

Exercise With and Without an Insulin Pump Among Children and Adolescents With Type 1 Diabetes Mellitus

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ABSTRACT. *Background.* The use of insulin pumps is becoming a popular technique for insulin delivery among patients with type 1 diabetes mellitus (T1DM), but there is no consensus regarding the guidelines for proper pump use during exercise.

Objective. To investigate the physiologic responses and risk of hypoglycemia among children and adolescents with T1DM when exercising with the pump on (PO) (50% of the basal rate) or pump off (PF).

Methods. Ten subjects with T1DM (6 female subjects and 4 male subjects), 10 to 19 years of age, performed prolonged exercise (40–45 minutes) on a cycle ergometer ~2 hours after a standard breakfast and an insulin (Lispro) bolus. Complex carbohydrates (20 g) were provided before and after the exercise. Each patient exercised once with PO and once with PF, in a randomized, crossover (single-blind) manner. During exercise and 45 minutes of recovery, subjects were monitored for cardiorespiratory, metabolic, and hormonal responses. Blood glucose concentrations were recorded for 24 hours after exercise, with a continuous glucose monitoring system, to document late hypoglycemic events.

Results. During exercise, blood glucose concentrations decreased by 59 ± 58 mg/dL (mean \pm SD: $29 \pm 24\%$) with PF and by 74 ± 51 mg/dL ($35.5 \pm 18\%$) with PO (not significant). No significant differences were found in cortisol, growth hormone, or noradrenaline levels between PO and PF. There were no differences in cardiorespiratory parameters, blood lactate concentrations, or free fatty acids concentrations between pump modes. Hypoglycemic events during exercise were asymptomatic and occurred for 2 subjects with PO and 2 with PF. Nine subjects had late hypoglycemia after PO, compared with 6 after PF (not significant).

Conclusions. We found no advantage for subjects with either PO or PF during exercise, and we noted that late hypoglycemia was more common than hypoglycemia during exercise. However, PO was associated with a trend of increased risk for late hypoglycemia. We recom-

mend that the pump be removed or turned off during prolonged exercise and that blood glucose concentrations be monitored for several hours after exercise, regardless of the pump mode. *Pediatrics* 2005;116:e348–e355. URL: www.pediatrics.org/cgi/doi/10.1542/peds.2004-2428; *type 1 diabetes mellitus, children and adolescents, insulin pump, exercise, hypoglycemia, maximal oxygen consumption rate, VO_{2max}* .

ABBREVIATIONS. CGMS, continuous glucose monitoring system; CSII, continuous subcutaneous insulin infusion; FFA, free fatty acid; GH, growth hormone; HR, heart rate; NA, noradrenaline; PF, pump off; PO, pump on; RER, respiratory exchange ratio; RPE, rate of perceived exertion; DM, diabetes mellitus; T1DM, type 1 diabetes mellitus; VO_{2max} , maximal oxygen consumption rate; VE , expired ventilation.

Type 1 diabetes mellitus (T1DM) usually presents during childhood or adolescence, with a peak age of 11 to 13 years. Of patients with longstanding disease, 40% to 50% develop microvascular or macrovascular complications. The treatment protocol for diabetes mellitus (DM) includes a triad of insulin, diet, and exercise.¹

To achieve tight metabolic control, insulin is delivered through either multiple daily insulin injections or continuous subcutaneous insulin infusion (CSII).² The use of CSII via insulin pump best simulates normal insulin secretion and has improved both the metabolic control and quality of life of diabetic patients.^{3–5} The use of the insulin pump has increased in recent years, especially among children and adolescents.

Physical activity plays an important role in the treatment protocol for DM. Among patients with T1DM, exercise has been found to improve metabolic control and to reduce exogenous insulin requirements. It may also prevent or delay late DM-related complications and improve longevity.^{6–8} Several factors influence the metabolic and hormonal responses to exercise among diabetic patients, such as the duration and intensity of exercise, the level of metabolic control, the type and dose of insulin delivered before exercise, the site of injection, and the timing of the previous insulin injection and food intake relative to the exercise. Accordingly, blood glucose levels can decline (the most common response), increase, or remain unchanged. Hyperinsulinemia prevents the appropriate increase in hepatic glucose production and accelerates the exercise-induced stimulation of

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glucose uptake into the contracting muscle. It also prevents the appropriate increase in lipid mobilization during exercise, leading to reduced availability of free fatty acids (FFAs) as metabolic fuel.⁷ Insulin resistance decreases with training among both adults and children. This physiologic effect is transient and depends on regular daily exercise.^{9–11} Therefore, it is recommended that regular exercise be part of the lifestyle of all diabetic patients.¹²

