Diet and Exercise in the Treatment of Obesity

Effects of 3 Interventions on Insulin Resistance

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Background: In short-term studies, diet and exercise both improve insulin sensitivity.

Objective: To determine the effects of a 48-week supervised diet and exercise program on weight and insulin sensitivity after initial weight loss and weight maintenance, and then subsequent weight regain over 96 weeks.

Methods: Forty-five obese women were randomly assigned to 1 of 3 treatment groups: (1) diet alone, (2) diet and aerobic training, and (3) diet and strength training. All subjects received the same 48-week group behavior modification program and diet (approximately 3879 kJ/d [approximately 925 kcal/d] for the first 16 weeks; approximately 6276 kJ/d [approximately 1500 kcal/d] thereafter). Exercising subjects were provided 3 supervised exercise sessions per week for the first 28 weeks and 2 sessions weekly until week 48. During weeks 48 to 96, subjects were unsupervised. Oral glucose tolerance tests were performed at baseline and weeks 16, 24, 44, and 96.

Results: Subjects across the 3 conditions achieved a mean weight loss of 13.8 kg by week 16, which was associated with decreased insulin levels (61.8% of baseline). There were no significant differences among groups in changes in body mass index, which is a measure of weight in kilograms divided by the square of the height in meters, weight, glucose tolerance, or insulin levels at weeks 16, 24, and 44. No additional beneficial effect of aerobic or strength exercise on insulin resistance, as reflected by serum insulin levels before and after a glucose load, was demonstrated. The 22 subjects who were studied at week 96 maintained a loss of approximately 10% of initial weight. Insulin levels, however, had returned to pretreatment levels.

Conclusions: This study confirms the beneficial effect of weight reduction on hyperinsulinemia in obese individuals. Participation in supervised exercise did not result in additional improvement in weight loss or insulin sensitivity. We also observed a marked increase in insulin levels with only partial weight regain. Determining the amount of sustained weight loss necessary for continued improvement in insulin sensitivity will require further study.

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Obese individuals are frequently insulin resistant. This is a serious public health problem since obesity is common, and insulin resistance and hyperinsulinemia are associated with an increased risk of the development of diabetes, hypertension, and atherosclerosis.1 Normal glucose tolerance is maintained in many obese individuals by increased insulin secretion, resulting in hyperinsulinemia.2 With weight loss, insulin resistance decreases, and basal and postprandial glucose and insulin levels are similarly reduced.3 Such improvements have been observed whether weight was lost with a low-calorie (ie, approximately 4185 to 6280-kJ/d [1000 to 1500-kcal/d]) or very low-calorie (approximately 1675 to 3350-kJ/d [400 to 800-kcal/d]) diet.4,6

Exercise also improves insulin sensitivity and glucose tolerance.7 Several long-term studies6-10 found improved insulin action in exercise-trained obese individuals, even in the absence of significant weight loss. These findings suggest that diet and exercise have independent effects on insulin resistance and that the combination of diet and exercise may produce greater benefits than treatment by diet alone.11

Our study examined changes in insulin resistance in 45 obese women who participated in a 48-week weight loss program as described previously.12 Subjects were randomly assigned to 1 of 3 conditions: (1) diet alone, (2) diet and aerobic exercise, or (3) diet and strength training. Strength training was included because of findings that it may be associ-
SUBJECTS AND METHODS

SUBJECTS

The 45 women who participated in this study were drawn from the first cohort of a larger study of diet and exercise as described previously.\(^1\) Subjects were 43.3 ± 1.1 years old (mean ± SEM), with a baseline weight of 96.9 ± 2.2 kg and a body mass index (BMI, a measure of weight in kilograms divided by the square of height in meters: weight (kg)/[height (m)]\(^2\)) of 35.9 ± 0.9. Before treatment they completed an initial interview in which the requirements of the study were described and subjects’ psychological status was assessed.\(^2\) Subjects also underwent a medical evaluation to identify contraindications including a recent myocardial infarction; a history of cerebrovascular, kidney, or liver disease; cancer; diabetes; pregnancy; or the use of medications known to affect weight or energy expenditure.\(^3\) In addition, they were asked if they had a first-degree relative with diabetes, hypertension, obesity, or coronary artery disease. In the final screening, all subjects completed a stress test to rule out cardiac abnormalities that might be exacerbated by exercise training. Subjects gave their written informed consent to participate. This study was approved by the institutional review boards of the SUNY Health Science Center at Syracuse and Syracuse University, Syracuse, NY.

