass index (in kg/m²) dropped from 37 to 34 in both groups. The mean percentage of ideal body weight dropped from 172% to 155% in the aspartate group and from 169% to 153% in the no-aspartate group. Although both groups had significant reductions in body weight (P < 0.0001), no significant differences were noted between groups with respect to percentage weight loss (P = 0.79).

A linear-regression model was used to test for treatment effect and to identify baseline factors that would predict better weight loss during the study. When both study groups were included in the model, only low baseline levels of self-reported hunger (P = 0.004) were predictive of a greater weight loss, with an adjusted r² of 4% for the model. During active weight loss, percentage weight loss was positively correlated with exercise (P = 0.0001) and self-reported eating control (ie, restricting) (P = 0.0001) and was negatively correlated with self-reported hunger (P = 0.005) (Table 3). In the aspartate group, percentage weight loss was positively associated with aspartate consumption (P = 0.004).

The relation between aspartate intake and body weight change at week 19 is illustrated in Table 4. The most favorable weight loss was observed for the group with the highest aspartate intake at the end of active weight loss. Differences in weight loss between participants consuming the most and the least aspartate were as large as 4% of initial body weight (4.5 kg). Similar intakes of energy and fat as well as similar levels of exercise were reported across the three groups.

Exercise
At baseline, participants in both the aspartate and no-aspartate groups reported completing an average of < 4 min of purposeful exercise per week. By the end of active treatment, all study participants reported similar and significant increases in exercise level compared with baseline (P < 0.0001). Total weekly minutes of purposeful exercise rose to 123.3 ± 132 in the aspartate group and to 142.3 ± 131 in the no-aspartate group. There were no significant differences in exercise levels between study groups.

Dietary intake
Mean intakes of selected nutrients at baseline and at the end of active weight loss for the aspartate and no-aspartate groups are shown in Table 5. There were no significant differences in mean nutrient intake between treatment groups at the end of active weight loss. Compared with baseline, however, energy intake, fat, protein, carbohydrate, sucrose, fiber, and saccharin intakes decreased significantly in both treatment groups.

Subjective measures
Desire for sweets decreased significantly in both groups from baseline to the end of active treatment (Table 6). Self-reported hunger did not differ from baseline in either treatment group. Eating control increased significantly in both treatment groups at week 19. There were no significant differences between study groups. Self-reported levels of eating control (ie, binging) were significantly correlated with both total energy intake (r = 0.19, P = 0.015) and total fat intake (r = 0.28, P = 0.0003) at the end of active weight loss as assessed by 3-d food records.

Intercurrent health events
Twenty (12 aspartate, 8 no-aspartate) intercurrent health events were reported during the 19 wk of dietary restriction. Each treatment group had three severe (requiring hospitalization or life-threatening) intercurrent health events. Among participants in the aspartate group, the severe intercurrent health events included gastric ulcer, vaginal bleeding, and severe back spasms, none of which were considered to be study-related. In the no-aspartate group, the severe intercurrent health events included drop in blood pressure, neurogenic bladder, and severe right calf pain. Only the decrease in blood pressure was considered to be study-related (secondary to weight loss).

Week 71
Aspartate intake
Daily aspartate intake among aspartate group participants was not significantly different from baseline at week 71 (Table 2). Among participants in the no-aspartate group, daily intake remained significantly lower at the end of follow-up (P = 0.004) compared with baseline intake. At week 71, aspartate intake remained significantly higher in the aspartate group than in the no-aspartate group (P = 0.004).

Body weight
Participants in the aspartate group experienced a 2.6-kg (2.6% of initial body weight) increase in weight during maintenance for a net weight loss of 8.1 ± 9.4% from baseline (P < 0.000). Those in the no-aspartate group gained 5.4 kg (5.4% of initial body weight) for a net weight loss of 5.1 ± 9.3% from baseline (P = 0.0001) (Figure 1). There was 80% power to detect a 5% difference in treatments for a two-sided hypothesis test with 5% Type 1 error.

