Brief Report

Glycemic Responses to Graded Exercise Testing in Adolescents Using Automated Insulin Delivery Systems

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Abstract

This study evaluated the glycemic responses to a graded exercise test (GXT) performed by 24 adolescents with type 1 diabetes (T1D) using automated insulin delivery (AID) systems. Each participant partook in a GXT on a bicycle ergometer until volitional exhaustion. Plasma glucose and lactate levels were measured during the GXT, whereas sensor glucose was monitored in the hours thereafter. Plasma glucose levels were stable throughout the GXT (overall change of -0.26 mmol/L [-5 mg/dL], $p = 0.593$), with no hypoglycemic events. Sensor glucose levels also remained stable and within the recommended glucose target ranges after the GXT for the remaining day and night, with only a few episodes of mild hypoglycemia. This study highlights the glycemic safety of performing GXT for adolescents utilizing AID systems.

Introduction

Graded exercise testing (GXT) is commonly used to assess cardiorespiratory fitness (CRF) in clinical and research settings, including among individuals with type 1 diabetes (T1D) [1]. Given the glycemic challenges that physical exercise often poses for people with T1D, profiling glucose responses during activity is necessary to inform management decisions that promote safety. Although previous studies have shown stable glucose responses during GXT in adults with T1D using various insulin treatment modalities [2], it is unclear if these findings apply to an adolescent population, as this has not been explored. Therefore, this study aimed to assess glycemic responses during and after a GXT in adolescents with T1D using automated insulin delivery (AID) systems, with the hypothesis that glycemia would remain stable during and after for both users of both AID systems.

Materials and methods

The main inclusion criteria were: age 13-17 years old, T1D diagnosis for ≥1 year, use of MiniMed 780G or Tandem Control-IQ for ≥3 months, and HbA1c of ≤75 mmol/mol (9 %). The main exclusion criteria were pregnancy or the desire to become pregnant. Participants were matched across the two AID systems on age, sex, and weight-adjusted total daily insulin dose (IU/kg/day).

After inclusion, participants performed a GXT on a workload-controlled ergometer (Vyntus, IntraMedic), following a set protocol that included 3-minute passive rest (start), 3-minute warm-up at 20 Watts (W), and subsequent one-minute increments in load (15, 20, or 25 W) until voluntary exhaustion. Upon reaching exhaustion, the workload was immediately reduced to 20 W for a 3-minute active recovery, followed by a final 3-minute passive recovery period (end). *Exercise mode and temporary target were not activated on the respective AID-systems.* The only precaution taken before starting the GXT was ensuring a plasma glucose (PG) level of ≥ 5.0 mmol/L (90 mg/dL).

During the GXT, venous-derived plasma samples were collected at rest, every 3 minutes during the progressive phase, at exhaustion, and after both recovery phases. Samples were analyzed immediately using the YSI 2500 Biochemistry Analyzer (YSI Inc., Yellow Springs, OH, USA) to measure point concentrations of plasma glucose (PG) and lactate (PLa). Continuous glucose monitoring (CGM) data were acquired from participants' own devices to record sensor glucose (SG) values throughout the test and for 24 hours afterward.

All statistical analyses were conducted using RStudio (version 4.2.2). Continuous variables were expressed as mean ± SD. Comparisons between two time points, as well as cardiopulmonary parameters measured during GXT, were performed using t-tests or Wilcoxon signed-rank test. To assess changes in PG, PLa, and SG concentrations over time, linear mixed-effects models were employed with time as a fixed effect and participant ID as a random effect. Models were adjusted for potential confounding

variables, including age, sex, and T1D duration. For analyses involving the inpatient setting, models were additionally adjusted for rescue carbohydrate intake. P-values of < 0.05 were considered statistically significant.

Results

A total of 24 adolescents with T1D (50% treated with MiniMed 780G and Tandem CIQ, respectively) completed the study. Baseline characteristics and key physiological responses to GXT at peak are presented in Table 1. Of the participants, 7 used Fiasp and 17 used Novorapid in their insulin pumps. There were no significant differences in baseline characteristics between users of each AID system, but males had significantly higher $\dot{V}O_{2peak}$ than females (males: 41.7 ±6.2 mL/kg/min vs. females: 34.7 ±4.8 mL/kg/min, p = 0.009).

