High-intensity Exercise in Men with Type 1 Diabetes and Mode of Insulin Therapy

Authors
Andrzej Gawrecki, Dariusz Naskret, Paweł Niedzwiecki, Anna Duda-Sobczak, Aleksandra Araszkiewicz, Dorota Zozulinska-Ziolkiewicz

Affiliation
Department of Internal Medicine and Diabetology, Poznan University of Medical Sciences, Poznan, Poland

Key words
type 1 diabetes, high intensity exercise, metabolic decompensation, hypoglycemia, continuous subcutaneous insulin infusion, multiple daily injections

accepted after revision 27.11.2016

Introduction
Regular exercise improves metabolic control and reduces the risk of chronic complications of diabetes, including cardiovascular events [5]. Therefore, physical exercise has long been an integral part of the treatment of type 1 diabetes (T1D) [26]. Guidelines of diabetes societies emphasize the benefits of physical activity, and propose solutions for insulin therapy and nutrition. However, patients’ behavior and therapeutic decisions relating to physical activity depend on many factors, including the metabolic control of diabetes, physical fitness, time of the day, and most of all, the duration and intensity of the exercise [34]. This is because the duration and intensity (i.e., light, moderate, or high) of the exercise will influence the plasma glucose levels in people with T1D. There are several positive molecular mechanisms related to intense exercise including increased mitochondrial biogenesis, stimulation of 5’AMP-activated protein kinase (AMPK) [32], enhanced production of glucose transporters GLUT-4 [28].

The biggest limitation and patients’ concern associated with physical activity in the treatment of diabetes is hypoglycemia [17]. Hypoglycemia not only occurs during physical exercise, but also in the subsequent hours. Hypoglycemia after short activity results mostly from the decrease in glycogen stores and relative high insulin level [18]. High-intensity exercise is highly dependent on glucose as a fuel, derived from either hepatic or muscle glycogenolysis. In obtaining energy at high intensity exercise dominates glucose, but also the energy source is a phosphate, beta-oxidation and glucose in circulation produced by the liver in glycogenolysis as well as gluconeogenesis. On the other hand, intense physical activity may cause hyperglycemia in patients with T1D, with some reports indicating that the maximal physical effort can lead to metabolic decompensation [10, 30, 34]. The causes of hyperglycemia are complex and result from the catecholamine response to intense exercise, as well as incorrect insulin dose or increased carbohydrate consumption associated with the fear of hypoglycemia [8]. Hyperglycemia caused by a high intensity physical activity can also occur a few hours after the event, which is related to the absence of physiological hyperinsulinemia and increased glucose production due to the catecholamine response [19]. Due to the potential for hypoglycemic and hyperglycemic events to occur, the modification of therapy in patients with T1D during physical activity has become of interest. In practice, different intensity of the exercise requires ingestion of a diversified amount of carbohydrates and adequate insulin dose adjustment [21]. In particular, patient’s attention must be given to the relation

Bibliography

Abstract
The purpose of this study was to evaluate the impact of high intensity exercise on glucose levels and risk of metabolic decompensation in males with type 1 diabetes (T1D), depending on the method of insulin administration. The study comprised 29 males (aged 25.3 ± 5.1 years; duration of diabetes 10.3 ± 3.2 years) treated with continuous subcutaneous insulin infusion (CSII) or multiple daily insulin injections (MDI). Treadmill exercise test was performed twice in each patient until subjective exhaustion as maximum according to the Borg scale. All the patients achieved ≥ 85% of the maximal heart rate. Distance during the test was 4 500 ± 1 400 m and 4 473 ± 1 559 m in the MDI and CSII groups, respectively, which was achieved in 31 ± 8 min. During the test and in the 6 h after, no clinically significant episodes of hypoglycemia occurred. Mean glucose levels did not exceed 10 mmol/L in most patients. The risk of the composite endpoint (hypoglycemia < 3.8 mmol/L, hyperglycemia ≥ 16.6 mmol/L, ketones ≥ 0.6 mmol/L, and lactate > 2.2 mmol/L) was higher in patients treated with MDI than CSII (OR3.75, 95%CI:1.22–11.52, p = 0.02). In conclusion, planned high intensity physical effort in men with well-controlled T1D is metabolically safe. CSII shows greater metabolic advantage over MDI during and after high intensity exercise in men with T1D.
between time of exercise and last bolus of insulin administration, frequently with the necessary intake of carbohydrates during and after exercise. Moreover, the demand for insulin requirement usually decreases after the start of regular physical activity. Indeed, proper adjustment of insulin therapy has successfully enabled patients with diabetes to perform intense sporting activities, including extreme sports [20, 31]. If not done well, adjusting the insulin dose may lead to glycemic instability and worsening of metabolic control of T1D.