Linear-regression analyses of weight change from baseline through week 71 and from the end of active weight loss through week 71 were used to identify prognostic factors (Table 3). A greater percentage weight loss was predicted by randomization for the aspartate treatment group (P = 0.05). Participation in the aspartate group was associated with a 3.5-kg (3.5%) advantage in weight maintained. Furthermore, percentage weight loss was positively correlated with exercise (r = 0.32, P = 0.005) and self-reported eating control (r = 0.37, P = 0.0001) but not with aspartate intake (r = 0.19, P = 0.07).
Exercise

At week 71, all participants reported significantly higher levels of purposeful activity than at baseline ($P = 0.0001$). Among aspartame subjects, the mean week-71 exercise level was significantly higher (48 ± 112 min/wk increase) than at week 19 ($P = 0.01$). The no-aspartame group did not significantly increase exercise levels from the end of active treatment (7 ± 176 min/wk). However, women in the aspartame and no-aspartame groups reported comparable amounts of weekly exercise at the end of maintenance: 177 ± 117 and 174 ± 138 min/wk, respectively.

Dietary intake

No significant differences existed between the two treatment groups with respect to selected nutrient intake at week 71 (Table 5). Compared with baseline, however, intake of total energy, fat, protein, fiber, and saccharin decreased significantly within both treatment groups at week 71, and intake of carbohydrate and sucrose decreased significantly within the aspartame group.

Subjective measures

At week 71, no significant differences existed between the treatment groups on any of the subjective variables (Table 6). As compared with baseline, desire for sweets and hunger did not differ significantly in either treatment group. Self-reported hunger did not differ from baseline in either treatment group. However, eating control increased significantly in both treatment groups at week 71. Self-reported levels of eating control (ie, binging) were significantly correlated with both total energy intake ($r = 0.31, P = 0.01$) and total fat intake ($r = 0.41$).

TABLE 3

Correlation coefficients ($r$) between percentage weight change and selected outcome variables for the aspartame group (Apm), no aspartame group (No), and all subjects.

<table>
<thead>
<tr>
<th></th>
<th>Baseline to end of AWL</th>
<th>Baseline to week 71</th>
<th>End of AWL to week 71</th>
<th>Baseline to week 175</th>
<th>End of AWL to week 175</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Apm</td>
<td>No</td>
<td>All</td>
<td>Apm</td>
<td>No</td>
</tr>
<tr>
<td>Number</td>
<td>82</td>
<td>81</td>
<td>163</td>
<td>52</td>
<td>49</td>
</tr>
<tr>
<td>Aspartame</td>
<td>0.32$^{2}$</td>
<td>-0.09</td>
<td>0.18$^{2}$</td>
<td>0.18</td>
<td>0.07</td>
</tr>
<tr>
<td>Exercise</td>
<td>0.34$^{2}$</td>
<td>0.26$^{2}$</td>
<td>0.30$^{2}$</td>
<td>0.52</td>
<td>0.15</td>
</tr>
<tr>
<td>Eating control</td>
<td>0.49$^{2}$</td>
<td>0.34$^{2}$</td>
<td>0.42$^{2}$</td>
<td>0.28</td>
<td>0.47</td>
</tr>
<tr>
<td>Hunger</td>
<td>-0.23$^{2}$</td>
<td>-0.22</td>
<td>-0.22$^{2}$</td>
<td>-0.05</td>
<td>-0.26</td>
</tr>
</tbody>
</table>

1 AwL, active weight loss.
2 $P \leq 0.01$.
3 $P \leq 0.05$.
4 $P \leq 0.001$.
5 $P \leq 0.001$.
TABLE 4
Change in weight, macronutrient intake, and exercise according to daily aspartame intake at the end of active weight loss

