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Insulin-Sensitivity Response to a Single Bout of Resistive Exercise in Type 1 Diabetes Mellitus

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Context: Little is known about the acute effects of resistance exercise on insulin sensitivity in people with type 1 diabetes. ***Design:*** Repeated-measures design with 2 independent variables: group (exercise and nonexercise control) and time (preexercise and 12 and 36 h postexercise). ***Setting:*** General Clinical Research Center, Temple University Hospital, Philadelphia, PA. ***Patients:*** 14 physically active subjects (11 men and 3 women) with type 1 diabetes. ***Intervention:*** The exercise group completed 5 sets of 6 repetitions of strenuous (80% 1-RM) quadriceps and hamstring exercises while the control group performed only activities of daily living. ***Main Outcome Measures:*** Insulin sensitivity was assessed with the euglycemic-hyperinsulinemic-clamp technique preexercise and 12 and 36 h postexercise. ***Results:*** Insulin-sensitivity values were not significantly different between the exercise and control groups (P = .92) or over time (P = .67). ***Conclusions:*** A single bout of strenuous resistance exercise does not alter insulin sensitivity in people with type 1 diabetes.

Keywords: blood glucose, weight training, insulin clamp

Effective management of metabolic control plays an important role in the health of people with type 1 diabetes. Regular exercise, insulin therapy, and dietary modifications are vital tools used to achieve this goal. There are many benefits of regular exercise for people with type 1 diabetes. These may include normalization of prevailing blood glucose levels and improvements in insulin sensitivity.[1]

Although the effects of aerobic exercise have been studied and shown to improve insulin sensitivity, there is limited published research on the effects of acute and chronic resistance exercise on insulin sensitivity.[2] Published research on resistance exercise and type 1 diabetes reports the effects of chronic resistance exercise on glycosylated hemoglobin (HbA1c) levels as a measurement of long-term metabolic control.[3–5] Chronic resistance exercise has been shown to either decrease[3,4] or have no effect[5] on HbA1c levels, but those studies did not evaluate insulin sensitivity.

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Hornsby[2] noted that little is known about the acute effects of resistance exercise on metabolic control, including insulin sensitivity in people with type 1 diabetes. In contrast, several researchers[6–8] evaluated the acute effects of aerobic exercise on metabolic control and insulin sensitivity in individuals with type 1 diabetes. Although an acute bout of prolonged, moderate-intensity aerobic exercise is reported to improve insulin sensitivity, this benefit is often associated with an increased risk of postexercise hypoglycemia in people with type 1 diabetes.[6,7,9–11] It is interesting that recent data suggest that the risk of postexercise hypoglycemia is less for patients with type 1 diabetes when intermittent, high-intensity (ie, sprint) exercise is added to prolonged, moderate-intensity aerobic exercise.[12,13] Thus the purpose of this study was to evaluate the acute effects of strenuous resistance exercise on insulin sensitivity in people with type 1 diabetes because both the potential benefits and the risks of this type of acute exercise stimulus are unknown for this population.

Methods

The study used a repeated-measures design. Independent variables were group (exercise and nonexercise control) and time (preexercise and 12 and 36 hours postexercise). The dependent variable was insulin sensitivity, which was measured by the euglycemic-hyperinsulinemic-clamp technique.

Subjects consisted of 11 men and 3 women with type 1 diabetes 19 to 36 years of age. Female subjects were studied during the follicular phase of the menstrual cycle to minimize the unpredictable effects menstrual hormones may have on metabolic control. Subjects were physically active but not engaged in a resistance-exercise program at the time of the study. They were screened for the absence of the following significant disease complications: moderate nonproliferative retinopathy, proliferative retinopathy, neuropathy, microalbuminuria >300 mg/24, or serum creatinine >1.2 mg/dL (106.1 μmol/L). All subjects read and signed an informed-consent form approved by Temple University Hospital's institutional review board. Demographic and physical characteristics of the subjects are listed in Table 1.