PROCEDURES

Subjects were randomly assigned to 1 of 3 treatment conditions: (1) diet and behavior therapy alone; (2) diet, behavior therapy, and aerobic training; or (3) diet, behavior therapy, and strength training (Table 1). For the first 28 weeks, all subjects attended weekly 90-minute group treatment sessions of 7 to 10 members each. From weeks 29 to 48, they attended 10 biweekly group sessions. Sessions were led by clinical psychologists as described previously.\(^4\) Subjects attended group sessions once every 3 months in the year following treatment.

DIET

All subjects were prescribed the same diet. They were asked to maintain their usual food intake during the first week. During weeks 2 to 17, they were prescribed a diet of approximately 3879 kJ/d (925 kcal/d) that consisted of 4 servings daily of a liquid meal replacement combined with a shelf-stable dinner entrée and 2 cups of salad. Each serving of the liquid diet provided 628 kJ (150 kcal), 13 g of protein, 11.2 g of carbohydrate, and 5 g of fat (Nutritional Formula, Sandoz Nutrition Co, Minneapolis, Minn). Each of the dinner entrées provided approximately 1255 kJ (approximately 300 kcal), 20 g of protein, 35 to 40 g of carbohydrate, and 7 g of fat (Health Recipes, Sandoz Nutrition Co).

Beginning at week 18, subjects decreased their consumption of the liquid diet while increasing consumption of conventional foods. The liquid supplement was eliminated first at breakfast, followed by the midafternoon meal, and then lunch. This occurred at weeks 18, 19, and 20, respectively, at which time subjects were prescribed approximately 4405 kJ/d (approximately 1053 kcal/d), approximately 4815 kJ/d (approximately 1150 kcal/d), and approximately 5235 kJ/d (approximately 1250 kcal/d), respectively. This refeeding protocol was supervised by a registered diettitian who co-led group sessions from weeks 17 to 26 and met with subjects once individually during weeks 21 to 23 to assist with meal planning. Beginning at week 22, subjects were instructed to consume a self-selected diet of approximately 6280 kJ/d (1500 kcal/d), with 12% to 15% of energy from protein, 55% to 60% from carbohydrate, and 25% to 30% from fat.

EXERCISE CONDITIONS

All subjects in the exercise conditions were provided 3 on-site, supervised training sessions per week (on nonconsecutive days) for the first 28 weeks, 2 workouts per week from weeks 29 to 48, and were unsupervised thereafter. Subjects exercised with members of their behavioral treatment groups.

Diet and Aerobic Training

Subjects (n = 14) in this condition participated in step aero-

ics. Each training session was preceded by a 5- to 10-

minute warm-up and followed by a 5-minute cool-down

period. Subjects began exercising for 12 minutes at week 1 and added 2 minutes to the routine each week so that by week 14 they performed 40 minutes of actual stepping. All subjects began using a 10-cm step; those who could exercise comfortably on either a 15- or 20-cm step did so beginning at week 5. Subjects were instructed to exercise at a moderate intensity level, as judged by a score of 11 to 15 on Borg Rating of Perceived Exertion Scale.\(^5\) Subjects in this condition agreed not to engage in resistance training at any time during the study. During weeks 29 to 48, they

showed that weight loss is associated with significant improvements in obesity-related health complications. Less, however, is known about long-term changes in health accompanying weight loss.