<table>
<thead>
<tr>
<th>Tertile</th>
<th>First (n = 27)</th>
<th>Second (n = 27)</th>
<th>Third (n = 27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspartame intake</td>
<td>Mean (mg)</td>
<td>75 ± 51</td>
<td>243 ± 60</td>
</tr>
<tr>
<td></td>
<td>Range (mg)</td>
<td>0–157</td>
<td>158–359</td>
</tr>
<tr>
<td>Weight loss</td>
<td>(kg)</td>
<td>6.5 ± 5.5</td>
<td>9.7 ± 7.0</td>
</tr>
<tr>
<td></td>
<td>(%)</td>
<td>6.8 ± 5.9</td>
<td>9.3 ± 6.4</td>
</tr>
<tr>
<td>Energy intake (kJ)</td>
<td></td>
<td>4695 ± 1799</td>
<td>5389 ± 1866</td>
</tr>
<tr>
<td>Fat intake (g)</td>
<td></td>
<td>32 ± 17</td>
<td>43 ± 26</td>
</tr>
<tr>
<td>Protein intake (g)</td>
<td></td>
<td>68 ± 22</td>
<td>72 ± 19</td>
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<tr>
<td>Carbohydrate intake (g)</td>
<td></td>
<td>138 ± 56</td>
<td>153 ± 44</td>
</tr>
<tr>
<td>Exercise (min/wk)</td>
<td></td>
<td>141 ± 173</td>
<td>125 ± 117</td>
</tr>
</tbody>
</table>

1 Patients were divided into tertiles based on aspartame intake at the last active-weight-loss visit.
2 $\bar{x}$ ± SD.

$P = 0.0005$ at the end of maintenance as assessed by 3-d food records.

Intercurrent health events

During maintenance, a total of 19 and 21 intercurrent health events were reported in the aspartame and no-aspartame groups, respectively. Among aspartame participants, 6, 1, and 11 were classified as mild, moderate, and severe, respectively. Only one event was considered to be study-related (reinjury of back secondary to increased physical activity). In the no-aspartame group, 1, 4, and 16 were classified as mild, moderate, and severe, respectively. Only two intercurrent health events were considered to be study-related. One woman with a history of gallstones underwent a cholecystectomy 9 mo after she entered the program; this participant had lost 6.8 kg during active weight loss and regained all her lost weight during the first 3 mo of maintenance. Another woman also underwent a cholecystectomy, also 9 mo after enrollment; after the active weight loss period, she had independently started a very-low-energy diet program, which may have led to the need for surgery.

Week 151

Although no significant difference from baseline aspartame intake was found in the aspartame group, daily aspartame intake in the no-aspartame group remained significantly lower at the end of follow-up (Table 2). Aspartame intake remained higher ($P = 0.02$) at week 175 (293 compared with 192 mg/d). All participants maintained purposeful activity of $\geq 3$ h/wk. The subjective measures of eating control in the no-aspartame group converged to the same values in the aspartame group as they regained their weight (Table 6). No new intercurrent health events were reported. The aspartame group had a mean weight loss of 5.1 kg (5.1%); the no-aspartame group had no net change in body weight from baseline. This difference between groups was significant ($P = 0.028$; Figure 1). The weight regain was also significantly different, 5.4% (5.4 kg) compared with 9.4% (9.4 kg) ($P = 0.046$).

DISCUSSION

Among obese women undergoing voluntary weight reduction, participation in a multidisciplinary weight-loss program that includes the use of aspartame-containing foods and beverages was as effective at promoting weight loss as was the same diet, exercise, and behavior program devoid of aspartame-containing products.

The more interesting results of this study, however, relate to the effect of aspartame on long-term control of body weight. The results of this 71-wk study and 2-y follow-up period showed that participation in a weight-control program that included the use of the high-intensity sweetener aspartame facilitated long-term maintenance of a reduced body weight. During the year after a 10-kg weight loss, women in the aspartame group experienced a 2.6-kg weight regain compared with women in the no-aspartame group, who regained about twice as much weight (5.4 kg); 2 y later, a mean weight loss of 5.1% had been achieved in the aspartame group. In our study, those participants who did not consume high-intensity sweeteners experienced no net change in body weight over the 175 wk they were monitored. These results are similar to those reported for adjunctive use of appetite control medication (25–28).