To date, reports on the effect of physical activity on diabetes control monitored with glycated hemoglobin (HbA1c) are inconsistent [16], with most studies only concerning moderate-intensity aerobic efforts [4, 11, 25]. While a meta-analysis by Kennedy et al. found no glycemic benefit of moderate-intensity exercise overall in people with T1D, further sub-analyses suggested that exercise may confer a glycemic benefit in the young and when undertaken for longer periods [15]. In addition, high-intensity efforts are typically not recommended, due to their suspected potential to cause decompensation of diabetes. Therefore, the knowledge and clinical experience concerning safety of high intensity exercise in patients with T1D is limited.

The aim of the study was to evaluate the effect of high-intensity exercise on glucose levels and the risk of metabolic decompensation in males with T1D. An additional goal of the study was to compare 2 methods of insulin delivery: continuous subcutaneous insulin infusion (CSII) using a personal insulin pump and multiple daily injections (MDI) using pens.

Material and Methods

Subjects

The study included males with T1D who were referred to a diabetes ward in order to educate and diagnose chronic complications. Written informed consent was obtained from all the participants before inclusion in the study. The study was approved by the ethics committee of the Poznan University of Medical Sciences. The study meets the ethical standards in sport and exercise [13].

Inclusion criteria were: T1D lasting from 5 to 15 years, treated for at least 3 months with intensive functional insulin therapy using a personal insulin pump or pen-type injectors; age 18–35 years; male sex; no other significant comorbidities; echocardiography result in the normal range; no hypoglycemia < 60 mg/dL (3.3 mmol/L) or acetonuria and glycosuria on the day of examination; and HbA1c ≤ 8.5%. Exclusion criteria were: presence of advanced chronic complications of diabetes, pre-proliferative retinopathy, proliferative retinopathy, diabetic maculopathy, neuropathy, diabetic nephropathy in stage III–V chronic kidney disease; metabolic decompensation of diabetes (severe hypoglycemia, diabetic ketoacidosis) in the last 10 days; important cardiovascular, respiratory, and mobility diseases; glucose before a standardized meal preceding the exercise > 200 mg/dL (11.1 mmol/L) or < 60 mg/dL (3.3 mmol/L), or < 70 mg/dL (3.8 mmol/L) with accompanying symptoms of hypoglycemia; postprandial glycosuria > 250 mg/dL (13.8 mmol/L) and the presence of ketones in the blood; or a body mass index (BMI) ≥ 30 kg/m². Patients were treated using CSII (CSII group) or MDI with pen-type injectors (MDI group).

All patients underwent a complete physical examination including anthropometric and blood pressure measurements. BMI was calculated from the following formula: BMI = weight (kg)/squared height (m²). Blood samples were collected in a fasting state using S-Monovette blood collection system. Serum total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglyceride (TG) levels were measured using standard methods. HbA1c was measured using high-performance liquid chromatography (HPLC) with the Variant Hemoglobin A1c Program (Bio-Rad Laboratories, Hercules, CA, USA).

Study protocol

Exercise tests were carried out in a hospital setting. Before inclusion in the study, resting transthoracic echocardiography and laboratory tests necessary for qualification were performed. In the outpatient setting and on the first day of admission to the diabetes ward, a test validating the basal insulin (the long-acting insulin) dose in the MDI group and the basal rate in patients treated with CSII was performed. Evaluation of glucose levels during an 8 h break between meals and at night was performed, assuming that changes in glucose levels will not exceed ± 30 mg/dL (1.7 mmol/L).