Hypoglycemia is the most common risk of exercise among diabetic patients. It may occur during exercise and/or several hours thereafter, owing to an increase in insulin sensitivity. Hyperglycemia, with or without ketosis, may also occur during exercise, mainly among patients with poor glycemic control.^{7,11} Unfortunately, fear of these situations often causes diabetic patients to refrain from physical activity. Usually patients are advised to inject insulin in accordance with planned physical activity, because adherence to exercise guidelines decreases greatly the risk of hypoglycemia or hyperglycemia.^{7,13}

The physiologic responses to exercise among healthy children have been investigated widely, and it is accepted that the physiologic responses of this population are different from those of adults.¹⁴ Most of the studies in the field of exercise physiology among patients with T1DM were conducted with adults. In addition, diabetic children and adolescents differ from the healthy pediatric population in their physiologic and metabolic responses to exercise. Young diabetic patients are characterized by impaired utilization of exogenous glucose as an energy source during exercise, despite high insulin levels,¹⁵ and by higher rates of perceived exertion (RPEs), which persist after glucose ingestion.¹⁶

Current exercise guidelines (eg, American Diabetes Association) for patients with T1DM are general and emphasize the importance of individual experimentation and support by a multidisciplinary medical staff. It is advised that exercise be individually tailored, taking into account the patient's interests, fitness level, and medical condition. Children, who are characterized by a wide range of glucose levels, and adolescents, who undergo hormonal changes that hamper metabolic control, require special attention and individual guidance. Nutrition and insulin doses need to be adjusted according to the time, type, intensity, and duration of exercise, preexercise glucose levels, and general metabolic control. Pump users are instructed to adjust the basal rate of insulin infusion during exercise.^{17,18} However, the proper adjustment of the insulin pump during exercise

among children and adolescents is not yet clear. This is especially crucial for this population, which engages characteristically in unplanned physical activity.

A better understanding of the physiologic and metabolic responses to exercise, with or without an insulin pump, may assist in providing proper guidelines for pump use during exercise. We therefore undertook the current study to investigate the cardiorespiratory, metabolic, and hormonal responses to controlled submaximal exercise, with the pump on (PO) (at 50% of the basal rate) and the pump off (PF), among children and adolescents with T1DM treated with CSII. In addition, we looked for differences in effort perception (RPE) and compared the occurrence of acute and late hypoglycemia.

METHODS

Subjects

Ten subjects (6 female subjects and 4 male subjects), 15.7 ± 3.0 years of age (range: 10–19 years), who had T1DM for ≥ 1 year participated in the study. All subjects had hemoglobin A1c levels of $<10\%$ and had been treated with an insulin pump for >3 months (Table 1). They were outpatients at the Institute for Endocrinology and Diabetes, National Center of Childhood Diabetes, Schneider Children's Medical Center of Israel. The research protocol was approved by the Ethics Committee for Clinical Investigation and by the Israeli Ministry of Health. Written informed consent was signed by all participants and by the parents of those <18 years of age.

Study Design

The study was conducted with a single-blind, randomized, case-crossover design. All subjects attended the laboratory on 4 occasions. The first visit included a detailed explanation of the study, a physical examination, determination of sexual development according to Tanner stage¹⁹ and BMI, blood sampling (complete blood count, iron, biochemical, lipid profile, and thyroid function tests and celiac screening), assessment of metabolic control (hemoglobin A1c and fructosamine levels), and urinalysis. Blood and urine samples were obtained to rule out hematologic, metabolic, and endocrinologic impairments and liver or kidney malfunction that could bias our results. During the second visit, the subjects underwent resting electrocardiography and determination of the maximal oxygen consumption rate ($\dot{V}O_{2max}$) on a cycle ergometer. During the third and fourth visits, the subjects cycled for 40 to 45 minutes at submaximal effort ($\sim 60\%$ of $\dot{V}O_{2max}$), with either PO (at 50% of the basal rate) or PF (0% of the basal rate), in a crossover design. The pump setting at the third visit was determined at random. Exercise was performed ~ 2 hours after a standard breakfast and a full insulin bolus, as determined by the patient according to carbohydrate count. Safety precautions were taken to ensure the appropriate glucose level before exercise (100–300 mg/dL, without ketosis) and to prevent hypoglycemia, according to the American Diabetes Association recommendations.¹⁷ Twenty grams of complex carbohydrates (cookies) were given to the participants before and 15 minutes after the exercise. Cardiorespiratory data and blood samples were obtained during

TABLE 1. Subjects' Characteristics

	Mean \pm SD	Range	Normal Values
Age, y	15.7 \pm 3.0	10.8–18.9	
DM duration, y	7.5 \pm 3.2	3–13.8	
Pump (CSII) duration, mo	15.2 \pm 9.4	6–36	
BMI, SD score	0.36 \pm 0.58	–0.6–1.2	
Hemoglobin A1c, %	8.1 \pm 0.8	6.5–9.5	4.3–5.8
Fructosamine, μ mol/L	405 \pm 53	320–499	205–285
$\dot{V}O_{2max}$, L/min	1.7 \pm 0.6	1.06–2.82	
$\dot{V}O_{2max}$, mL/(kg·min)	30.3 \pm 5.2	23.4–39.2	

exercise and after 45 minutes of recovery. Thereafter, blood glucose levels were recorded with a continuous glucose monitoring system (CGMS) and with multiple blood glucose self-tests for 24 hours, along with documentation of insulin boluses and meals.