Starting PG was similar between the two AID systems (780G: 7.2 ±1.8 mmol/L [130 ±32 mg/dL] vs. CIQ: 8.4 ±2.5 mmol/L [151 ±45 mg/dL], p = 0.180) and remained unchanged throughout exercise in both groups (overall change -0.26 mmol/L [-5 mg/dL], p = 0.593), while PLa increased significantly but equally in both groups (start: 1.0 ±0.3 vs. end: 9.0 ±2.0 mmol/L, p < 0.001) (Figure 1, Panel A). There was no effect of age, sex, diabetes duration or AID system on either of the outcome variables. There were no hypoglycemic events throughout GXT, but three individuals experienced level 2 hyperglycemia (PG >13.9 mmol/L [>250 mg/dL]).

Higher starting PG was associated with higher end PG (r = 0.487, 95% CI: 0.400 to 0.574, p <0.001), as well as the overall change in PG over GXT (r = -0.261, 95% CI: -0.331 to -0.192, p <0.001). Half of the participants experienced a decline in PG during GXT (Δ -1.5 ±1.2 mmol/L [-27 ±22 mg/dL]) whilst the other half experienced a rise (Δ +1.2 ±0.6 mmol/L [+22 ±11 mg/dL]).

In the three hours post-GXT, SG levels revealed one level 2 hypoglycemia event (nadir SG: 2.9 mmol/L [52 mg/dL]), and six level 1 hypoglycemic events, equally distributed between the two pump systems (three in 780G and three in Control-IQ). In the same period, glycemia remained within targets, and no differences between the two AID systems were observed (Figure 1, Panel D). In the overnight period (00:00–06:00) following GXT, there were no events of level 2 hypoglycemia but four events of level 1 hypoglycemia, again with an equal distribution between the two AID systems. Overnight, glucose remained stable and within targets, with no significant differences between AID groups (Figure 1, Panel F). Additionally, there were no differences in glycemic outcomes between the night preceding the GXT and the night following.

Discussion

This study is the first to evaluate glycemic responses during and after GXT in adolescents with T1D using AID systems. Results showed that PG values remained stable throughout GXT with no hypoglycemic events. Additionally, SG remained within recommended ranges in the immediate (+3 hours) and extended (overnight) time frames after test completion.

These results match previous T1D-adult studies that used in-clinic GXT testing [1]. Additionally, they confirm that glycemic responses remain stable during a GXT and expand on this finding to include an adolescent population using the latest diabetes technology. In our study, we confirmed relatively stable and near-normal glycemic outcomes during the test, with no hypoglycemic events. Additionally, we tracked SG values before and after the GXT, which provided new insight into glycemic responses over a longer time frame and supported the initial findings of glycemic stability. This study was the first in this age group to use this treatment approach and confirm its effectiveness. We found that SG levels fell within glycemic targets throughout the immediate post-exercise and overnight periods, even when no restrictions were placed on everyday life. In previous work involving GXT, participants were asked to adhere to certain preparatory measures (e.g., fasting for two hours prior to GXT and having no hypoglycemia within 24 hours before), however, in this study no such preparation was put in place. One of the major barriers for children and adolescents with T1D participating in exercise is the fear of developing hypoglycemia [3,4]. The results of this study may help reassure healthcare professionals, families, and individuals with T1D that engaging in shorter sessions (around 20 minutes) of high-intensity exercise is unlikely to lead to major glycemic disturbances for those utilizing the latest insulin therapy regimes. However, it should be noted that this type of activity is not widely practiced among adolescents and usually results in more stable glycemic outcomes – largely due to the adrenaline response - compared to moderate-intensity exercise. Even so, data remain limited in this age group using AID systems and therefore could help guide in less common scenarios. Recently published consensus guidelines concentrated on exercise for individuals with T1D using AID systems [4]. These guidelines outline how various types and durations of exercise, along with AID systems, affect the necessary preparations for achieving safe glycemic outcomes. Our study can now build on the understanding that brief, high-intensity physical exertion—even in a controlled test setting like a GXT—may require less advanced preparation in adolescents with T1D, which could inform future exercise guidance.

Although adolescents with T1D generally have lower fitness levels than healthy controls, the values in our study were somewhat higher than the reported average for this population [5]. Notably, however, the average VO_{2peak} in our group was close to the threshold associated with a significantly increased risk of developing cardiovascular disease (CVD) [6].