Patients were provided with the Guardian Real Time (Medtronic) system of continuous glucose monitoring (CGM). A sensor was inserted 24 h before the first exercise test. Calibration was performed using the Contour TS glucose meter (Bayer HealthCare Diabetes Care), in accordance with the study protocol.

All subjects completed a progressive exercise test on the h/p/cosmos Para Graphics® treadmill 2 times (on the second and fourth day after the CGM sensor was inserted). Each high intensity exercise test was initiated in the 90th minute after ingestion of a standardized meal, prepared by a qualified dietitian, containing 90 g of carbohydrates. One day standard meal was preceded by an insulin bolus in dose balancing carbohydrates and on the second day the bolus of insulin was reduced by 30%, which is consistent with the recommendations [1, 24]. The data from both exercise tests were taken to analysis. The patients began the exercise test by walking at 3 km/h. The speed of the treadmill increased by 2 km/h for every 3 min. All subjects finished the exercise test at maximum treadmill speed of 11 km/h. There was no increase in the treadmill incline, as the test was supposed to respond to everyday life. The exercise tests were conducted until the patient perceived the maximum exhaustion according to the Borg scale which was objectively rated with patients’ heart rate. All the subjects achieved ≥ 85% of the maximal heart rate (HR) for the patient’s age [23], which was calculated from the formula Heart Rate Limit = 220-age. The mean HR during the exercise was 93 ± 13/min; in: 5th min 108 ± 15/min; 10th min 151 ± 19/min; 15th min 171 ± 16/min; 20th min 179 ± 15/min; 25th min 180 ± 13/min; 30th min 183 ± 14/min.

Glucose levels were monitored using the glucometer (Contour TS Bayer HealthCare Diabetes Care) at 10 min intervals during the test and then every hour for the next 6 h. Simultaneously, glycaemia was monitored using the CGM system. During the exercise and the subsequent 6 h observation, the patients consumed 20 g of simple carbohydrates if the measured glucose was < 70 mg/dL (3.8 mmol/L) and symptoms of hypoglycemia occurred, or when blood glucose was < 60 mg/dL (3.3 mmol/L) even in the absence of symptoms. The presence of ketones in capillary blood was controlled using a test strip and glucometer (Optium Xido Abbott Lab-
The study design is shown in Fig. 1.

**Table 1** Characteristics of patients with T1D in the MDI and CSII groups.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>MDI (n = 14)</th>
<th>CSII (n = 15)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>26.9 ± 4.5</td>
<td>23.7 ± 5.1</td>
<td>0.08</td>
</tr>
<tr>
<td>Duration of T1D (years)</td>
<td>10.4 ± 2.6</td>
<td>10.2 ± 3.7</td>
<td>0.90</td>
</tr>
<tr>
<td>Basal insulin dose/basal rate (U/kg body weight)</td>
<td>0.22 ± 0.06</td>
<td>0.25 ± 0.05</td>
<td>0.14</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>80.2 ± 6.1</td>
<td>79.6 ± 9.6</td>
<td>0.84</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>182 ± 7</td>
<td>180 ± 6</td>
<td>0.60</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.3 ± 2.1</td>
<td>24.4 ± 2.3</td>
<td>0.93</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>120 ± 9</td>
<td>119 ± 8</td>
<td>0.76</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>75 ± 9</td>
<td>77 ± 7</td>
<td>0.64</td>
</tr>
<tr>
<td>Hba1c (%)</td>
<td>7.1 ± 0.7</td>
<td>7.0 ± 0.4</td>
<td>0.53</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>4.9 ± 1.0</td>
<td>4.7 ± 1.0</td>
<td>0.83</td>
</tr>
<tr>
<td>HDL (mmol/L)</td>
<td>1.6 ± 0.3</td>
<td>1.5 ± 0.3</td>
<td>0.56</td>
</tr>
<tr>
<td>LDL (mmol/L)</td>
<td>3.0 ± 0.8</td>
<td>2.8 ± 0.9</td>
<td>0.64</td>
</tr>
<tr>
<td>TG (mmol/L)</td>
<td>1.0 ± 0.3</td>
<td>0.9 ± 0.3</td>
<td>0.73</td>
</tr>
</tbody>
</table>

Results are presented as mean ± SD.

