Improved Glycemic Control After Supervised 8-wk Exercise Program in Insulin-Dependent Diabetic Adolescents

RON STRATTON, PhD, DON P. WILSON, MD, ROBERT K. ENDRES, MD, AND DAVID E. GOLDSTEIN, MD

Eight insulin-dependent adolescents (4 boys, 4 girls) participated in an 8-wk program of supervised exercise, and 8 matched controls were encouraged to exercise on their own without supervision. All 16 subjects were asked to follow a standard ADA diet plan, kept a self-reported log of caloric intake, and met with a dietitian weekly to review their diets. Exercise for the supervised subjects was scheduled between the routine afternoon snack and the evening meal, and subjects were asked not to consume additional food on exercise days. After the 8-wk program, glycemic control, as measured by glycosylated serum albumin and blood glucose values (but not by glycosylated hemoglobin), improved in the supervised-exercise group despite reduced daily insulin dosage. Cardiorespiratory fitness, as measured by voluntary maximum treadmill time (Bruce protocol) and submaximal exercise heart rates, also improved. No changes were observed in the unsupervised control group. *Diabetes Care* 10:589–93, 1987

The importance of exercise in diabetes management has been recognized for centuries (1). In the post-insulin era, exercise has been formally assigned a place with insulin and diet, forming the familiar triad of therapy commonly employed in diabetes management (2).

Our study was designed to evaluate parallel responses in glycemic control to an 8-wk program of supervised, moderate exercise aimed at improving cardiorespiratory fitness. Glycemic control was assessed by glycosylated serum albumin and glycosylated hemoglobin. Because of its shorter half-life, measurement of glycosylated serum albumin should allow detection of glycemic changes earlier than glycosylated hemoglobin (3). For this study, additional snacks were not used to compensate for exercise, in favor of scheduling of exercise with routine food intake and blood glucose monitoring. Reductions in daily insulin dosage were used to avoid hypoglycemia, if necessary.

MATERIALS AND METHODS

Subjects. Sixteen Caucasian adolescents (8 boys, 8 girls) with insulin-dependent diabetes mellitus (IDDM) served as subjects. Baseline descriptive statistics are included in Table 1. All were on a split-mixed regimen of regular and NPH insulin, with subcutaneous injections by needle before the morning and evening meals. No preference was given to injection sites on scheduled exercise days. All subjects had been previously instructed in the daily self-management of their diabetes. Exercise history varied from sedentary individuals to school athletes. Informed consent was obtained from all participants and their parent or guardian before the study, in compliance with the institutional review board. The subjects were each randomly assigned to either the control or experimental group, resulting in four boys and four girls in each group.

Evaluation and exercise program. Initial evaluation for all 16 subjects included fasting morning blood samples for glycosylated hemoglobin, glycosylated albumin, total albumin, glucose, cholesterol, triglycerides, and high-density lipoprotein (HDL) cholesterol; treadmill stress test (Bruce protocol, voluntary maximum); skinfolds (British Indicators calipers—tricep, subscapular, midaxilla, iliac crest, abdominal, thigh, and in males, pectoral); height; and weight.

Each subject also met with a dietitian, and a standard ADA diet was reviewed and outlined. All subjects demonstrated adequate knowledge of the diet. Each was asked to maintain the diet throughout the study with no additional food intake on exercise days. Exercise was scheduled after school, after the regular afternoon snack and before the evening meal. Subjects were instructed that blood glucose would be monitored, and adjustments in insulin dosage would be made if necessary to avoid hypoglycemia that may result from an increase in activity. All subjects kept a record of daily caloric

TABLE 1
Baseline characteristics and comparisons (Student's *t* test) of supervised-exercise and control subjects

	Supervised exercise	Control
Age (yr)	15.1 ± 1.2	15.5 ± 0.9
Duration IDDM (yr)	3.7 ± 2.1	5.5 ± 3.3
Weight (kg)	59.0 ± 6.1	60.4 ± 8.7
Height (cm)	160.2 ± 7.5	164.3 ± 5.2
Sum of skinfolds (mm)	136.2 ± 60.6	122.7 ± 44.6
Fasting blood glucose (mg/dl)	218.1 ± 116.5	240.4 ± 115.2
Glycosylated hemoglobin (%)	10.1 ± 2.2	11.7 ± 2.9
Glycosylated serum albumin (%)	5.0 ± 3.6	4.9 ± 3.9
Plasma albumin (g/dl)	4.5 ± 0.2	4.5 ± 0.2
Total daily insulin (U)	55.9 ± 12.5	61.1 ± 14.8
Bruce treadmill time (min)	12.1 ± 1.5	12.4 ± 2.0
Submax heart rate (bpm)*	175.0 ± 11.8	168.1 ± 12.9
Cholesterol (mg/dl)	213.9 ± 35.1	234.3 ± 65.4
Triglycerides (mg/dl)	100.8 ± 110.9	98.7 ± 59.0
HDL cholesterol (mg/dl)	42.4 ± 8.2	44.4 ± 10.3