Subjects were instructed to abstain from prolonged exercise for at least 24 hours before the exercise tests. The interval between the submaximal exercise tests was at least 7 days, during which the subjects were instructed to continue their regular lifestyles and treatment protocols.

Insulin Protocol

All subjects used short-acting insulin (Lispro, Eli Lilly, Indianapolis, IN) delivered through an insulin pump (MiniMed 508; MiniMed, Northridge, CA; or H-TRONplus V100; Disetronic, Burgdorf, Switzerland). The insulin bolus at breakfast before the exercise session was not reduced, to comply with the simulation of unplanned physical activity. During exercise with PO, the basal rate of insulin infusion was 50% of the usual dose; during exercise with PF, the basal rate was set at 0%. Subjects were unaware of the pump mode (PO or PF, single-blind design). Within 5 minutes after termination of exercise, the insulin basal rate was returned to the original setting; that is, the pump delivered a full basal dose of insulin during recovery.

Procedures

All subjects exercised on a constant-power electronic cycle ergometer (model ER 900; Ergoline, Windhagen, Germany). Expired gas was analyzed with a computerized metabolic system consisting of oxygen and carbon dioxide analyzers (models S-3A and CD-3A; Applied Electrochemistry, Pittsburgh, PA) and a heated Fleisch-type pneumotachometer (model 47304A; Hewlett Packard, Palo Alto, CA). The analyzers were calibrated with precision calibration gases (16.0% oxygen and 5.0% carbon dioxide) and the pneumotachometer with a precision 3.0-L calibration syringe (Vacumed, Ventura, CA). Expired gas parameters included expired ventilation (\dot{V}_E), oxygen consumption rate ($\dot{V}O_2$), carbon dioxide production rate, and respiratory exchange ratio (RER) ($RER = \text{carbon dioxide production rate}/\dot{V}O_2$). Cycle load, pedaling frequency, and heart rate (HR) were monitored continuously and recorded every 20 seconds.

Submaximal Exercise

The exercise protocol consisted of cycling on the ergometer at submaximal effort ($\sim 60\%$ of $\dot{V}O_{2\max}$) for 40 to 45 minutes. Cardiorespiratory parameters were recorded during the last 3 minutes of each 10-minute interval (10, 20, and 30 minutes), during the last 3 minutes of exercise, and during 3 minutes of recovery. Subjects were connected to the metabolic system 3 minutes before the end of each interval, data were collected for 3 minutes, and the subjects were then disconnected. RPE was documented in every phase of the workload with the Borg scale.²⁰ Venous blood was drawn from a forearm vein through an indwelling catheter before, during (10, 20, and 30 minutes), and at the termination of exercise and during recovery (at 15 and 45 minutes), for the determination of glucose, lactate, FFAs, cortisol, growth hormone (GH), noradrenaline (NA), and insulin concentrations. At each time, a droplet of blood was analyzed immediately for the glucose level with a Glucometer Elite meter (Bayer Diagnostics, Tokyo, Japan), for safety reasons, and for the lactate level with a Biosen 5030 analyzer (EKF, Hamm, Germany).

CGMS

A subcutaneous glucose sensor (MiniMed) was inserted in the lower abdomen, opposite the side of the insulin pump catheter, and was connected to a beeper-sized monitor. Glucose levels were recorded during exercise and for the following 24 hours. The monitor recorded data every 10 seconds, and an average glucose value was stored in memory every 5 minutes. The CGMS does not display glucose readings in real time but provides data for review with a personal computer after the entire recording (up to 72 hours) is completed. The range of sensor glucose readings is 40 to 400 mg/dL.^{21–23}

Blood Sample Analyses

Blood samples were placed in an ice-water slurry for additional analysis. Glucose levels were analyzed with the glucose oxidase

reaction (model 917 autoanalyzer; Hitachi, Tokyo, Japan; reagent from Roche, Basel, Switzerland). Insulin, GH, and cortisol levels were analyzed with chemiluminescent assays (Immulite 2000; Diagnostics Products, Los Angeles, CA), and NA levels were analyzed with high-performance liquid chromatography (Coulochem 5100E electrochemical detector; ESA, Chelmsford, MA). FFAs levels were determined with radioactive nickel labeling (beta counter; Hewlett Packard). Urine ketones were tested with Ketostix test strips (Bayer Diagnostics).

