Carbohydrate Requirements for Prolonged, Fasted Exercise With and Without Basal Rate Reductions in Adults With Type 1 Diabetes on Continuous Subcutaneous Insulin Infusion

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OBJECTIVE

Exercising while fasted with type 1 diabetes facilitates weight loss; however, the best strategy to maintain glucose stability remains unclear.

RESEARCH DESIGN AND METHODS

Fifteen adults on continuous subcutaneous insulin infusion completed three sessions of fasted walking (120 min at 45% VO_{2max}) in a randomized crossover design: 50% basal rate reduction, set 90 min pre-exercise ($-90_{min}50\%_{BRR}$); usual basal rate with carbohydrate intake of 0.3 g/kg/h (CHO-only); and combined 50% basal rate reduction set at exercise onset with carbohydrate intake of 0.3 g/kg/h (Combo).

RESULTS

Combo had a smaller change in glucose (5 ± 47 mg/dL) versus CHO-only (−49 ± 61 mg/dL, $P = 0.03$) or $-90_{min}50\%_{BRR}$ (−34 ± 45 mg/dL). The $-90_{min}50\%_{BRR}$ strategy produced higher β-hydroxybutyrate levels (0.4 ± 0.3 vs. 0.1 ± 0.1 mmol/L) and greater fat oxidation (0.51 ± 0.2 vs. 0.39 ± 0.1 g/min) than CHO-only (both $P < 0.05$).

CONCLUSIONS

All strategies examined produced stable glycemia for fasted exercise, but a 50% basal rate reduction, set 90 min pre-exercise, eliminates carbohydrate needs and enhances fat oxidation better than carbohydrate feeding with or without a basal rate reduction set at exercise onset.

Prolonged exercise in a fasted state may be preferable for people with diabetes since it increases lipid oxidation and is associated with better glucose stability than nonfasted exercise (1,2). On the basis of consensus, individuals with type 1 diabetes on continuous subcutaneous insulin infusion (CSII) can attempt to prevent hypoglycemia during fasted exercise by supplementing with carbohydrates and/or by performing a temporary basal rate reduction (3). The objective of this study was to compare three common strategies used for fasted exercise in individuals on CSII.

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RESEARCH DESIGN AND METHODS

This study conformed to the standard set by the Declaration of Helsinki and was approved by York University research ethics board (ClinicalTrials.gov, NCT04383015). Eligibility criteria included participants aged 18–65 years with type 1 diabetes (≥18 months), on CSII, and with HbA_{1c} ≤9.9% (85 mmol/mol). Maximal aerobic capacity (VO_{2max}) was determined (4); participants wore a continuous glucose monitor (Dexcom G5; Dexcom, San Diego, CA) and used a standardized glucose meter to measure blood glucose levels during exercise (Contour Next Link; Ascensia Diabetes Care, Parsippany, NJ).

Participants arrived at the laboratory fasted (0700–1045 h) with blood glucose between 72 and 270 mg/dL. Females were studied in early follicular phase. The following hypoglycemia minimization strategies were tested in a randomized crossover design:

A. A 50% basal rate reduction, set 90 min pre-exercise ($-90_{min}50\%_{BRR}$)
B. Carbohydrate intake of 0.3 g/kg/h, with usual basal rate (CHO-only)
C. A 50% basal rate reduction set at exercise onset, along with carbohydrate intake of 0.3 g/kg/h (Combo)

Experimental visits consisted of 120 min of treadmill walking at 40–50% of individual heart rate reserve (5). Blood glucose concentration was measured pre-exercise, at baseline, every 15 min during exercise, and postexercise using the standardized glucose meter. Carbohydrate (Skittles; Mars Inc.) was provided on the basis of body weight every 30 min if glycemia was <180 mg/dL during exercise (CHO-only and Combo strategies only). If glucose was <70 mg/dL, 12 g of carbohydrate were provided, followed by 15 min of rest, and exercise resumed when glucose was >70 mg/dL. A portable metabolic system (K5; COSMED, Rome, Italy) was worn intermittently to estimate substrate utilization (6), and the rate of perceived exertion (Borg 0–10 scale) was recorded every 15 min during exercise. To protect against postexercise hypoglycemia, participants reduced bolus insulin by 25% at the first meal postexercise and set a 20% basal rate reduction for 6 h overnight (3).

Saliva was collected pre- and postexercise to measure free cortisol (Cortisol Saliva ELISA; Crystal Chem, Elk Grove Village, IL). Plasma capillary samples were also collected at 0, 65, and 140 min of exercise for glucagon levels (Glucagon ELISA; Mercodia, Uppsala, Sweden).

On the basis of a two-sided type I error level of 0.05, we calculated that 12 participants would be needed to detect a mean change in blood glucose of 18 mg/dL during exercise with 80% power. A one- or two-way repeated-measures ANOVA was used where appropriate. Statistical significance was set at $P < 0.05$, and a Tukey post hoc test was used if significance was found. All data are presented as mean ± SD unless otherwise stated.