Table 1 Demographic and Physical Characteristics of the Exercise and Control Group Participants, Mean ± SD

Variable	Exercise group (n = 7)	Control group (n = 7)
Age (y)	23.4 ± 4.0	26.3 ± 6.7
Height (cm)	174.4 ± 6.8	176.0 ± 8.2
Weight (kg)	81.9 ± 13.8	77.5 ± 13.5
Percent body fat	14.7 ± 6.1	16.1 ± 8.8
Baecke physical activity score[a]	9.1 ± 1.2	8.5 ± 1.3
Percent glycosylated hemoglobin	6.8 ± 1.5	8.3 ± 2.6
Years since type 1 diagnosis	5.9 ± 5.5	7.1 ± 3.9

[a] Baecke scores range from 3 to 15: A score of 3 reflects a low level of physical activity and a score of 15 reflects a high level of physical activity.

One-Repetition-Maximum Test

A one-repetition-maximum (1-RM) test was done on the quadriceps and hamstring muscle groups using the Body Masters TM system (Model 110 leg-extension apparatus and Model 112 standing leg-curl apparatus, Body Masters Sport Industries, Inc, Rayne, LA). After each successful lift, the resistance was increased 2.3 kg. The 1-RM was the most weight a subject could lift through the full range of motion. Subjects rested 3 minutes between test repetitions.

Blood Glucose Assessment

Blood glucose levels were measured in milligrams per deciliter, and testing was conducted before and after the 1-RM test using the One Touch Profile glucometer (Lifescan, Inc, Milpitas, CA). This was done to reduce the risk of exercise-induced hypoglycemia or exacerbating preexisting hyperglycemia. Subjects with a blood glucose level of 100 to 240 mg/dL were allowed to complete the 1-RM testing. Any subject with a blood glucose reading below 100 mg/dL was given approximately 20 g of carbohydrates, and the level was reassessed in 15 minutes. If the blood glucose reading was above 240 mg/dL the subject did not complete any further testing and was rescheduled for another day. None of the subjects required carbohydrate supplementation before 1-RM testing.

Euglycemic-Hyperinsulinemic Clamp

A euglycemic-hyperinsulinemic clamp was used to assess total-body insulin sensitivity preexercise and postexercise. During the application of the euglycemic-hyperinsulinemic clamp, plasma insulin was raised to a physiological postprandial level and maintained while 20% dextrose (Abbott Laboratories, North Chicago, IL) was infused at a variable rate to maintain a predetermined blood glucose level. Albumin was added to the insulin-infusion mixture to prevent the hormone from sticking to the plastic tubing surface. The glucose-infusion rate (GIR) is an index of total-body insulin sensitivity. As a means of standardizing this measure, GIR was measured in milligrams per kilogram of total body weight per minute.[14]

To minimize the effects of circadian rhythm on insulin sensitivity, each euglycemic-hyperinsulinemic-clamp application started and finished at a similar time of day (between 8 AM and 12 PM). A researcher began the procedure by inserting a polyethylene catheter into the subject's dorsal forearm vein for blood sampling. The forearm was wrapped in a heating blanket to increase blood flow. A second catheter was placed in the contralateral forearm vein for the infusion of insulin and glucose. Regular human insulin (Humulin R, Eli Lilly, Indianapolis, IN) was infused at a rate of 1 $mU \cdot kg^{-1} \cdot min^{-1}$ for 4 hours starting at 0 minutes. Blood glucose concentrations were maintained at approximately 110 mg/dL (6.1 mmol/L) by using a variable-rate infusion with 20% glucose as previously described.[14] Blood samples were drawn for free insulin every 60 minutes, and glucose concentrations at 15-minute intervals, for 4 hours. Blood glucose concentrations were determined every 15 minutes with a Beckman glucose analyzer (Palo Alto, CA), and glucose infusions were adjusted accordingly. The GIR needed to maintain euglycemia was used as an index of insulin sensitivity.

HbA1c Assessment

HbA1c was assessed as a measure of long-term metabolic control. For this measure, subjects pierced a finger to obtain a blood droplet. The blood droplet was then placed on a DCA HbA1c cartridge (DCA Analyzer, Bayer, Corp, Leighton, PA) that was inserted into a DCA 2000+ analyzer (Bayer, Corp). A reading was obtained 10 minutes later. The HbA1c value was measured as a percentage and has a normal range of 4% to 6%.