$\dot{V}O_{2\max}$ Determinations

$\dot{V}O_{2\max}$ determinations were based on an incremental cycling workload (starting load of 20–40 W, depending on the subject's age, with increments of 10–20 W every 2 minutes), at a constant rate (~ 60 cycles per minute), until volitional exhaustion or the subject could no longer maintain the required pedaling rate. $\dot{V}O_{2\max}$ was determined as the mean of the 2 consecutive highest $\dot{V}O_2$ measurements.

Statistical Analyses

Results are presented as mean \pm SD. Descriptive statistics and Spearman correlation tests were applied. Data were then analyzed with analysis of variance for repeated measures. The Fisher-Irwin exact test was used to compare the proportion of late hypoglycemic events between the 2 pump modes. BMDP statistical software was used for computations. The significance level was set at $P \leq .05$.

RESULTS

Preexercise Parameters

Exercise (mean 58% of $\dot{V}O_{2\max}$) started 111 ± 11 minutes (PF) or 112 ± 17 minutes (PO) after breakfast and insulin bolus (4.7 ± 2.2 U before PF and 4.0 ± 2.2 U before PO; not significant). Two subjects received an extra 1 U because their glucose levels were >300 mg/dL (without ketosis) ~ 1 hour before exercise. The preexercise HRs were 86 ± 9 beats per minute (PF) and 85 ± 9 beats per minute (PO). Fructosamine levels were 376 ± 53 $\mu\text{moles/L}$ and 396 ± 53 $\mu\text{moles/L}$, respectively (not significant). No significant differences were found between PF and PO in any preexercise blood parameters. With PO, the insulin basal rate ranged from 0.2 to 0.8 U/hour (mean: 0.55 ± 0.18 U/hour).

Cardiorespiratory Responses

No differences were found between PF and PO in HR, \dot{V}_E , $\dot{V}O_2$, or RER. The HR was 162 ± 8 beats per minute at the end of exercise with PF and 158 ± 8 beats per minute with PO. After 45 minutes of recovery, the HRs were 88 ± 7 beats per minute and 87 ± 9 beats per minute, respectively. \dot{V}_E was 29.9 ± 6.8 L/minute at the end of exercise with PF and 30.3 ± 6.9 L/minute with PO. The mean $\dot{V}O_2$ was 1.0 ± 0.28 L/minute with PF (58% of $\dot{V}O_{2\max}$) and 0.98 ± 0.28 L/minute with PO (57% of $\dot{V}O_{2\max}$). The mean RERs were 1.02 ± 0.03 and 1.01 ± 0.05 with PF and PO, respectively.

RPE

RPE increased from 11.8 ± 2 (fairly light to somewhat hard) to 15.5 ± 2.2 (hard) during exercise with PF and from 10.6 ± 2.3 (very light to fairly light) to 15.3 ± 1.8 (hard) with PO. The differences between conditions were statistically insignificant.

Metabolic Responses

Glucose

The results of the metabolic responses are illustrated in Fig 1. Glucose levels decreased during ex-