There were no significant differences between the groups. There were eight subjects (4 boys, 4 girls) in each group.
*Heart rate at completion of 10th min, Bruce treadmill protocol.

intake and met with the dietitian each week to review their food intake. These self-reports indicated adequate knowledge and adherence to the diet by all subjects.

The control subjects were instructed as to the importance of regular exercise and were given an outline of a recommended exercise program, including frequency (3–6 days/wk), duration (20–60 min), and various recommended activities including jogging, cycling, swimming, basketball, and tennis. They were asked to exercise regularly on their own. The experimental subjects came to the hospital exercise area for 30–45 min of supervised exercise, 3 days/wk for 8 wk. Exercise activities included highly aerobic activities such as jogging on a motorized treadmill or riding a cycle ergometer on 2 of the days. On 1 of the 3 days, subjects were allowed to choose activities such as basketball, recreational swimming, or resistance exercise machines. Blood glucose was measured before and after exercise on at least two of the three weekly sessions in capillary blood samples taken by fingerstick and tested with reagent strips and a meter (AccuChek, Biodynamics, Indianapolis, IN). All 16 subjects repeated the initial evaluation procedure at the end of the 8-wk program.

Analytic methods. All venous blood samples were obtained in the postabsorptive state after a 10-h fast. Plasma samples were stored at −80°C until analyzed. Plasma glucose was determined by the Worthington assay. Total plasma albumin was determined by a colorimetric method (Lancer, St. Louis, MO). Total glycosylated hemoglobin concentrations were determined by the microcolumn technique with preincubation in saline to remove the labile fraction (ion exchange, Isolab, Akron, OH). Glycosylated serum albumin was determined at the University of Missouri with boronic acid affinity chromatography. Blood lipid analyses were performed at the Mayo Clinic laboratory.

One male subject in the control group had grossly lipidemic blood samples (cholesterol 478 and 368 mg/dl, triglycerides 2032 and 1092 mg/dl, HDL 14 and 19 mg/dl, before and after the study, respectively). This made determination of glycosylated serum albumin and total plasma albumin in this subject impossible by our methods. These values were therefore excluded from statistical analyses, leaving 7 subjects for the control group for blood lipids, glycosylated serum albumin, and total plasma albumin.

Baseline comparisons of the two groups were made with Student's *t* test for independent samples. The effects of the 8-wk treatment were statistically analyzed by two-way (groups × treatment) analyses of variance with repeated measures (test-retest). Simple comparisons were used to determine within-group differences on test-retest when a significant repeated-measures effect or treatment × repeated measures interaction was observed. Values from blood glucose monitoring in the first 3 wk of the exercise program were compared with values from the last 3 wk by Student's *t* test. All data are reported as means ± SD.

RESULTS

Refer to Table 1 for a summary of between-group comparisons on baseline evaluation. No baseline differences were observed. All test-retest comparisons are summarized in Table 2.

Cardiorespiratory fitness and body composition. Analysis of variance of maximum voluntary Bruce treadmill time revealed a significant repeated-measures effect [$F(1,14) = 4.43$, $P < .05$]. Simple comparisons revealed a significant increase in treadmill time for the supervised-exercise group from 12.1 ± 1.5 to 13.6 ± 2.0 min [$F(1,7) = 6.62$, $P < .05$], with no statistically significant change for the control group.

Submaximal heart rates, based on the heart rate observed at the completion of the 10th min of the Bruce treadmill protocol, were also evaluated as a reflection of cardiorespiratory fitness. Analysis of variance revealed a significant treatment × repeated measures interaction [$F(1,14) = 4.53$, $P < .05$]. Simple comparisons revealed a significant decrease in submaximal heart rate for the supervised-exercise group from 175.0 ± 11.8 to 160.8 ± 12.8 beats/min [$F(1,7) = 13.2$, $P < .01$]. The small mean decline for the control group was not statistically significant.

Analyses of variance were not statistically significant for height, weight, or sum of skinfolds.