The results of this study support those of Porikos et al (11, 12), Tordoff and Alleva (13), and Evans (29), which suggest that aspartame may facilitate the control of body weight. This study, however, is the first large, randomized, outpatient clinical trial to show that aspartame consumption as part of a multidisciplinary weight-control program can facilitate long-term control of body weight. This finding has important clinical implications given the poor long-term success rates of dietary treatment of obesity (30).

In the present study, women in both treatment arms lost equal amounts of weight: 10 kg (10% of initial body weight). According to correlation analysis, consumption of more aspartame by the aspartame group was predictive of greater weight loss during active weight loss. This is an important finding because > 71% of dieters consume foods containing low-energy sweeteners (10). Laboratory studies in which aspartame replaces sugar have found that if the energy reduction is substantial, compensation will be incomplete and there will be some reduction in daily energy intake (11, 29, 31–33). Indeed, compared with the aspartame participants in the lowest tertile for aspartame consumption (Table 4), the participants in the highest tertile lost an additional 4.5 kg (0.22 kg/wk), theoretically equivalent to a difference in daily intake of 1046 kJ (250 kcal) over the duration of the dieting phase. Although energy intake (as measured by a 3-d food diary) was not significantly different between the lowest and highest tertiles (Table 4), it is well documented that obese individuals report consuming very close to their prescribed energy intakes (34, 35) and underreport food intake (33, 36). Other factors associated with greater weight loss in both treatment groups during the dieting phase included increased exercise, greater self-reported eating control (restricting), and reduced hunger.

At week 71, treatment group assignment (aspartame and no-aspartame) was a significant determinant of weight maintenance. Thus, participants in the aspartame group experienced a 3.5% (of initial body weight) advantage with respect to weight maintenance. Although aspartame intake was signifi-
TABLE 5
Selected daily nutrient intake through week 71, by treatment group

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n = 81)</th>
<th>Week 19 (n = 66)</th>
<th>Week 71 (n = 35)</th>
<th>Baseline (n = 80)</th>
<th>Week 19 (n = 62)</th>
<th>Week 71 (n = 32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kJ)</td>
<td>8506 ± 301</td>
<td>5326 ± 193²</td>
<td>6058 ± 402²</td>
<td>7933 ± 247</td>
<td>5084 ± 172</td>
<td>6033 ± 29‡</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>86 ± 4</td>
<td>39 ± 2²</td>
<td>54 ± 5²</td>
<td>79 ± 3</td>
<td>38 ± 2²</td>
<td>49 ± 5²</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>81 ± 3</td>
<td>73 ± 2²</td>
<td>69 ± 4²</td>
<td>80 ± 2</td>
<td>70 ± 2²</td>
<td>68 ± 3²</td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>226 ± 8</td>
<td>155 ± 6²</td>
<td>169 ± 10²</td>
<td>210 ± 8</td>
<td>149 ± 6²</td>
<td>177 ± 10</td>
</tr>
<tr>
<td>Sucrose (g)</td>
<td>38 ± 2</td>
<td>20 ± 1²</td>
<td>28 ± 3¹</td>
<td>37 ± 2</td>
<td>23 ± 2²</td>
<td>36 ± 5</td>
</tr>
<tr>
<td>Fiber (g)</td>
<td>17 ± 1</td>
<td>15 ± 1²</td>
<td>14 ± 1²</td>
<td>15 ± 1</td>
<td>14 ± 1²</td>
<td>13 ± 1²</td>
</tr>
<tr>
<td>Saccharin (mg)</td>
<td>15 ± 3</td>
<td>9 ± 3²</td>
<td>5 ± 3²</td>
<td>10 ± 3</td>
<td>3 ± 2²</td>
<td>5 ± 3²</td>
</tr>
</tbody>
</table>