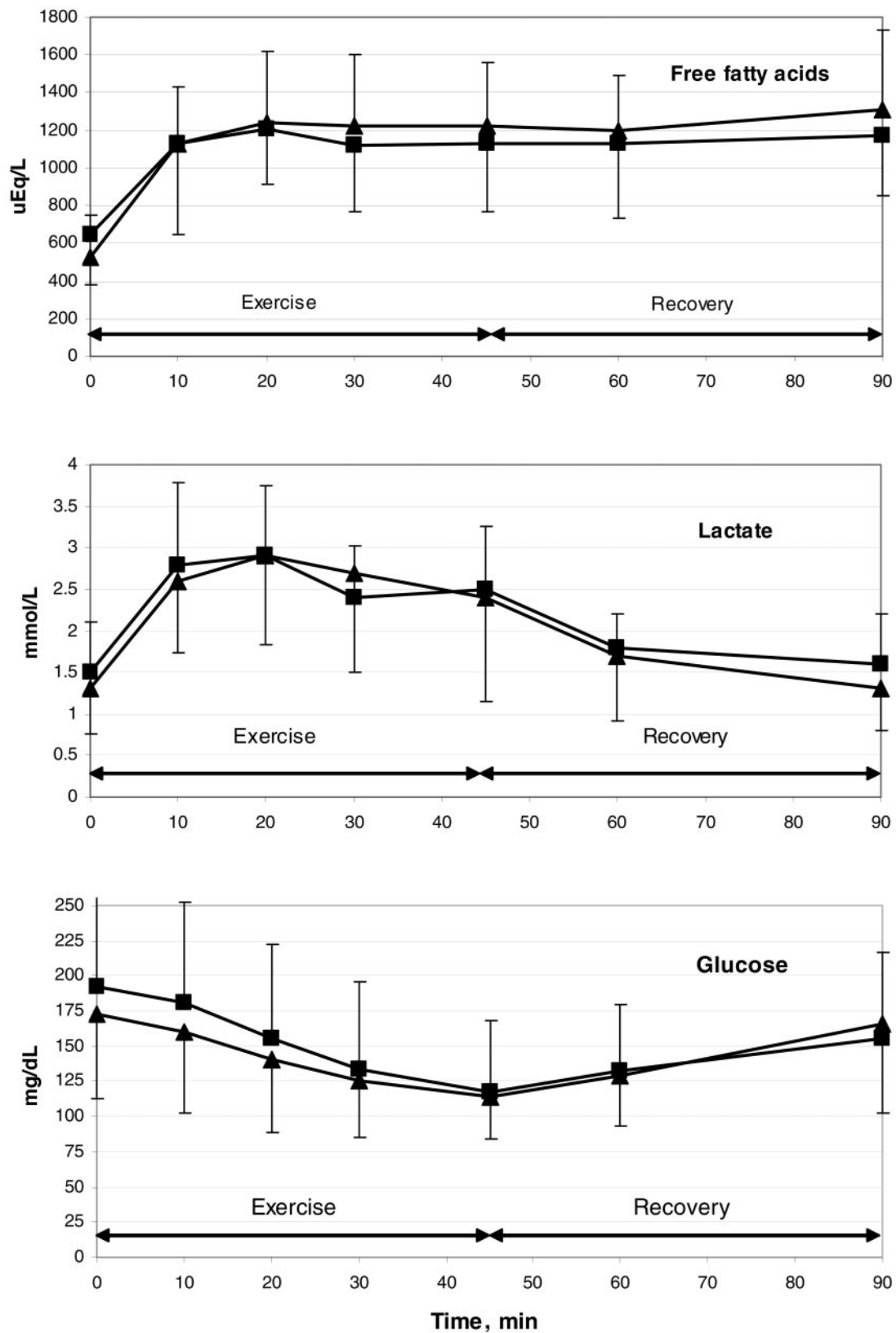


Fig 1. Metabolic responses among young subjects with T1DM during submaximal exercise (~60% of $\dot{V}O_{2max}$) and recovery, with PF (▲) and PO (■). Data are presented as mean \pm SD. No significant differences were found between PF and PO conditions.

ercise under both conditions (range: 7–77%), except for 1 patient who had an 18% increase with PF. During exercise, blood glucose levels decreased by

59 \pm 58 mg/dL (mean \pm SD: 29 \pm 24%) with PF and by 74 \pm 51 mg/dL (35.5 \pm 18%) with PO (not significant). The lowest values were observed generally at

the end of exercise (mean: 114 ± 30 mg/dL with PF and 118 ± 50 mg/dL with PO). There were no significant differences in absolute glucose levels [$F(6,54) = 0.93$, $P = .48$] or relative (percentage) changes [$F(6,54) = 1.09$, $P = .38$] between the PF and PO conditions.

Lactate

The highest lactate levels were measured at 10 or 20 minutes, except for 1 patient who exhibited the highest value at the end of exercise. The highest lactate level was 2.9 ± 1.1 mmol/L with PF and 2.9 ± 0.8 mmol/L with PO, and levels returned to preexercise values at 45 minutes of recovery. There was no significant difference between the 2 conditions.

FFAs

The highest FFAs values were measured at 20 minutes of exercise (1243 ± 377 μ Eq/L with PF and 1208 ± 298 μ Eq/L with PO). The highest value during exercise with PF was followed by another peak (1306 ± 427 μ Eq/L) at 45 minutes of recovery, compared with stabilization with PO. There was no significant difference between the 2 conditions.

Hormonal Responses

Cortisol

The results of the hormonal response are illustrated in Fig 2. Cortisol levels increased during exercise under both conditions, attaining their highest levels at 15 minutes of recovery, ie, 390 ± 145 nmol/L ($164 \pm 78\%$) after exercise with PF and 431 ± 147 nmol/L ($210 \pm 89\%$) after exercise with PO. Cortisol levels tended to increase more during exercise and recovery with PO, compared with PF ($P = .086$).

GH

Preexercise GH levels varied widely (0.1 – 21.7 ng/mL), and levels increased markedly during exercise under both conditions. The highest levels ranged between 7.3 and 68 ng/mL and were attained usually at the end of exercise (mean: 28.6 ± 22 ng/mL [$4069 \pm 5913\%$] with PF and 25 ± 15 ng/mL [$9220 \pm 18531\%$] with PO). There was no significant difference between the PF and PO conditions.

NA

Under both conditions, NA levels peaked ($\sim 200\%$) at the end of exercise (782 ± 322 pg/mL with PF and 763 ± 272 pg/mL with PO). The peak was followed by a nadir of $\sim 80\%$ to 90% of preexercise values at 15 minutes of recovery. There were no significant differences in NA levels or relative (percentage) changes between the 2 conditions.