RESULTS

A total of 15 adults (36 ± 15 years, 9 females, BMI 25.0 ± 5.5 kg/m^2, HbA_{1c} 6.9 ± 0.9% [52 ± 10 mmol/mol], VO_{2max} 43.3 ± 10.5 mL/kg/min) completed the study. Diabetes duration was 17 ± 12 years, and total daily insulin dose was 0.5 ± 0.1 units/kg. All participants were on CSII (67% Omnipod; Insulet Corporation, Acton, MA).

Participants covered 7.3 ± 0.3 miles during 120 min of treadmill walking at 46 ± 5% of their heart rate reserve. Fat oxidation was higher in $-90_{min}50\%_{BRR}$ (0.51 ± 0.2 g/min) versus CHO-only (0.39 ± 0.1 g/min, $P = 0.04$) (Supplementary Table 1). β-Hydroxybutyrate levels were highest in $-90_{min}50\%_{BRR}$ (0.4 ± 0.3 mmol/L) followed by Combo (0.3 ± 0.2 mmol/L) and CHO-only (0.1 ± 0.1 mmol/L, $P < 0.05$). Net calorie loss was higher in $-90_{min}50\%_{BRR}$ (860 ± 240 kcal) versus CHO-only (709 ± 217 kcal) and Combo (737 ± 201 kcal, both $P < 0.01$) (Supplementary Table 1).

During $-90_{min}50\%_{BRR}$, fewer carbohydrates (1 ± 3 g) were consumed versus CHO-only (38 ± 19 g) and Combo (30 ± 17 g, both $P < 0.001$) (Fig. 1*A*). Carbohydrate intake was 0.25 ± 0.1, 0.01 ± 0.0, and 0.20 ± 0.1 g/kg/h for the CHO-only, $-90_{min}50\%_{BRR}$, and Combo strategies, respectively.

Glucose level at exercise start averaged 166 ± 54, 162 ± 63, and 160 ± 67 mg/dL for the $-90_{min}50\%_{BRR}$, CHO-only, and Combo strategies, respectively ($P > 0.05$) (Fig. 1*B*). At 90 min of exercise, Combo had higher glucose than $-90_{min}50\%_{BRR}$ ($P = 0.03$). After 105 min of exercise until 20 min of recovery, Combo had higher glucose versus the other strategies (all $P < 0.01$) (Fig. 1*B*). The change in glucose during exercise was greater in those with higher baseline glucose levels (Supplementary Fig. 1), averaging −34 ± 49, −49 ± 61, and 5 ± 47 mg/dL for the $-90_{min}50\%_{BRR}$, CHO-only, and Combo strategies, respectively ($P = 0.02$). CHO-only had two (13%) participants develop hypoglycemia versus one (7%) each in the other two strategies. Time in range (70–180 mg/dL) during exercise was 76 ± 34%, 82 ± 24%, and 62 ± 37%, in $-90_{min}50\%_{BRR}$, CHO-only, and Combo, respectively. Rate of perceived exertion was lower in Combo versus the other two strategies (both $P < 0.01$).

Serum cortisol fell from pre- to postexercise in CHO-only and Combo but not in $-90_{min}50\%_{BRR}$ (Supplementary Table 1). Plasma glucagon increased from pre- to postexercise in $-90_{min}50\%_{BRR}$ (15.1 ± 8.9 to 30.9 ± 22.3 pg/mL, $P = 0.002$) and Combo (11.7 ± 7.0 to 22.7 ± 19.2 pg/mL, $P = 0.08$) (Supplementary Table 1).

Time in range during the 12 h of recovery was lower in Combo (64 ± 19%, $P = 0.05$) and in $-90_{min}50\%_{BRR}$ (60 ± 25%, $P = 0.08$) as compared to a rest day (76 ± 15%) (Supplementary Fig. 2). However, time in range for 24 h postexercise was similar among strategies.

CONCLUSIONS

Performing a basal rate reduction before exercise in the postabsorptive state is the standard of care for people with type 1 diabetes on CSII (3,7). Unfortunately, the majority of individuals on CSII do not do this for usual exercise, relying more on carbohydrate feeding (8). We show here that a 50% basal rate reduction, set 90 min pre-exercise, is more effective than carbohydrate feeding, with or without a basal rate reduction at exercise onset, for the maximization of net caloric expenditure while still preserving glycemic stability during prolonged, fasted exercise. We also show that a 50% basal rate reduction at exercise onset, along with some carbohydrates (30 ± 17 g/2 h), can maintain glycemia if the basal rate reduction is not set 90 min in advance. Carbohydrate feeding in the 2nd hour of prolonged exercise may not be required if the basal rate reduction is set at