**Statistical analysis**

The statistical analysis was performed using Statistica PL version 8.0. The normality of the distribution of results was assessed with the Lilliefors test. As the analyzed parameters were normally distributed, parametric tests were used for further analyses. Results are presented as numbers and percentages, as well as mean values and standard deviations (SD). In the case of numeric variables, differences between subgroups were analyzed using the Student's t-test. The differences in the qualitative data were assessed using the Chi² test. The logistic regression model was used to assess the impact of the type of therapy on the occurrence of the composite endpoint (defined as the occurrence during the study of one or more of the parameters, such as blood glucose ≥ 300 mg/dL (16.6 mmol/L) or < 70 mg/dL (3.8 mmol/L), ketones ≥ 0.6 mmol/L or lactate concentration in the blood > 2.2 mmol/L). A p < 0.05 was considered statistically significant.

**Results**

**Patient characteristics**

The study group consisted of 29 males aged 25.3 ± 5.1 years, with a mean duration of diabetes of 10.3 ± 3.2 years, treated since diagnosis with intensive functional insulin therapy. In the studied group, 15 men were treated using personal insulin pumps (CSII group), and in 14 men insulin therapy was carried out using pen-type injectors (MDI group). In the MDI group, 7 patients used a long-acting insulin analog (glargine), including 4 people administering it in one evening injection. 7 patients used intermediate-acting insulin (Neutral Protamine Hagedorn, NPH) insulin in 2 injections per day. All patients reported irregular amateur sport activity. None of the patients smoked cigarettes. Patients in the MDI and CSII groups did not differ significantly in terms of the parameters examined (Table 1).

**Changes in blood glucose levels during the exercise test**

During the exercise test, the MDI and CSII groups covered a similar distance (4500 ± 1400 m and 4473 ± 1559 m, respectively; p > 0.05). In both groups, the duration of test was 31 ± 8 min. Blood glucose levels during the exercise test were significantly higher at the beginning of the test and in 10th and 20th minute in the CSII group vs. the MDI group (10.0 ± 3 mmol/L vs. 7.9 ± 2.9 mmol/L, p = 0.007, and 7.8 ± 2.6 mmol/L vs. 6.3 ± 2.7 mmol/L, p = 0.04, in the 10th and 20th minute, respectively; Fig. 2). At the end of the test, glucose levels were lower than before exercise and did not differ between the 2 groups (6.6 ± 2.8 mmol/L vs. 6.1 ± 2.2 mmol/L, p = 0.43, in the CSII and MDI groups, respectively; Fig. 2). The mean differences in glucose levels between the beginning and the end of the test were significantly higher in patients treated with CSII than MDI (3.9 ± 2.7 mmol/L vs. 2.1 ± 2.4 mmol/L, p = 0.015). In addition, the mean blood glucose levels monitored during the test using the CGM were higher in the CSII group compared to the MDI group (10.1 ± 3.2 mmol/L vs. 8.4 ± 2.3 mmol/L, p = 0.023). However, the short time of exercise testing and high glycemic variability should be taken into account, which could affect the accuracy of the results assessed by CGM.

**Changes in blood glucose levels after the exercise test**

Mean glucose levels measured using a glucometer increased gradually after the exercise test in the following hours of observation (Fig. 2). However, glucose levels measured 6 h after the end of physical exercise did not differ significantly between the 2 groups (9.9 ± 4.1 mmol/L vs. 11.3 ± 3.9 mmol/L, p = 0.19, in the CSII and MDI group, respectively; Fig. 2). Similar observations were made.
when analyzing mean glucose levels using CGM: while glucose levels gradually increased in the hours after exercise, the mean glucose levels in 3 designated time intervals did not differ significantly between the MDI and CSII groups (▶ Fig. 3).

**Changes in serum lactate and capillary blood ketone levels during and after the exercise test**

Significantly higher mean levels of serum lactate were found after the exercise test in the patients in the MDI group compared to the CSII group (9.07 ± 3.35 mmol/L vs. 6.03 ± 3.41 mmol/L, p = 0.001). However, before exercise and after 6h of observation, mean plasma lactate levels did not differ between the 2 groups (1.86 ± 0.49 mmol/L vs. 1.60 ± 0.46 mmol/L, p = 0.05, and 1.21 ± 0.69 vs. 1.0 ± 0.55 mmol/L, p = 0.21, respectively). In addition, the average ketone concentrations after 6h of observation were within the reference range; however, significantly higher levels of ketone bodies were found in patients treated with MDI after 6h of observation than those treated with CSII (0.44 ± 0.42 mmol/L vs. 0.23 ± 0.19 mmol/L, p = 0.015).