Glycemic control. Analysis of variance of glycosylated serum albumin revealed a significant treatment × repeated measures interaction [$F(1,13) = 13.6$, $P < .01$]. Simple comparisons revealed a significant decline in glycosylated serum albumin for the supervised-exercise group from 5.03 ± 3.6 to 4.20 ± 3.2% [$F(1,7) = 14.7$, $P < 0.01$], with no significant change for the control group. Analyses of variance were not statistically significant for total plasma albumin, glycosylated hemoglobin, or fasting blood glucose.

Daily insulin dosage (total U/day) was reduced in five of

TABLE 2
Effects of 8-wk exercise program

	Supervised exercise			Control*	
	Before	After	P	Before	After
Bruce treadmill time (min)	12.1 ± 1.5	13.6 ± 2.0	.05	12.4 ± 2.0	12.6 ± 2.5
Submax heart rate (bpm)†	175.0 ± 11.8	160.8 ± 12.9	.01	168.1 ± 12.9	165.1 ± 20.6
Total daily insulin (U)	55.9 ± 12.5	50.8 ± 13.5	.06‡	61.1 ± 14.8	61.1 ± 14.8
Glycosylated albumin (%)	5.0 ± 3.6	4.2 ± 3.2	.01	4.9 ± 3.9	5.0 ± 3.8
Plasma albumin (g/dl)	4.5 ± 0.2	4.4 ± 0.3	NS	4.5 ± 0.2	4.5 ± 0.2
Glycosylated hemoglobin (%)	10.1 ± 2.2	9.9 ± 2.4	NS	11.7 ± 2.9	11.4 ± 2.9
Fasting glucose (mg/dl)	218.1 ± 116.5	206.0 ± 115.8	NS	240.4 ± 115.2	213.9 ± 136.4
Sum of skinfolds (mm)	136.2 ± 60.6	129.3 ± 50.9	NS	122.7 ± 44.6	123.6 ± 39.8
Cholesterol (mg/dl)	213.9 ± 35.1	214.5 ± 66.1	NS	234.3 ± 65.4	223.3 ± 65.4
Triglycerides (mg/dl)	100.8 ± 110.9	85.6 ± 51.7	NS	98.7 ± 59.0	123.6 ± 95.9
HDL cholesterol (mg/dl)	42.4 ± 8.2	42.9 ± 8.0	NS	44.4 ± 10.3	40.3 ± 10.8
Weight (kg)	59.0 ± 6.1	60.0 ± 5.7	NS	60.4 ± 8.7	60.6 ± 8.5
Height (cm)	160.2 ± 7.5	161.0 ± 7.1	NS	164.3 ± 5.2	165.3 ± 5.7

Comparison of test-retest values in supervised-exercise subjects and nonsupervised (control) subjects. Statistically significant changes were determined by simple comparisons after significant repeated-measures effect or repeated measures × treatment interaction on ANOVA. NS, not significant.
*Differences were not significant for control subjects.
†Heart rate at completion of 10th min, Bruce treadmill protocol.
‡Five of 8 supervised-exercise subjects reduced their daily insulin dosage, whereas other 3 remained constant. Insulin dosage remained constant in all control subjects. ANOVA revealed significant repeated measures × treatment interaction ($P < .05$).

the eight supervised-exercise subjects and remained constant in the other three. Daily insulin dosage remained constant in all eight control subjects. Analysis of variance revealed a significant treatment times repeated measures interaction [$F(1,14) = 4.58$, $P < .05$]. The decline for the supervised-exercise group from 55.9 ± 12.5 to 50.8 ± 13.5 U/day approached significance [$F(1,7) = 4.58$, $P < .06$].

Results of preexercise blood glucose monitoring in the supervised-exercise group revealed a significant decline in mean blood glucose values (mg/dl) in the last 3 wk of the exercise program from those in the first 3 wk (198.0 ± 75 to 160.8 ± 69 mg/dl; $t = 2.53$, df = 97, $P < .01$).

Lipids. Analyses of variance were not statistically significant for cholesterol, triglycerides, or HDL cholesterol.

DISCUSSION

In adequately insulinized, well-controlled diabetic subjects, exercise induces a decline in blood glucose (1). This acute decline is primarily attributed to increased muscle fuel consumption as glucose becomes a primary source of fuel for the exercising muscles (1,4). If exercise is of sufficient duration and intensity to deplete glycogen stores, the enhanced muscle glucose uptake continues in the hours after exercise as glycogen stores are repleted (1,4). As a result, most people with IDDM must consider dietary supplements, insulin reduction, and/or timing of exercise with food intake to accommodate physical activity (5). Exercise also appears to enhance the body's sensitivity to insulin (4,6,7), particularly if the exercise is habitual and aerobic (4).

