Acute Exercise-Induced Glucose Change During an Exercise Program in Type 2 Diabetes

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- **PURPOSE:** Supervised exercise programs have been demonstrated to improve overall glycemic control but less well characterized is the evolution of glucose response to exercise during an exercise program. We addressed this issue, using an observational cohort design, among overweight adults with type 2 diabetes. We hypothesized that during the course of the program, glucose levels during exercise would become more stable, as insulin sensitivity improved. Among adults with type 2 diabetes, glucose levels often decline acutely during exercise.
- **METHODS:** Thirty-five adults with type 2 diabetes underwent capillary blood glucose (CBG) testing before and after supervised exercise during a 24-week program (48 sessions). After-exercise CBG values were subtracted from before-exercise values (CBG difference). Through repeated measures analysis, we examined CBG difference, before-exercise values, and after-exercise values during the program. Assuming that some initial period of exercise training is necessary to impact CBG difference, in exploratory analyses, we varied the time period analyzed (eg. Weeks 2–24, Weeks 3–24, etc).
- **RESULTS:** CBG difference appeared stable throughout the program when all available data were considered. In models that examined periods following Week 11, however, the magnitude of CBG difference declined progressively, as did before-exercise values. After-exercise values remained stable for all time periods examined.
- **CONCLUSIONS:** Our exploratory analyses suggest that following 11 weeks of exercise supervision, before-exercise CBG values decline progressively but after-exercise values remain stable, resulting in a progressive decline in CBG difference.

K E Y W O R D S

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Physical activity is a critical component in the management of type 2 diabetes (T2D).[1] Participation in an exercise program has been shown to improve glycemic control[2] and cardiorespiratory fitness,[3] contributing to the long-term prevention of cardiovascular disease.[4] Less well characterized is the evolution of acute glucose change during exercise over the course of a supervised exercise program. In contrast to individuals without diabetes, patients with T2D experience an acute reduction in blood glucose levels during moderate to vigorous exercise.[5–8] Glucose levels in patients with T2D may decline even during the short periods (<15 minutes) of exercise characteristic of exercise stress testing.[9]

Possible mechanisms include (1) blunted hepatic glucose production[7] and (2) increased peripheral glucose utilization.[5,6] We postulated that men and women with T2D participating in a supervised exercise program may experience improved glucose handling, leading to more stable glucose levels during exercise. To our knowledge, this possibility has not been assessed previously. Using before- and after-exercise CBG values collected during the course of a 24-week supervised exercise program, we conducted an observational cohort study to assess the impact of exercise training on glucose change during exercise among overweight adults with T2D.

METHODS

The present analysis included data from adults with T2D who completed 3 or more sessions of a 24-week supervised exercise program between January 2003 and November 2004 as part of a Canadian Institutes of Health Research–funded clinical trial assessing the impact of supervised exercise on weight change and cardiovascular risk factors among overweight adults with T2D.[10] As previously described,[10] 42 trial participants were randomized to 1 of 2 interventions: dietary counseling alone and combined with a supervised exercise program. Those randomized to dietary counseling alone were offered an identical exercise program in gratitude for participation following completion of the trial. All procedures were approved by the institutional review board of McGill University.

Exercise sessions were conducted at the Cardiovascular Health Improvement Program, McGill University cardiac rehabilitation unit, and were supervised by an exercise physiologist (40 minutes of cardiovascular exercise: treadmill, cycling, or cross trainer; 15 minutes of stretching). Capillary blood glucose (CBG) was assessed before and after each exercise session, using One Touch Ultra glucometers (Lifescan Canada, Johnson & Johnson). Patients were given fruit juice or glucose tablets if their CBG level was less than 4 mmol/L. Heart rate was monitored and maintained at 65% to 85% of the maximum rate achieved during a maximal exercise stress test conducted at baseline. Supervised sessions occurred 3 times per week during the first 8 weeks, twice per week during the next 8 weeks, and once a week during the final 8 weeks of the program. Participants were encouraged to continue to exercise for at least 135 minutes per week for the entire 24-week intervention, even as the frequency of supervised exercise sessions was reduced. Although most participants completed the 48 exercise sessions over a 24-week period, in some cases, make-up sessions were scheduled between Weeks 24 and 30 for sessions cancelled before Week 24 as a result of holidays or inclement weather.