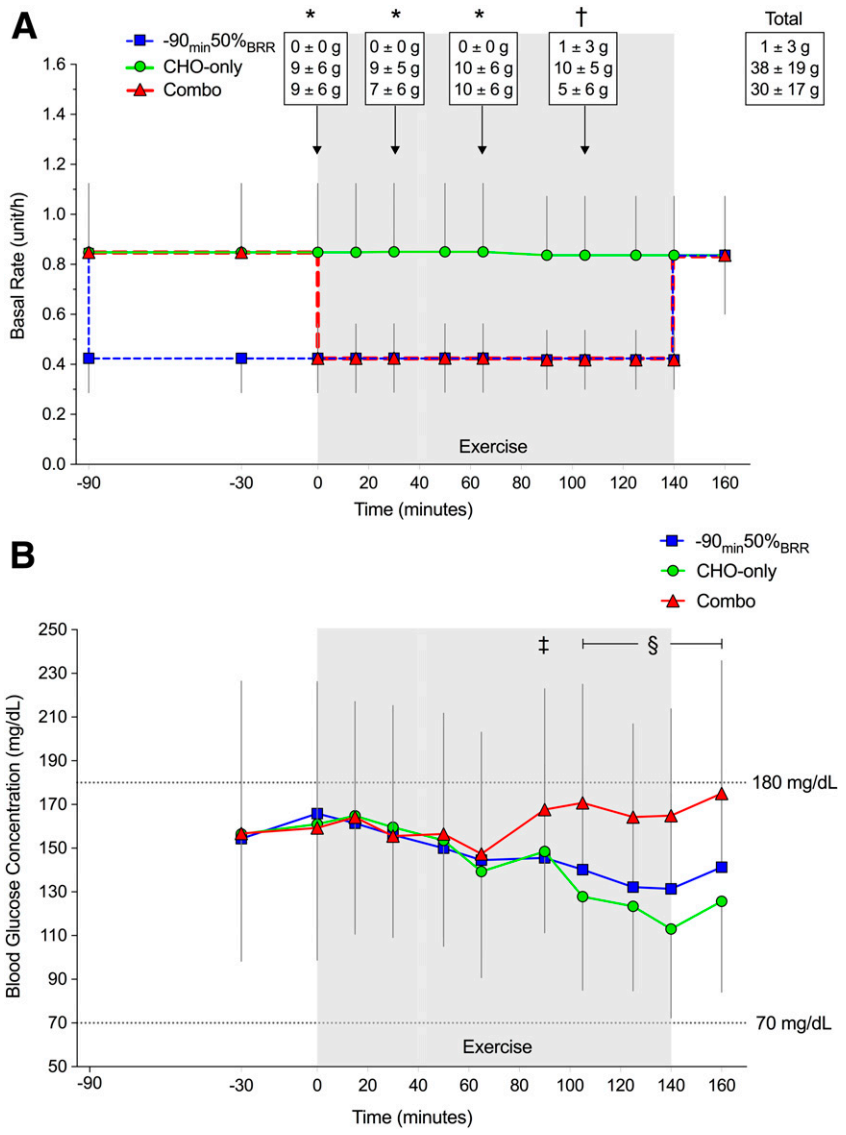

Figure 1—*A*: Insulin basal rate profile and absolute carbohydrate intake amounts across treatment strategies. *B*: Absolute whole-blood glucose concentrations during exercise across three strategies. Dashed lines denote the target glycemic range. Data are mean ± SD ($n = 15$). *$-90_{min}50\%_{BRR}$ significantly different; †all significantly different; ‡Combo vs. $-90_{min}50\%_{BRR}$; §Combo vs. $-90_{min}50\%_{BRR}$ and CHO-only ($P < 0.05$).

exercise onset, since we found that glucose levels begin to rise when the two strategies are combined. While the Combo strategy had the most glycemic stability during exercise, it also had the lowest time in range since it tended to elevate glucose postexercise (Supplementary Fig. 2), particularly in those who were in target range before (Supplementary Fig. 1).

An individualized approach to insulin management and carbohydrate feeding for exercise is needed for people with type 1 diabetes (3). Some individuals may do well with basal rate suspension for some forms of exercise (9) or with a basal rate reduction set closer to exercise (10,11). Carbohydrate needs are also highly variable because of a number of factors, including exercise intensity, insulin regimen, and performance goals (3). Nonetheless, we found that carbohydrate intake of 0.3 g/kg/h appears to be a reasonable starting prescription for fasted exercise in active adults with type 1 diabetes on CSII who do not adjust their basal insulin, albeit glycemic results were variable (Supplementary Fig. 1). In the $-90_{min}50\%_{BRR}$ strategy, 14 (93%) of the 15 participants exercised for 120 min without any carbohydrate needs. This, along with the reduction in insulin delivery, was associated with higher lipid use and ketone production, which may help with fat loss (12).

In summary, the more proactive approach to reduce basal insulin delivery 90 min pre-exercise for individuals on CSII may eliminate snacking needs and effectively increases fat oxidation, thereby increasing net energy expenditure. Future studies should determine whether this approach is favorable for weight control and glycemic stability when exercise of different forms and intensities occur.

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Author Contributions. S.M.M. was responsible for data collection, interpretation of data, and analysis. S.M.M., D.P.Z., R.P., N.C.D'S., T.V., T.T.L., and M.C.R. contributed feedback and revisions for the final manuscript. S.M.M., D.P.Z., and M.C.R. designed the study and wrote the manuscript. D.P.Z., R.P., and N.C.D'S. assisted in the data collection. N.C.D'S. assisted with assays. M.C.R. is the guarantor of this work and, as such, had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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