Skinfold Thickness Assessments

Skinfold thickness was assessed using a Lange skinfold caliper (Beta Technology, Cambridge, MD). The sums of 3 gender-specific anatomical sites were used for body-fat estimates by skinfold thickness: chest, abdomen, and thigh for men and triceps, suprailiac area, and thigh for women.[15] Body fat was calculated from the body-density value using the equation developed by Siri.[16]

Physical Activity Status

Current physical activity status was assessed using the modified Baecke physical activity questionnaire,[17] on which scores could range from 3 to 15. A score of 3 reflects a low level of physical activity, and a score of 15 reflects a high level of physical activity. The modified Baecke physical activity questionnaire is reliable for assessing physical activity during work, sports, and leisure time ($r = .89$).[18]

Data collection was completed over a period of 5 days. A period of 96 hours separated day 1 from day 2. Beginning with day 2 through day 5, subjects were hospitalized for a total of 4 consecutive days.

Day 1. Subjects were assigned randomly to either an exercise or a control group. The primary investigator measured and recorded each subject's age, height, weight, skinfold thickness, blood glucose level, HbA1c value, years since diabetes diagnosis, and quadriceps and hamstring 1-RMs. Levels of physical activity were assessed via the modified Baecke physical activity questionnaire.[17] Blood glucose levels were measured before each 1-RM test, and only participants with an acceptable blood glucose level were permitted to complete the 1-RM test.

Day 2. Subjects were admitted to Temple University's General Clinical Research Center (GCRC) 96 hours after completion of day 1. A 96-hour waiting period after the completion of the 1-RM test was used because several authors have shown that any improvements in insulin sensitivity caused by a prior exercise session are limited to 48 hours postexercise.[19] The primary goal of day 2 was to nearly normalize subject's blood glucose levels using intravenous insulin. Energy requirements were determined using the Harris-Benedict equation,[20] and while in the GCRC subjects consumed a controlled diet consisting of approximately 55% carbohydrates, 30% fats, and 15% proteins. Subjects were weighed on a daily basis to ensure that they maintained their weight throughout the study.

Days 3–5. Starting with day 3 and continuing through day 5, subjects completed consecutive euglycemic-hyperinsulinemic-clamp procedures (ie, preexercise, 12

hours postexercise, and 36 hours postexercise). The euglycemic-hyperinsulinemic-clamp technique was used to quantify insulin sensitivity and was conducted at a similar time each day.

In the evening on day 3, subjects in the exercise group completed the resistance-exercise protocol, which consisted of 5 sets of 6 repetitions using a weight equal to 80% of the 1-RM for both the quadriceps and hamstring muscle groups. A rest period of 4 minutes was given between sets. Subjects in the control group were allowed to perform activities of daily living but did not exercise during this time period.

Data analyses were conducted using descriptive and inferential statistics. Independent Student *t* tests were used to analyze the demographic and physical characteristics, as well as the exercise and control groups' free-insulin concentrations and blood glucose levels at each of the 3 euglycemic-hyperinsulinemic clamps. Two 1-factor analyses of variance (ANOVA) with repeated measures were used to analyze body weight during the study period. A 2×3 factorial ANOVA with repeated measures was used for the GIR analysis. Independent variables in this analysis were group (ie, exercise and control) and time (ie, preexercise and 12 and 36 hours postexercise). An α of .05 was used for all statistical analyses.

Results

There were no significant differences between the 2 groups in demographic characteristics, physical characteristics, and physical activity score (Table 1). Separate 1-factor (group) ANOVAs with repeated measures indicated no significant changes in body weight during the study period for the exercise ($F_{3,18} = .96$, $P = .43$) or control groups ($F_{3,18} = 3.0$, $P = .06$).