Statistical Analyses

All statistical analyses were performed using SAS version 9.1. CBG difference was calculated for each session by subtracting the after-exercise CBG value from the before-exercise CBG value. Each participant contributed up to 48 values for CBG difference (ie, corresponding to the 48 sessions during the supervised program). We examined change in CBG difference over time through sequential linear mixed effects models (repeated measures analysis; PROC MIXED).[11] Time periods examined through sequential models were Week 1 to end of program; Week 2 to end of program; Week 3 to end of program; and so on until the final week of training, under the assumption that some previously undefined initial period of exercise training would be necessary before the magnitude of CBG difference would begin to be affected. Using a similar analytic approach, we assessed the evolution of before-exercise and after-exercise CBG values during the exercise program. Models were adjusted for gender, baseline hemoglobin A1c, sulfonylurea use, and diabetes duration (self-report). However, as these adjustments did not substantively alter the results, only the unadjusted models are presented.

RESULTS

Forty-two men and women with T2D participated in the original trial, and 35 of these individuals are included in the present analysis (Figure 1). Participants were middle-aged, overweight, and

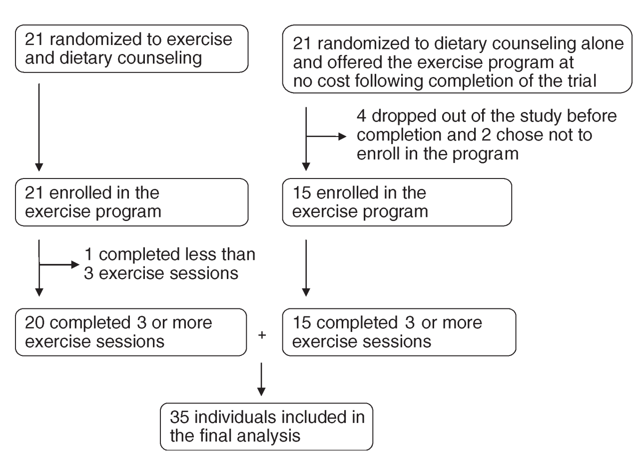

Figure 1. Participant flowchart.

Table 1 • BASELINE CHARACTERISTICS OF PARTICIPANTS INCLUDED IN THE ANALYSIS

Age, mean (SD), y	51 (8)
Female, *n* (%)	18 (51)
Body mass index, mean (SD), kg/m^2	37 (6)
Diabetes duration, mean (SD), y	3 (3)
Hemoglobin A_{1c}, mean (SD), %	6.9 (1)
Glucose-lowering medications	
Sulfonylurea use, *n* (%)	15 (43)
Metformin use, *n* (%)	27 (77)
Thiazolidinedione use, *n* (%)	5 (14)
Cardiovascular risk factors	
Systolic blood pressure, mean (SD), mm Hg	130 (16)
Diastolic blood pressure, mean (SD), mm Hg	82 (10)
Total cholesterol/high-density lipoprotein ratio, mean (SD)	4.2 (1.2)
Exercise stress test workload, mean (SD), metabolic equivalents	8.8 (2.1)

generally had good glycemic and blood pressure control at baseline (Table 1).

As calculated using all available session values for all 35 subjects, the mean before-exercise and after-exercise CBG values were 8.6 (0.4) mmol/L and 6.8 (0.3) mmol/L, respectively, and the mean CBG difference was 1.8 (0.2) mmol/L. Among the 35 participants considered, 25 completed the program by Week 24; 8 completed the program between Weeks 24 and 26; and 2 completed the program between Weeks 26 and 30.

Over the entire exercise program, as computed through a linear mixed effects model using all available data, the CBG difference did not change significantly over time (0.02 mmol/L/wk; 95% confidence interval [CI], −0.05 to 0.003 mmol/L/wk). In the model examining the time period following Week 11, the rate of change of CBG difference was significant at −0.06 mmol/L/wk (95% CI, −0.11 to −0.003 mmol/L) (Table 2). Significant reductions in CBG difference over time were also computed through