**Incidence of single endpoints among MDI and CSII patients**

During exercise and in the 6h after, we noticed 11 episodes of hypoglycemia < 70 mg/dL (3.8 mmol/L) in the MDI group and 9 episodes in the CSII group (p = 0.45). However, no severe hypoglycemia episodes and no episodes of clinically significant hypoglycemia were noted. All hypoglycemia episodes resolved after the consumption of carbohydrates. There was no difference in the number of episodes of hyperglycemia (> 16.6 mmol/L) or high lactate concentrations (> 2.2 mmol/L) between the MDI and CSII groups. A significantly higher incidence of elevated levels of ketone bodies was observed in the MDI group after 6h (▶ Table 2). The relative risks of the individual endpoints are shown in ▶ Fig. 4.

**Comparison of the composite endpoint among MDI and CSII patients**

The risk of the composite endpoint (hypoglycemia < 70 mg/dL [3.8 mmol/L] and/or hyperglycemia ≥ 300 mg/dL [16.6 mmol/L] and/or lactate ≥ 2.2 mmol/L and/or ketones ≥ 0.6 mmol/L) was al-
served in either the MDI or CSII groups during the exercise test and [29]. Despite this, no clinically significant hypoglycemia was ob-

mately explained by the action of the morning dose of intermedi-

cate-acting insulin (NPH). It is also likely that the insulin is absorbed

partly maintained within a safe range. These lower blood glucose levels

expected as the test was performed 90 min after bolus ad-

most 4 times higher in the MDI group than in the CSII group, with

an odds ratio (OR) of 3.75, 95 % confidence interval (CI) of 1.22–

11.52, p = 0.02; (Fig. 4).

Discussion

Adequate preparation and planning is essential for the safety of ex-

ercise in patients with T1D. The results of the 58 progressive exer-

cise tests in this study confirm that performing high intensity phys-

ical exercise in patients with T1D is safe. However, the obtained re-

sults might be partially associated with the relatively good

metabolic control of diabetes in this particular study group.

In this study, patients with T1D reached at least 85 % of the heart

rate limit while running on a treadmill and rated their exertion as

the maximum in the Borg scale [6]. During exercise, mean glucose

levels in particular minutes of physical effort decreased, but were

maintained within a safe range. These lower blood glucose levels

were expected as the test was performed 90 min after bolus ad-

ministration of a fast-acting insulin analogue. Moreover, in patients

treated with pens, glucose levels before and at the beginning of the exercise test were lower than those treated with CSII, which can be partly explained by the action of the morning dose of interme-

ciate-acting insulin (NPH). It is also likely that the insulin is absorbed

more quickly during exercise when patients are treated using MDI

[29]. Despite this, no clinically significant hypoglycemia was ob-

served in either the MDI or CSII groups during the exercise test and

in the 6 h after. While it was expected that the subjects would ex-

perience a number of hypoglycemic events in the 6 h after high in-

tensity exercise, instead, glucose levels increased in both groups
during this time. Patients did not have any correction of the hyper-

glycemia, did not eat meals, and stayed in the hospital ward avoid-

ing physical effort. This increase in glucose levels occurred despite

the start of the test at the 90th minute following a bolus of insulin

and its maximum effect. It should also be noted that the basal rate

in the CSII group and the basal insulin dose in MDI group were not

reduced on the test day. Physical exercise at high intensity did not

cause clinically important hypoglycemia in the 90th minute after a

bolus administration, therefore during the maximum effect of in-

sulin. Thus, performing high intensity exercise at different times

after insulin bolus should also be safe, however might be related to

higher risk of hyperglycemia.