1 x ± SEM, ², ³ Significantly different from baseline; ² P = 0.0001, ³ P = 0.001.

significantly lower in the aspartame group than in the no-aspartame group at week 71, aspartame intake did not correlate with weight maintenance (P = 0.07). Greater weight maintenance was positively correlated with both exercise and eating control. Other studies have identified exercise as a significant predictor of weight maintenance (37–39). Exercise increases energy expenditure, reduces body fat, and may offset some of the drop in metabolic rate associated with dietary restriction (40–42). Exercise has also been reported to improve mood and self-esteem, possibly increasing dietary compliance (43). However, exercise levels were comparable between the two treatment groups at all time points and thus cannot explain the smaller weight regain by the aspartame group compared with the no-aspartame group. Self-reported eating control was also positively associated with weight outcome; self-reported eating control (which measures the degree with which someone is restricting their intake) could be predictive of weight maintenance over the long term.

Identifying the mechanism by which aspartame affects body weight regulation was not an aim of the present study. However, sensory-specific satiety (the alteration of food preferences through prefeeding of a particular food) may explain how low-energy sweeteners enhance weight loss (44, 45). Appetite may be controlled by satisfying sweetness without overconsumption of sucrose and/or fat. Woolley et al (46) showed that use of a sugar substitute may satisfy the hedonic need for sweetness as effectively as sugar itself and could result in decreased energy consumption. Thus, aspartame may work to promote long-term weight maintenance by satisfying the increased sensory responsiveness found in obese subjects who have reduced their weight (47) and by satisfying the desire for sweet taste without adding energy.

During the study, no differences were found between groups with respect to desire for sweats or hunger, although desire for sweets decreased significantly in both groups at the end of the dietary-restriction phase (Table 6). The aspartame diet may have reduced the desire for sweets by providing ample low-energy sweetness as part of the program and, despite earlier claims to the contrary (48–50), aspartame was not associated with an increase in hunger at any time during the study. It should be emphasized that aspartame has not been found to increase food intake acutely [0–120 min after preload ingestion (51) and over several hours (10 h)] (31). In the present study, the greater the weight loss the greater the hunger in both treatment groups as determined by multivariate analysis. This makes intuitive sense: it is well documented that, in general, energy restriction leads to increased hunger (33, 52, 53). We hypothesize that the greater weight loss associated with increased hunger would require greater dietary restraint, which is supported by the increase in self-reported eating control.

Aside from the predicted 1% incidence of symptomatic gallbladder disease (54), no clinically significant intercurrent health events occurred. The use of dexfenfluramine, recently approved for prolonged use in the treatment of medically significant obesity, is associated with significant side effects (26–28). Compared with dieting alone, use of the medication is associated with diarrhea (17.9% compared with 7.3%), somnolence (7.1% compared with 3.4%), and dry mouth (12.5% compared with 5%). Indeed, 7% of subjects had to discontinue use of the medication because of adverse events, and the primary pulmonary hypertension odds ratio was 23–46 to 1 (55). None of these adverse effects were reported with the adjunctive use of aspartame, yet significant weight loss was achieved.

TABLE 6
Subjective measures at baseline, end of active weight loss (AWL), and weeks 71 and 75