RESULTS

WEIGHT LOSS

Subjects in all 3 groups lost weight during the first 16 weeks of treatment (Figure 1). At week 16, the mean weight loss was 13.8 kg, and this weight loss was main-

ated with better maintenance of fat-free mass during weight loss than is diet alone or diet and aerobic exer-

ise.\(^6\) Subjects were assessed after an initial 16 weeks of consuming a portion-controlled diet of approximately 3879 kJ/d (approximately 925 kcal/d) and at weeks 24 and 44 when they were prescribed an approximately 5025-

to 6280-kJ/d (approximately 1200 to 1500-kcal/d) diet of conventional foods. Twenty-two of the 45 women were assessed approximately 1 year after treatment (ie, week 96). This last measurement provided an opportunity to assess the effects on insulin and glucose levels of long-term changes in body weight when subjects had stopped dieting and exercising regularly. Short-term studies\(^7\) have

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were assisted in developing a personal program of aerobic exercise to replace the third exercise session that was deleted from their supervised training. During the initial 24 weeks of the study, subjects in this group attended a mean ± SEM of 73.8% ± 4.7% (n = 16 subjects) of possible exercise sessions, which decreased to 65.8% ± 8.4% (n = 12 subjects) from weeks 25 to 40. From weeks 48 to 96, subjects were encouraged to continue exercising but were not supervised. Seven subjects returned at week 96 for final assessments.

Diet and Resistance Training

These subjects (n = 16) engaged in resistance training using equipment from Universal Gym Equipment (Cedar Rapids, Iowa). The circuit of exercises targeted the large muscle groups. At week 1 subjects were familiarized with the equipment, and at week 2 they performed 1 set each on the bench press, latissimus pull down, chest fly, shoulder press, leg extension and curl; leg press, arm curls, and extensions; and sit-ups and back extensions. Subjects performed the exercises with a resistance that allowed them to do 10 or more repetitions but not more than 14. Initial workouts lasted approximately 20 minutes exclusive of the 5- to 10-minute warm-up and cool-down periods. From weeks 3 to 14, an extra set of each of the exercises was added to the routine so that each subject eventually did 2 sets of each exercise at each session. By the end of week 14, subjects engaged in weight training for approximately 40 minutes per session. This time was held constant from weeks 14 to 48 but resistance was increased whenever subjects were able to perform more than 14 repetitions for 2 consecutive sets. Subjects agreed not to initiate aerobic training at any time during the study. During weeks 29 to 48, they were assisted in developing a personal program of resistance training to replace the third session deleted from the supervised practice. During the initial 24 weeks of the study, subjects in this group attended a mean ± SEM of 73.8% ± 4.7% (n = 16 subjects) of possible exercise sessions, which decreased to 65.8% ± 8.4% (n = 12 subjects) from weeks 25 to 40. From weeks 48 to 96, subjects were encouraged to continue exercising but were not supervised. Six subjects from this group returned at week 96 for final assessments.

Diet Alone

Subjects (n = 15) in this condition agreed not to engage, during the study, in any program of regular activity that resembled the aerobic or strength training conditions. A review of their weekly activity logs indicated that none of the subjects initiated such training. Subjects were allowed to maintain habitual lifestyle activities, such as occasionally playing tennis, bowling, or going for a walk at lunch time but all agreed not to increase the frequency or intensity of such activities. Nine of these subjects participated in the week 96 assessment.

ORAL GLUCOSE TOLERANCE TESTS

Baseline oral glucose tolerance tests were performed after an overnight fast at the Clinical Research Unit of University Hospital, Syracuse, NY. These tests were repeated at the end of the approximately 3879-kJ/d (925-kcal/d) diet period (week 16) and at weeks 24, 44, and 96. For each test, subjects received a 75-g glucose load orally, and glucose and insulin levels were drawn at 0, 30, 60, 90, 120, and 180 minutes. Serum glucose levels were measured using a hexokinase ultraviolet method (Paramax 7202X, Dade, Irving, Calif), and insulin levels were measured using a human insulin–specific radioimmunoassay kit (Linco Research Inc, St Louis, Mo). All 45 subjects returned for the 24-week visit, and 36 subjects were studied at week 44 and 22 at week 96. At each visit, fasting weight and sitting blood pressure were obtained. Baseline characteristics are listed in Table 1.

BLOOD PRESSURE

Blood pressure was assessed on the same schedule as oral glucose tolerance tests. Blood pressure was measured using a sphygmometer (Tycos sphygmometer, Welch Allyn, Arden, NC) once at each visit with subjects fasted and rested, in the seated position.