Means and standard deviations for free-insulin concentrations, blood glucose levels, and GIRs during the last hour of the euglycemic-hyperinsulinemic-clamp procedure are described in Table 2. Independent *t* tests indicated no significant differences between the exercise and control groups' preexercise and 12- and

Table 2 Free Insulin Concentrations (FIC), Blood Glucose (BG) Levels, and Glucose-Infusion Rates (GIR) During the Last Hour of the Euglycemic-Hyperinsulinemic Clamps for the Exercise and Control Groups, Mean ± SD

Variable	Group	Preexercise	12 h postexercise	36 h postexercise
FIC (pmol/L)	Exercise	405.0 ± 77	384.0 ± 104	360.0 ± 94
	Control	362.0 ± 38	319.0 ± 64	312.0 ± 53
BG (mg/dL)	Exercise	111.0 ± 8	117.0 ± 9	106.0 ± 9
	Control	111.0 ± 8	112.0 ± 7	109.0 ± 5
GIR ($mg \cdot kg^{-1} \cdot min^{-1}$)	Exercise	8.5 ± 3	8.9 ± 2	9.0 ± 3
	Control	9.4 ± 3	8.5 ± 3	8.2 ± 2

n = 7 in each group.

36-hour postexercise insulin concentrations and blood glucose levels. A 2 × 3 ANOVA with repeated measures indicated no significant interaction ($F_{1,2}$ = 1.72, P = .20) or main effects (group: $F_{1,2}$ = .01, P = .92; time: $F_{1,2}$ = .40, P = .67) for the GIRs.

Discussion

The results of this investigation indicate that a single bout of strenuous resistance exercise does not improve insulin sensitivity in people with type 1 diabetes at 12 and 36 hours postexercise. Because there were similarities between the exercise and control groups' anthropometric traits, metabolic control, duration of disease, physical activity status, insulin concentrations, and blood glucose levels, the GIR method allowed for accurate insulin-sensitivity comparisons to be made between the 2 groups.

Although the current findings are not directly comparable to other acute-exercise data because of differences in the exercise stimulus, the findings are consistent with recent data published on insulin sensitivity in people with type 1 diabetes and people without diabetes. Peltoniemi et al[8] reported no effect of a single bout of prolonged, low-intensity (ie, 10% 1-RM) intermittent isometric leg exercise on insulin sensitivity in type 1 patients with diabetes. In agreement, Nuutila et al,[21] using a similar exercise and testing protocol, reported no effect of an acute bout of exercise on insulin sensitivity in nondiabetics. Chapman et al[22] used a resistance-exercise stimulus similar in intensity to that of the current project (ie, 10 repetitions at 75% 1-RM) in nondiabetic subjects and also reported no effect of the exercise bout on insulin sensitivity.

In contrast to the current data, several resistive-exercise-training studies with nondiabetics and subjects with type 2 diabetes reported an improvement in insulin insensitivity.[23–29] It is interesting that all the subjects in these resistive-training studies were either insulin resistant (type 2 diabetes) or at risk for insulin resistance because they were older, sedentary, overweight/obese, or a combination of these characteristics. Thus the physical and conditioning characteristics of our subject population may have contributed to the lack of an acute effect on insulin sensitivity.

Engaging in prolonged moderate aerobic exercise carries the risk of an immediate and extended postexercise hypoglycemic event for people with type 1 diabetes.[6,7,9,10,30] The current finding of a lack of improvement in insulin sensitivity after resistive exercise presents a favorable exercise option by suggesting that strenuous resistive exercise carries a lower risk of a postexercise hypoglycemic event. This proposition is supported by other data that demonstrate a blunting effect of other forms of high-intensity exercise (ie, intermittent high-intensity sprint exercise) on postexercise hypoglycemia.[12,13] However, this suggestion is accompanied by the caution that the current subject population consisted of physically active people with type 1 diabetes in good glycemic control. Thus, future research examining the effects of acute resistive exercise using type 1 subjects who are not physically active and/or in poor glycemic metabolic control is warranted before a generalize recommendation can be made.

Conclusion

The results of this study indicate that a single bout of strenuous resistance exercise does not affect insulin sensitivity in physically active people with type 1 diabetes who are in good glycemic control. This finding may negate some of the potential benefits of this form of exercise for people with type 1 diabetes (ie, decreased insulin dosages and/or risk of hyperglycemia), but it presents the possible benefit of reducing the risk of a postexercise hypoglycemic event. Furthermore, it proposes that, given the documented hypoglycemic risk associated with aerobic exercise, people with type 1 diabetes who can only exercise late in the day should consider resistive exercise as a safer option.

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