Table 2 • RATES OF CHANGE IN CAPILLARY BLOOD GLUCOSE DIFFERENCE AND BEFORE- AND AFTER-EXERCISE GLUCOSE VALUES

	CBG difference, mmol/L		Before-exercise CBG, mmol/L		After-exercise CBG, mmol/L	
	Rate of Change, mmol/L/wk	95% Confidence Interval	Rate of Change, mmol/L/wk	95% Confidence Interval	Rate of Change, mmol/L/wk	95% Confidence Interval
0 to program end	−0.02	−0.05 to 0.003	0.009	−0.03 to 0.05	0.008	−0.02 to 0.03
1 to program end	−0.006	−0.03 to 0.02	0.01	−0.03 to 0.05	0.02	−0.008 to 0.04
2 to program end	−0.007	−0.04 to 0.02	0.02	−0.03 to 0.06	0.02	−0.008 to 0.04
3 to program end	−0.01	−0.04 to 0.02	0.01	−0.03 to 0.06	0.02	−0.005 to 0.05
4 to program end	−0.02	−0.05 to 0.01	0.003	−0.04 to 0.04	0.02	−0.007 to 0.04
5 to program end	−0.01	−0.04 to 0.02	0.006	−0.03 to 0.05	0.02	−0.009 to 0.04
6 to program end	−0.02	−0.05 to 0.01	0.000007	−0.04 to 0.04	0.02	−0.008 to 0.04
7 to program end	−0.02	−0.06 to 0.01	−0.002	−0.04 to 0.04	0.02	−0.009 to 0.05
8 to program end	−0.02	−0.06 to 0.02	−0.009	−0.05 to 0.03	0.02	−0.02 to 0.05
9 to program end	−0.02	−0.07 to 0.02	−0.02	−0.07 to 0.03	0.006	−0.03 to 0.04
10 to program end	−0.04	−0.09 to 0.01	**−0.05**	−0.10 to −0.001	−0.009	−0.05 to 0.03
11 to program end	**−0.06**	−0.11 to −0.003	**−0.06**	−0.11 to −0.004	0.004	−0.03 to 0.04
12 to program end	**−0.08**	−0.14 to −0.01	**−0.09**	−0.15 to −0.02	−0.002	−0.05 to 0.04
13 to program end	**−0.10**	−0.18 to −0.03	**−0.10**	−0.17 to −0.03	0.007	−0.04 to 0.06
14 to program end	−0.08	−0.17 to 0.00002	**−0.09**	−0.16 to −0.008	0.005	−0.05 to 0.06
15 to program end	−0.09	−0.19 to 0.005	**−0.10**	−0.19 to −0.01	−0.003	−0.07 to 0.06
16 to program end	−0.09	−0.20 to 0.03	−0.08	−0.19 to 0.02	0.01	−0.06 to 0.09
17 to program end	**−0.14**	−0.24 to −0.03	**−0.13**	−0.23 to −0.02	0.02	−0.06 to 0.11
18 to program end	**−0.13**	−0.25 to −0.01	−0.11	−0.23 to 0.02	0.02	−0.08 to 0.13
19 to program end	−0.09	−0.25 to 0.06	−0.07	−0.23 to 0.09	0.02	−0.11 to 0.16
20 to program end	−0.13	−0.35 to 0.08	−0.16	−0.37 to 0.05	−0.02	−0.20 to 0.16
21 to program end	−0.24	−0.54 to 0.06	**−0.31**	−0.6 to −0.01	−0.08	−0.33 to 0.18
22 to program end	−0.12	−0.48 to 0.23	−0.25	−0.6 to 0.1	−0.11	−0.43 to 0.20
23 to program end	0.09	−0.30 to 0.48	−0.15	−0.59 to 0.29	−0.21	−0.57 to 0.15
24 to program end	0.19	−0.24 to 0.61	−0.02	−0.49 to 0.45	−0.26	−0.63 to 0.12

Abbreviation: CBG, capillary blood glucose.
Statistically significant values are indicated in boldface.

Table 3 • RATES OF CHANGE IN CAPILLARY BLOOD GLUCOSE DIFFERENCE AND BEFORE- AND AFTER-EXERCISE GLUCOSE VALUES OF PARTICIPANTS WHO COMPLETED 11 OR MORE WEEKS OF THE SUPERVISED EXERCISE PROGRAM

Weeks Included in Analyses	Rate of Change in CBG Difference, mmol/L/wk	95% Confidence Interval
0 to program end	−0.002	−0.03 to 0.02
1 to program end	−0.005	−0.03 to 0.02
2 to program end	−0.006	−0.04 to 0.02
3 to program end	−0.01	−0.04 to 0.02
4 to program end	−0.02	−0.05 to 0.01
5 to program end	−0.02	−0.05 to 0.01
6 to program end	0.02	−0.01 to 0.05
7 to program end	−0.02	−0.06 to 0.01
8 to program end	−0.02	−0.06 to 0.02
9 to program end	−0.02	−0.07 to 0.02
10 to program end	−0.04	−0.09 to 0.01
11 to program end	**−0.06**	−0.11 to −0.003
12 to program end	**−0.08**	−0.14 to −0.01
13 to program end	**−0.10**	−0.18 to −0.03
14 to program end	−0.08	−0.17 to 0.00002
15 to program end	−0.09	−0.19 to 0.005
16 to program end	−0.09	−0.20 to 0.03
17 to program end	**−0.14**	−0.24 to −0.03
18 to program end	**−0.13**	−0.25 to −0.01
19 to program end	−0.09	−0.25 to 0.06
20 to program end	−0.13	−0.35 to 0.08
21 to program end	−0.24	−0.54 to 0.06
22 to program end	−0.12	−0.48 to 0.23
23 to program end	0.09	−0.30 to 0.48
24 to program end	0.19	−0.24 to 0.61

Abbreviation: CBG, capillary blood glucose.
Statistically significant values are indicated in boldface.

models that examined intervals beyond 12 weeks, 13 weeks, 17 weeks, and 18 weeks (Table 2).