STATISTICAL ANALYSES

The SPSS statistical software (Statistical Package for Social Science, SPSS Inc, Chicago, Ill) was selected to analyze the data. A preliminary analysis of variance showed that there were no significant differences in baseline characteristics among the 3 conditions. Two-way analysis of variance was used to determine the differences on insulin levels on family history and time, as well as their interaction. A series of 1-way analyses of variance was used to determine the group differences in body weight, BMI, glucose levels (area under the curve [AUC]), and insulin levels (AUC). The Duncan test was used to determine specific differences among groups. Statistical significance was set at P<.05.

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groups throughout the course of the study (Figure 2 and Figure 3). Fasting glucose levels and AUC glucose decreased slightly after weight loss, but this change was not significant.

INSULIN LEVELS

At the beginning of the study, mean fasting insulin levels were 15.4 ± 1.0 mU/L. Fasting insulin levels and AUC insulin at baseline did not differ significantly among groups. After the initial weight loss (week 16), fasting insulin levels decreased to a mean ± SEM of 10.6 ± 0.6 mU/L (P < .001), and AUC insulin decreased to 61.8% of baseline (P < .05; Figures 2 and 3). The insulin levels then remained stable from weeks 16 to 44 (Figures 2 and 3). There were no significant differences in changes in insulin levels (fasting or AUC) among the strength training, aerobic exercise, or diet alone groups at any time.

Week 96 Assessment

The AUC insulin levels were compared at weeks 0, 44, and 96 for the 22 subjects who completed all assessments. There was a significant decrease from week 0 to week 44 (Figure 4). Fasting and AUC insulin levels then rose in 19 (86%) of 22 subjects. Insulin levels increased from weeks 44 to 96, such that the AUC at week 96 was not significantly different from baseline. This is in contrast to weight, which remained stable from weeks 44 to 96. Therefore, weight regain was associated with the return of hyperinsulinemia, despite subjects maintaining a weight loss of approximately 10% of initial weight.

Family History

The presence of a first-degree relative with diabetes, hypertension, obesity, or coronary artery disease was determined as described earlier. Insulin levels were analyzed for subjects with or without a family history of these conditions at baseline and week 44. No significant differences in insulin levels (AUC) were found for subjects with a family history of diabetes, hypertension, or coronary artery disease. At baseline, however, insulin levels (AUC) were significantly higher in subjects with a family history of obesity (n = 39) compared with those without a family history (n = 6) (P = .004). Differences were not significant at week 44.

BLOOD PRESSURE

Analyses of blood pressure data showed no significant changes in systolic blood pressure over the course of the study. However, significant changes in diastolic blood pressure were demonstrated with weight loss (Table 2, P < .02). There were significantly lower diastolic blood pressures at 16, 24, and 44 weeks compared with baseline, but not at 96 weeks. No significant differences in changes in blood pressure among treatment groups were found.
Exercise would produce significantly larger weight losses than treatment by diet alone, a prediction that was not confirmed in this study or our larger study of 128 women.12 Two factors may have contributed to our failure to observe additive effects of diet and exercise. First, subjects may not have exercised at sufficient intensity or duration to yield an effect. Positive results might have been obtained during the first 28 weeks if subjects had exercised 4 or 5 times a week, rather than only 3 times. Such a high frequency of training, however, is not realistic for most obese clinic patients. A second more likely explanation is that the 3879-kJ/d (925-kcal/d) diet that subjects consumed during the first 16 weeks induced such large, rapid reductions in weight and insulin levels, such as to mask any possible effects of exercise. Studies of both very low-energy diets4,5 and gastric surgery19 have shown that severe caloric restriction alone produces marked improvements in insulin and glucose levels, long before sub-

Figure 2. Changes in mean serum glucose and insulin concentrations during oral glucose tolerance tests in obese women treated with diet and behavior therapy alone (Diet Alone); diet, behavior therapy, and aerobic exercise (Aerobic Exercise); and diet, behavior therapy, and strength training (Strength Training) at baseline (circles) and after 16 weeks (squares), 24 weeks (triangles), and 44 weeks (diamonds).
Projects have lost significant amounts of weight. We believe that the potential additive effects of diet and exercise are most likely to be observed when obese individuals are subjected to minimal caloric restriction and lose modest amounts of weight. Andersen and colleagues recently reported that obese individuals who reduced their BMI by 2.16 by the combination of diet and exercise experienced significantly larger reductions in insulin levels than did those treated by diet alone.