Insulin

Insulin levels increased during exercise, attaining their highest values at 20 minutes ($107 \pm 13\%$ with PF and $110.5 \pm 14.5\%$ with PO), and then decreased to approximately preexercise levels at the end of exercise. Insulin levels declined more during recovery, reaching $72 \pm 12\%$ (after PF) and $79 \pm 11\%$ (after

PO) at the end of recovery (Fig 3). There was no significant difference between the pump conditions in either insulin levels [$F(6,54) = 1.57$, $P = .17$] or percentage changes [$F(6,54) = 0.87$, $P = .52$].

Hypoglycemia

Acute Hypoglycemia

Glucose levels of <70 mg/dL, with or without symptoms, were considered hypoglycemia. The chemistry laboratory results were used for analysis. Hypoglycemia (50 – 64 mg/dL) occurred during exercise for 2 subjects with PF and 2 with PO, all asymptomatic (these subjects continued exercising). Three of the hypoglycemic events occurred at 30 minutes of exercise and 1 at 20 minutes. All 4 subjects had preexercise glucose levels of 84 to 111 mg/dL; only 1 consumed a sweet drink before exercise, because of a glucose reading of <100 mg/dL (glucometer check). The exercise sessions with a hypoglycemic event began at lower glucose levels and higher insulin levels (for 3 subjects, 10 – 50% higher) than the other sessions performed by the same subjects.

Late Hypoglycemia

Analysis of the CGMS data showed that all subjects had 1 to 3 late hypoglycemic events (glucose levels between 50 and 70 mg/dL), after either PF or PO, that were symptomatic in part and occurred generally 2.5 to 12 hours after exercise. Nine subjects (90%) had late hypoglycemic episodes after exercise with PO, compared with 6 (60%) with PF (not significant).

DISCUSSION

Children engage frequently in unplanned physical activity. Our study was designed to mimic unplanned exercise. We demonstrated a risk for late hypoglycemia among children and adolescents with T1DM treated with pumps, regardless of the pump mode.

Guidelines for pump use during and after exercise are general and, to the best of our knowledge, no published data exist concerning exercise with different pump settings among this population. Sonnenberg et al²⁴ investigated the effect of exercise on glucose levels among 7 male subjects, 15 to 31 years of age, with T1DM treated with insulin pumps. The subjects performed moderate exercise for 60 minutes on a cycle ergometer with 5 different insulin (soluble, regular) protocols. The authors found that hypoglycemia during exercise could be prevented only when the premeal insulin bolus was reduced by 50% and basal insulin infusion during exercise was discontinued. To reduce late hypoglycemic reactions after exercise, the best measure proved to be a reduction of the basal insulin infusion rate by 25% during postexercise hours. Rabasa-Lhoret et al²⁵ found that, among subjects with well-controlled T1DM who were receiving intensive insulin therapy with a basal (Ultralente)-bolus (Lispro) insulin regimen, the risk of hypoglycemia during postprandial exercise of different intensities and different durations could be minimized with appropriate reduction of the premeal