One of this study's key strengths is its innovative approach, featuring three notable aspects: 1) unlike previous studies that only looked at in-clinic glucose levels, this study offers valuable insights into longer-term outcomes, 2) by using two different and widely used AIDs, it provides up-to-date

information, and 3) it builds on previous findings in adults by applying them to an adolescent population. However, important points to consider are the potential healthy user bias, which might make for difficulty in generalizing findings, as well as the lack of control imposed in the post-clinic period.

In conclusion, from a glycemic perspective, the GXT was safe for adolescents using AID systems, leading to consistent glucose responses both in-clinic and in the hours following. These results suggest that, when starting at an appropriate glycemic level, adolescents with T1D can perform brief, unplanned physical activity with less concern about glycemic fluctuations.

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Statement of Ethics

The study was conducted according to the Declaration of Helsinki, and all procedures were approved by the National Research Ethics Committee of Denmark (approval number H-22025766) and the Danish Data Protection Agency (approval number P-2022-311). All participants were provided with full written and verbal descriptions, and written, informed consent was obtained from parents and participants.

Conflict of Interest Statement

JS has served as an educator for Medtronic. She has received funding from Medtronic and Novo Nordisk. JS owns shares in Novo Nordisk, JS has received fees for speaking on behalf of Medtronic, Sanofi Aventis, Rubin Medical, and Novo Nordisk. KN serves as an adviser to Medtronic, Abbott, Convatec, and Novo Nordisk; owns shares in Novo Nordisk; has received research grants to the institution from Novo Nordisk, Zealand Pharma, Dexcom, and Medtronic; and has received fees for speaking from Medtronic and Novo Nordisk.

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Author Contributions

EBL, OMM, RB, AGR, KN and JS contributed to the conception and design of the study. EBL, OMM, ST and MZS contributed to the attribution of the data. EBL, OMM and AGR were responsible for data analyses. All authors were responsible for data interpretation. EBL wrote the original draft of the manuscript. All authors contributed to revising the article. All authors provided final approval of the version to be published.

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Table 1

		MiniMed 780G (N = 12)	Tandem Control-IQ (N = 12)	Overall (N = 24)
Baseline Characteristics	*Age (Years)*	15.1 ±1.51	14.8 ±1.7	15.0 ±1.57
	Sex (% Male)	8 (66.6%)	8 (66.6%)	16 (66.6%)
	T1D Duration (Years)	7.4 ±3.6	7.5 ±3.3	7.5 ±3.4
	BMI (kg/m^2)	22.1 ±2.36	20.4 ±1.81	21.2 ±2.24
	Systolic Blood Pressure (mmHg)	128 ±13	124 ±8	126 ±11
	Resting Pulse (BPM)	66 ±9	71 ±14	68 ±12
	HbA1c (mmol/mol)	52 ±8.9	53 ±5.2	53 ±7.1
	HbA1c (%)	6.9 ±0.8	7.0 ±0.5	7.0 ±0.6
	TIR (%)	70.0 ±11.1	62.5 ±6.4	66.3 ±9.6
	TITR (%)	48.2 ±13.5	40.1 ±3.3	44.2 ±10.4
	Total Daily Dose (IU/day)	57.7 ±8.9	60.3 ±13.8	59.0 ±11.5
	Total Daily Dose/Bodyweight (IU/kg/day)	0.88 ±0.14	0.98 ±0.19	0.93 ±0.17
	Types of Insulin (% using Novorapid)	7 (58%)	10 (83%)	17 (71%)
GXT Characteristics	*VO2peak (ml/kg/min)*	40.7 ±5.6	38.6 ±7.9	39.6 ±7.0
	AT relativized to VO_{2peak} (%)	48.0 ±6.5	46.8 ±4.1	47.4 ±5.3
	VE, peak (L/min)	90.3 ±31.3	86.8 ±23.2	88.6 ±27.5
	RER, peak	1.2 ±0.1	1.1 ±0.1	1.2 ±0.1
	HR, peak (bpm)	193 ±8	184 ±29	188 ±22
	Power, peak (W/kg)	3.3 ±0.4	3.3 ±0.8	3.3 ±0.6
	Total Test Duration (mins)	23.5±2.9	22.8±3.0	23.2 ±3.1