Despite these acute and chronic influences of exercise, the literature is far from unanimous in clearly demonstrating beneficial effects on glycemic control. Whereas Campaigne et al. (8) demonstrated a decrease in glycosylated hemoglobin in children completing a 12-wk exercise program, a second study failed to reveal similar effects in adolescents, although profiles of blood lipids improved (9). Similarly, other studies have failed to demonstrate significant changes in glycosylated hemoglobin, although other health and fitness parameters improved (10–12).

The failure to demonstrate lower glycosylated hemoglobin values may be at least partly due to the emphasis on increased food consumption to protect against exercise-induced hypoglycemia. Zinman et al. (11) reported a significant increase in caloric intake among their subjects on exercise days, commenting that "several patients clearly indicated that during exercise days they could 'liberalize' their diet and considered this one of the advantages of regular exercise."

Another possible reason for failure to demonstrate glycemic improvement associated with exercise may be the sensitivity of the glycosylated hemoglobin measurement. Due to the long survival time of red blood cells (120 days), changes may not be readily apparent after 8–12 wk of thrice-weekly moderate exercise, particularly if diet and exercise are adjusted to compensate for the glycemic effects of the activity. In a study of much longer duration, Peterson et al. (13) demonstrated a steady decline in glycosylated hemoglobin in 10 IDDM patients participating in an 8- to 10-mo program of supervised exercise and glucose monitoring.

In agreement with previous studies, our results suggest that cardiorespiratory fitness improves after supervised exercise of

moderate duration, frequency, and intensity in IDDM adolescents. Unlike most previous studies, our subjects were instructed not to consume additional food before exercise. In five of the eight exercising subjects, a gradual modest decrease in total daily insulin was used, whereas daily insulin remained constant for the other three. No significant changes were observed in blood lipids, weight, or skinfolds, although this is perhaps not surprising considering the relatively short 8-wk duration of the exercise program.

As with most previous studies, mean glycosylated hemoglobin did not change in either the exercising or control group. A significant mean decline in glycosylated serum albumin was observed in the supervised-exercise group, however. In addition, blood glucose concentrations before exercise revealed significantly lower values in the last 3 wk of the exercise program compared with those of the first 3 wk, despite a reduction in insulin dosage in most subjects. Jones et al. (3) studied newly diagnosed diabetic patients and found glycosylated serum albumin to be a sensitive index of metabolic response to therapeutic intervention in the first 8 wk after diagnosis. Our results suggest that this test is similarly sensitive in established patients following a program emphasizing exercise for improving fitness and glycemic control.

Convertino et al. (14) demonstrated an increase in total plasma albumin associated with daily 2-h exercise training sessions for 8 days, a result that could potentially influence the percentage of glycosylated albumin measured. Despite measurable improvement in physical fitness during our 8-wk program, neither the supervised-exercise group nor the control group had any change in their total plasma albumin concentrations. Thus, a dilutional effect on the percentage of glycosylated albumin is unlikely.

In addition to the exercise activities, other factors may have influenced the improved metabolic control observed. All subjects met with the dietitian weekly, and experimental subjects also participated in supervised exercise 3 days/wk. As a result, the supervised-exercise subjects interacted more frequently with the clinic staff. In addition, absolute dietary compliance is difficult, if not impossible, to confirm in this type of study. We further recognize and have recently reported on problems with self-reported information in the adolescent population (15). Aside from these restrictions, however, we did not observe any difference in reports of caloric consumption nor in anthropometric measurements.

Our 8-wk program of moderate thrice-weekly supervised exercise in IDDM adolescents was associated with improved physical fitness as well as improved glycemic control, as measured by glycosylated serum albumin and blood glucose values, despite a reduction in daily insulin dosage in five of the exercising subjects and a constant daily insulin dosage in the other three. Additional food intake on exercise days was avoided by selective scheduling of exercise sessions and reduction in insulin dosage, if necessary. We conclude that improved cardiorespiratory fitness does occur in IDDM adolescents during a supervised 8-wk program of moderate exercise. Furthermore, parallel improvement in glycemic control can be demonstrated by changes in glycosylated serum albumin.

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From the Department of Family Practice, Children's Medical Center (R.S.), the Department of Pediatrics, H. Allen Chapman Research Institute of Medical Genetics (D.P.W.), and the Department of Pediatrics, St. Francis Health Institute (R.K.E.), University of Oklahoma Tulsa Medical College, Tulsa, Oklahoma; and the Department of Child Health, University of Missouri School of Medicine, Columbia, Missouri (D.E.G.).

Address correspondence and reprint requests to Ron Stratton, PhD, Children's Medical Center, 5300 East Skelly Drive, Tulsa, OK 74135.

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