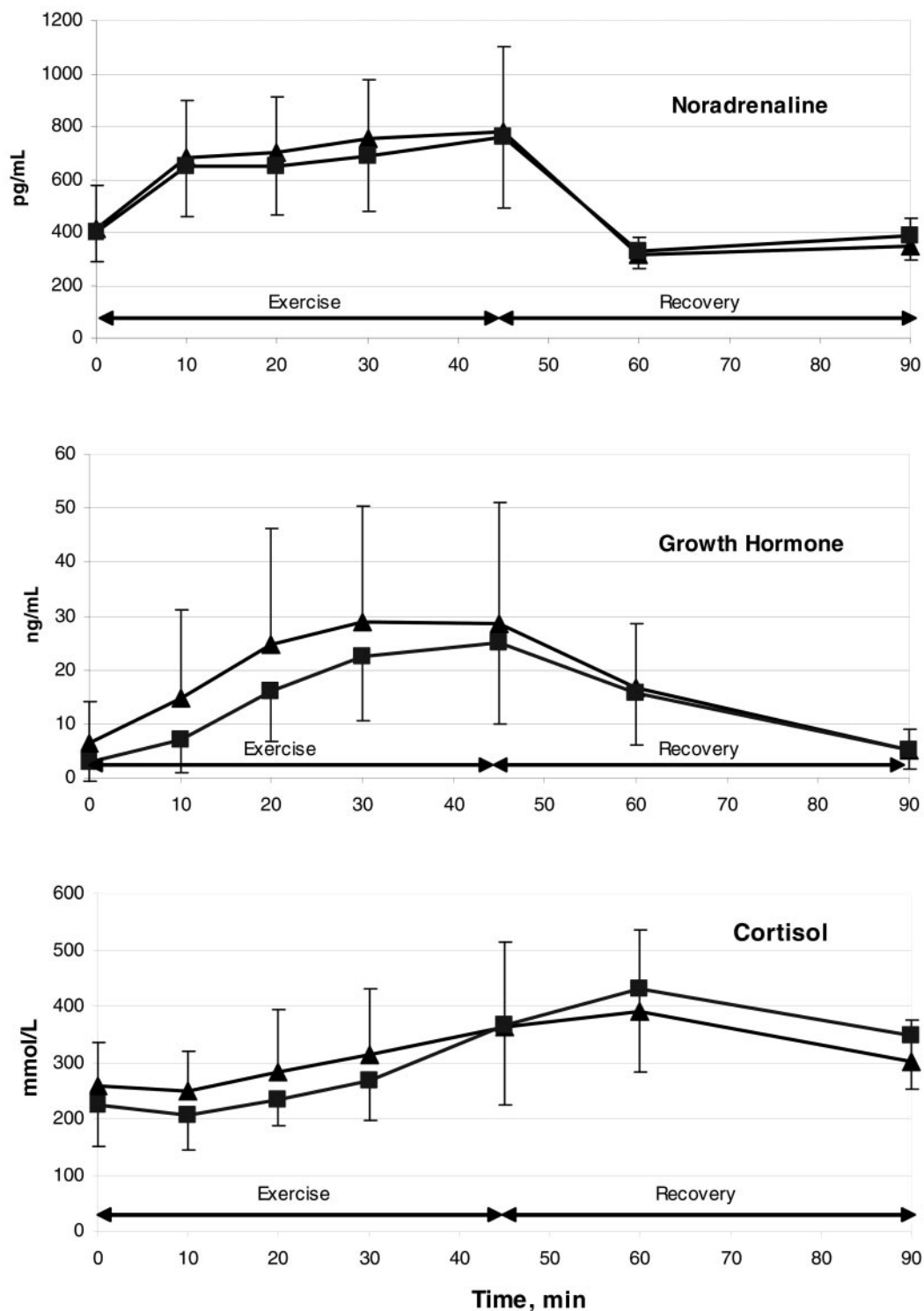


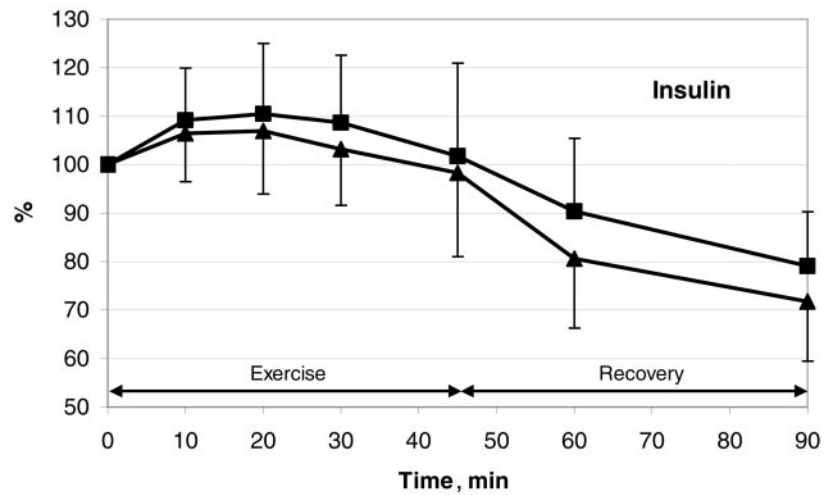
Fig 2. Hormonal responses among young subjects with T1DM during submaximal exercise (~60% of $\dot{V}O_{2max}$) and recovery, with PF (\blacktriangle) and PO (\blacksquare). Data are presented as mean \pm SD. No significant differences were found between PF and PO conditions.

insulin Lispro dose. Of course this demands preplanning of the exercise.

The unique aspects of the present study are the simulation of unplanned exercise (after breakfast with a full-dose insulin bolus), the age of these CSII-treated patients (pediatric group), the insulin used (Lispro), and the multiplicity of physiologic parameters. Our study demonstrates that, among young diabetic subjects, late postexercise hypoglycemia is a

much more common phenomenon than hypoglycemia during exercise. This indicates that the pump condition (0–50% of the basal rate) is probably not a major risk factor for hypoglycemia during exercise, although exercise with PO may pose an increased risk of late hypoglycemia, when insulin sensitivity is increased. The insulin basal rate, which was not reduced after exercise under the conditions of this study, might have contributed to the high frequency

Fig 3. Relative (percentage) changes in insulin levels among young subjects with T1DM during submaximal exercise ($\sim 60\%$ of $\dot{V}O_{2\max}$) and recovery, with PF (\blacktriangle) and PO (\blacksquare). Data are presented as mean \pm SD. No significant differences were found between PF and PO conditions.



of postexercise hypoglycemia. We observed a trend toward a greater decline in glucose levels during exercise with PO, with a slower increase during recovery. Edelman et al²⁶ studied the effect of interruption of insulin infusion on exercise-induced hypoglycemia among 7 adult subjects with SCII-treated T1DM. The authors concluded that, even after 3-hour interruption of the basal-rate insulin infusion, moderate postprandial exercise might lead to hypoglycemia if there is relative hyperinsulinism.