We assessed insulin levels (before and after a glucose load) after initial weight loss and subsequent weight regain over a 96-week period. We found that although our subjects’ weight remained almost 10% below baseline at week 96, insulin levels were not similarly reduced. With weight regain over the follow-up year, insulin levels returned to their previously elevated baseline levels, despite the maintenance of a large weight loss. These results suggest that a 5% to 10% weight loss in the absence of improved eating and exercise habits may not improve insulin resistance. Wing and Jeffery observed more favorable long-term changes in insulin levels with weight regain. Thus, additional studies are needed to determine the long-term effects on health of modest weight losses.

It is possible that a weight threshold exists, such that a specific BMI must be attained or a certain magnitude of weight loss must be maintained to continue to achieve metabolic benefit. A BMI of less than 29.7 was reported by Barakat and colleagues to be associated with improvement in insulin sensitivity, whereas higher breakpoint BMIs were correlated with diastolic and systolic blood pressure. In our subjects, BMI decreased from 36 at baseline to 30.5 at week 44, and then increased to 32.7 at week 96. The final BMI at week 96 was above the threshold BMI for insulin sensitivity suggested by Barakat et al. It is therefore possible that people with lower baseline and post-weight loss (weight maintenance) BMIs would have sustained improvement in insulin sensitivity with a similar absolute amount of weight loss and weight regain. Subjects studied by Wing and Jeffery were less obese at baseline than our patients and maintained an average BMI at follow-up of less than 29.7.

Genetic factors contribute to the development of the insulin-resistance syndrome, diabetes, and cardiovascular disease. A previous study of obese middle-aged women found that a parental history of diabetes or hypertension was associated with hyperinsulinemia, independent of BMI. In this study, insulin levels (AUC) were higher at baseline for subjects with a first-degree relative with obesity, but were not significantly different at baseline for those with first-degree relatives.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Baseline</th>
<th>16 wk</th>
<th>24 wk</th>
<th>44 wk</th>
<th>96 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>42</td>
<td>43</td>
<td>45</td>
<td>36</td>
<td>21</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>121.5 ± 2.8</td>
<td>115.2 ± 2.5</td>
<td>114.2 ± 2.2</td>
<td>118.1 ± 2.6</td>
<td>119.1 ± 3.5</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>81.1 ± 1.7</td>
<td>74.7 ± 1.7</td>
<td>73.8 ± 1.4</td>
<td>74.6 ± 1.7</td>
<td>77.0 ± 3.2</td>
</tr>
</tbody>
</table>

*Values are mean ± SEM. Total number of subjects at baseline n = 45.
†Significantly different from baseline (P < .05; 1-way analysis of variance).
with diabetes, hypertension, or coronary heart disease. Responses to weight loss did not differ in those with or without a family history of these insulin-resistant conditions.

Women in this study and in our larger investigation who were treated by diet and exercise did not maintain their weight losses (1 year after treatment) any better than those treated by diet alone. Randomized trials are divided between those who have or not found that an initial program of supervised exercise training facilitates long-term weight control. By contrast, virtually all correlational studies, including our own, have found that patients who reported exercising frequently during follow-up maintained larger long-term weight losses. This finding underscores the need to find methods of improving exercise adherence once subjects have completed formal treatment.

In conclusion, we found improvement in insulin sensitivity with weight loss in obese women. Subjects in the exercising groups had similar weight losses as those treated by diet alone. We observed no significant differences in changes in insulin levels between subjects who were enrolled in the diet alone or supervised exercise groups (aerobic or strength training). The partial weight regain that was observed in all treatment groups by week 96 was accompanied by an increase in insulin levels, with a return to elevated baseline levels. Determination of whether a greater specific amount of weight loss needs to be maintained or whether a defined BMI threshold must be achieved to preserve improvements in insulin sensitivity will require additional study.

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