<table>
<thead>
<tr>
<th></th>
<th>Aspartame</th>
<th>No aspartame</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hunger</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>4.0 ± 0.3</td>
<td>4.1 ± 0.3</td>
</tr>
<tr>
<td>End of AWL</td>
<td>4.0 ± 0.3</td>
<td>4.2 ± 0.3</td>
</tr>
<tr>
<td>Week 71</td>
<td>4.2 ± 0.3</td>
<td>4.3 ± 0.3</td>
</tr>
<tr>
<td>Week 175</td>
<td>6.0 ± 0.4</td>
<td>6.6 ± 0.3</td>
</tr>
<tr>
<td>Desire for sweets</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>5.2 ± 0.3</td>
<td>5.3 ± 0.3</td>
</tr>
<tr>
<td>End of AWL</td>
<td>4.0 ± 0.3</td>
<td>4.3 ± 0.4</td>
</tr>
<tr>
<td>Week 71</td>
<td>5.0 ± 0.4</td>
<td>4.6 ± 0.4</td>
</tr>
<tr>
<td>Week 175</td>
<td>5.3 ± 0.4</td>
<td>5.4 ± 0.4</td>
</tr>
<tr>
<td>Eating control</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>3.5 ± 0.3</td>
<td>4.0 ± 0.3</td>
</tr>
<tr>
<td>End of AWL</td>
<td>6.0 ± 0.3</td>
<td>6.2 ± 0.3</td>
</tr>
<tr>
<td>Week 71</td>
<td>4.3 ± 0.4</td>
<td>4.9 ± 0.4</td>
</tr>
<tr>
<td>Week 175</td>
<td>4.9 ± 0.4</td>
<td>5.2 ± 0.4</td>
</tr>
</tbody>
</table>

1 x ± SEM, n in brackets. Scores are based on a scale of 0 (none) to 10 (severe); eating control (0 = binging; 10 = restricting).

², ³, ⁴ Significantly different from baseline: ² P < 0.01, ³ P < 0.0001, ⁴ P < 0.05.
Although studies conducted in a free-living population provide greater applicability of results, such research is limited by lack of control. This study would have been improved by more rigorous compliance with the aspartame assignment during the maintenance phase. Although participants were instructed to continue to use or not use aspartame based on their original assignment, women in the aspartame group had a small decrease in their intake of aspartame, and women in the no-aspartame group significantly increased their intake of aspartame during maintenance.

Another limitation of this study relates to the generalizability of these results. Participants of this study were highly motivated, well-educated, middle-to-upper-middle class, white women willing to invest a great deal of time and effort in this program. The generalizability of these results to men and women from other socioeconomic and ethnic groups is not known and would require further study.

Although no attempt was made to blind the participants or researchers to the treatment group assignment, we do not believe that this decision limited this study. Prior research found that knowing whether a food was sweetened with aspartame or sugar had no influence on short-term food intake or perceived appetite; both informed and uninformed subjects responded similarly (31). In addition, the objective of this study was to evaluate whether the addition of aspartame to a standard multidisciplinary weight-control program could facilitate weight loss and long-term control of body weight in an outpatient setting. Because most Americans consume aspartame-sweetened products regularly (10), the only way to include a comparison group was to instruct them specifically to abstain from the use of aspartame, which would disclose their group assignment. Similarly, the intensive counseling in the use of aspartame-sweetened products would have alerted intervention subjects to their group assignment. Unless all food were to be provided to all participants, true blinding could not have been achieved.

Attaining and maintaining appropriate body weight can have significant beneficial effects on physical and emotional health and well-being (3–9). The complex nature of body-weight regulation makes it impossible to attribute the success of a diet to a particular component. However, the results of this study showed that whereas it was not necessary to consume aspartame to achieve medically significant weight loss, consumption of higher amounts of aspartame was associated with greater weight loss among obese, middle-aged women using aspartame as part of a weight-loss program. More important, however, participation in a multidisciplinary weight-maintenance program that included aspartame and exercise was associated with better long-term control of body weight. This study has provided evidence that a safe and cost-effective alternative to pharmacologic management exists for the long-term weight management of obesity.

We thank research nurse Martha Pontes and research assistant Brenda Conway for their supervision of the outpatient clinical services and dedication to the execution of the study protocol; Michelle Kienholz for reviewing and editing the manuscript; and all the subjects who participated and continue to participate in this study.

REFERENCES