Our findings emphasize the importance of preexercise complex carbohydrates ingestion and postexercise blood glucose monitoring and insulin dose reduction, as recommended by the American Diabetes Association.¹⁷ Increasing the bedtime snack the night after the exercise might also be considered.

The increase in serum insulin levels during exercise in both pump conditions can be explained, at least partially, by the decrease in plasma volume during exercise.²⁷ In addition, the possibility of accelerated insulin absorption from the pump catheter site exists, although there are no published data to support this assumption. Obviously, insulin levels do not decrease, and there is not the considerable increase that may be seen during similar exercise among diabetic subjects treated with injections, because of enhanced absorption from the injection site.^{28,29} Insulin levels returned to preexercise levels at the end of exercise with PF and PO, but the decline during recovery tended to be slower after exercise with PO. This suggests that PF or PO may influence both insulin levels and the rate of decline in the early postexercise period. No correlation was found between the change in insulin levels and the postbreakfast bolus dose or the basal rate (PO)/bolus ratio, meaning that the bolus dose or the basal rate should not influence the decision regarding pump settings during exercise.

This study showed that there was no difference in cardiorespiratory responses and effort perception (RPE) during submaximal exercise among young diabetic subjects treated with insulin pumps, whether exercise was performed with PF or PO. RER values were ~ 1.0 under both pump modes, which is higher than expected for healthy individuals who exercise

at $\sim 60\%$ of their $\dot{V}O_{2\max}$.^{30,31} These results suggest that young diabetic subjects performing submaximal exercise rely more on carbohydrate fuel for energy expenditure than do nondiabetic subjects, which is in agreement with the results reported by Broderick et al,³² who demonstrated higher RER among 12 subjects with T1DM during prolonged (90-minute) submaximal (60% of $\dot{V}O_{2\max}$) exercise, compared with 8 normal control subjects, corresponding to a smaller proportion of energy used from fat oxidation.

The results of the other metabolic and hormonal responses were not significantly different between PF and PO modes but, when exercise with PF was compared with PO, we assumed that serum insulin levels would be lower with PF. However, this assumption was correct for only one half of the subjects. A reasonable explanation is that exercise was performed on different days. Preexercise insulin levels are correlated primarily with prebreakfast levels, the postbreakfast bolus dose, and the time interval between the bolus dose and exercise. To overrule this bias and to understand better the influence of insulin on the responses to exercise, we categorized the subjects according to their serum insulin levels (low versus high) during exercise (not PF versus PO). The minimal difference was set at 10%, leaving 9 subjects for analysis. Analysis of the data showed that there were increases in GH relative (percentage) changes [$F(6,54) = 2.84, P = .018$] and in absolute cortisol levels [$F(6,54) = 2.45, P = .036$] at the higher insulin condition. These findings suggest that, when insulin levels are higher during exercise, more intense hormonal feedback is needed to maintain glucose levels and/or to facilitate energy substrate production and/or utilization (eg, FFAs). No differences were observed in any of the other cardiorespiratory, metabolic, or hormonal variables.

The present study was designed to mimic an unplanned, prolonged, morning exercise session (defined as a duration of 40–45 minutes) performed ~ 2 hours after breakfast. Additional research with different age groups and Tanner stages, at different times during the day, and with more subjects is needed to confirm our findings and to establish firm

guidelines, because the use of insulin pumps among youngsters is increasing.

CONCLUSIONS

We conclude that unplanned, prolonged (40 to 45 minutes), submaximal exercise, performed ~2 hours after breakfast (and most likely after any other meal), is equally performed, perceived, and safe (in terms of acute hypoglycemia) under the 2 pump modes. Moreover, we suggest that a working pump during exercise has no benefit, because it exposes the subject to higher insulin levels that may augment hormonal feedback. In addition, late hypoglycemia is more common than hypoglycemia during exercise. However, PO was associated with a trend of increased risk for late hypoglycemia.

We recommend that the pump be removed or turned off during unplanned prolonged exercise for the convenience of young diabetic patients, eliminating the need to change basal rates and possibly decreasing the risk of late hypoglycemia. This is in adjunct with the general recommendations of preexercise complex carbohydrate ingestion, postexercise blood glucose monitoring, and insulin dose reduction, as well as increases in the bedtime snack to prevent late hypoglycemic events.

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