Changes in before-exercise CBG values generally paralleled the changes in CBG difference, with before-exercise CBG values changing over time at a rate of −0.05 mmol/L/wk (95% CI, −0.10 to −0.001 mmol/L/wk) beyond 10 weeks of training (Table 2). There was also a significant reduction in before-exercise glucose values in models that considered the intervals beyond 11 weeks, 12 weeks, 13 weeks, 14 weeks, 15 weeks, and 17 weeks (Table 2). In contrast to CBG difference and before-exercise CBG values, after-exercise CBG values remained stable throughout the supervised exercise program (Table 2) for all time periods considered.

To examine the possibility that individuals who completed more than 11 weeks of the exercise program responded differently to the program, we repeated our analyses including only the 28 individuals who completed more than 11 weeks of exercise training. Similar results were obtained (Table 3).

DISCUSSION

Analysis suggests that among overweight adults with T2D who are not receiving insulin therapy, glucose levels during exercise become progressively more stable following 11 weeks of supervised exercise, attributable to progressive reduction in before-exercise glucose values combined with stable after-exercise values. Although the analysis involved "multiple testing" of CBG difference following variable periods of exercise program participation, findings are unlikely to be spurious, given that the significant reduction CBG difference did not occur randomly over the 24-week period but only following 11 weeks of training. This is consistent with the hypothesis that some period of regular exercise is necessary before glucose handling during exercise is impacted.

Previous studies that have examined glucose handling during exercise have not examined the evolution of this handling over the course of a supervised exercise program. In one such study, Kang and colleagues[6] demonstrated that the magnitude of glucose change during exercise is greater among individuals who begin exercising at a higher glucose level. Consistent with this, in our study we observed that as the before-exercise glucose levels declined following 11 weeks of training, the CBG difference diminished. Giacca and colleagues[5] have suggested that higher before-exercise glucose levels may directly provoke an abnormal increase in glucose utilization.

A limitation of this study was the absence of information on the time elapsed since the last meal. Poirier and colleagues[7,8] examined CBG during 1 hour of ergocycle exercise in men with T2D. There was no change in glucose level during exercise when participants exercised in a fasting state. Among those who exercised without fasting, the reduction in glucose levels during exercise was greatest among those who had eaten 4 to 8 hours before exercise.[7,8] The time elapsed since the last meal appears to impact glucose change during exercise even when before-exercise glucose levels are similar.[8] Future study is necessary to (1) confirm our observation that exercise-induced changes in glucose levels become less pronounced following 11 weeks of exercise training and (2) assess whether this relationship is impacted by time and content of the last meal. This study would have been strengthened by information addressing the timing of oral hypoglycemic agents, physical activities before the exercise session, and venous blood sampling in place of CBG testing.

Nonetheless, findings suggest that in addition to increasing insulin sensitivity and overall glycemic control, as demonstrated in previous studies,[2,12–14] exercise training may improve glucose handling during exercise. More stable glucose values during exercise may reduce the risk of exercise-induced symptomatic hypoglycemia in diabetic patients. Symptoms of hypoglycemia include tremor, diaphoresis, palpitations, confusion, and loss of consciousness; such symptoms may occur at glucose levels of less than 4 mmol/L.[15] Fear of hypoglycemia may constitute a barrier to regular exercise in diabetic patients. The American Diabetes Association recommends that diabetic patients monitor their blood glucose response to exercise and adjust food and medication to prevent hypoglycemic episodes.[16] The knowledge that regular exercise may eventually lead to (1) more stable glucose values and (2) a corresponding reduction in the need for CBG testing may encourage continued exercise participation among overweight adults with T2D not receiving insulin.

Replication of the results of these analyses, namely, that glucose values during exercise tend to become more stable following 11 weeks of training, would provide patients with T2D with information that may further encourage them to embark on and persist with a regular program of exercise as part of a general effort to maximize their physical activity. An optimal level of physical activity has the potential not only to improve glycemic control but also to reduce the risk of heart disease, stroke, and death in this high-risk population of patients.

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