We found that glucose levels after 6 h were significantly higher

than at the end of the exercise test and the beginning of the obser-

vation. While hyperglycemia after intense physical exercise has pre-

viously been described in numerous publications evaluating the

effect of aerobic, anaerobic, and combined training for diabetes

control [10, 30], no observation lasting 6 h has been conducted so

far after high intensity exercise. Yardley et al. showed greater in-

creases in glucose throughout 6-h recovery in type 1 diabetic pa-

tients using MDI compared to CSII [33], however after standar-

dized aerobic exercise. Hyperglycemia may be a cause of failure to

improve the control of T1D in people who are physically active. In-

deed, the occurrence of hyperglycemia during sport makes it diffi-

cult to demonstrate the beneficial effects of exercise on diabetes

control. Physical exercise at high intensity induces significant pro-

duction of catecholamines, which in turn promote, increase blood

glucose levels. This situation is especially evident in patients with

T1D with chronic poor control of glycemia and may lead to the de-

velopment of diabetic ketoacidosis. Intensified ketosis in healthy

subjects is a physiological phenomenon, while occurrence of this

process in patients with T1D requires control. Based on previous

publications, it was assumed that very intense exercise (> 90 % VO2max)

could lead to decompensation of diabetes and ketoacidosis

[9, 12]. However, we found that high-intensity physical exhaus-

tion caused no greater risk of diabetic ketoacidosis. The concentra-

tions of ketones assessed in the capillary blood were in the normal

range at the end of the exercise test and after 6 h of observation.

We measured ketones in the capillary blood in this study, as this al-

 lows for quicker identification of metabolic disorders than the de-

termination of ketones in the urine [24]. Therefore, our results con-

firm that, with proper treatment of T1D, the exercise at high inten-

sity does not cause decompensation of diabetes and the occurrence

of diabetic ketoacidosis.

Despite this, we also found that, ketone concentration after 6 h

was significantly higher in MDI patients compared to those with

CSII. For patients using pen-type injectors, a subcutaneous depos-

it of intermediate-acting insulin (NPH) or long-acting insulin ana-

logue is formed, and physical activity causing enhanced blood flow

can increase the absorption of insulin from the subcutaneous tis-

sue [29]. Faster absorption of insulin could explain the lower glu-

cose levels observed in the MDI group at the beginning of the test

and the lower insulin concentrations 6 h after the test. Therefore,

a lower concentration of insulin after 6 h may result in a higher con-

most 4 times higher in the MDI group than in the CSII group, with

an odds ratio (OR) of 3.75, 95 % confidence interval (CI) of 1.22–

11.52, p = 0.02; (Fig. 4).

Discussion

Adequate preparation and planning is essential for the safety of ex-

ercise in patients with T1D. The results of the 58 progressive exer-

cise tests in this study confirm that performing high intensity phys-

ical exercise in patients with T1D is safe. However, the obtained re-

sults might be partially associated with the relatively good

metabolic control of diabetes in this particular study group.

In this study, patients with T1D reached at least 85 % of the heart

rate limit while running on a treadmill and rated their exertion as

the maximum in the Borg scale [6]. During exercise, mean glucose

levels in particular minutes of physical effort decreased, but were

maintained within a safe range. These lower blood glucose levels

were expected as the test was performed 90 min after bolus ad-

ministration of a fast-acting insulin analogue. Moreover, in patients

treated with pens, glucose levels before and at the beginning of the exercise test were lower than those treated with CSII, which can be partly explained by the action of the morning dose of interme-

ciate-acting insulin (NPH). It is also likely that the insulin is absorbed

more quickly during exercise when patients are treated using MDI

[29]. Despite this, no clinically significant hypoglycemia was ob-

served in either the MDI or CSII groups during the exercise test and

in the 6 h after. While it was expected that the subjects would ex-

perience a number of hypoglycemic events in the 6 h after high in-

tensity exercise, instead, glucose levels increased in both groups
during this time. Patients did not have any correction of the hyper-

glycemia, did not eat meals, and stayed in the hospital ward avoid-

ing physical effort. This increase in glucose levels occurred despite

the start of the test at the 90th minute following a bolus of insulin

and its maximum effect. It should also be noted that the basal rate

in the CSII group and the basal insulin dose in MDI group were not

reduced on the test day. Physical exercise at high intensity did not

cause clinically important hypoglycemia in the 90th minute after a

bolus administration, therefore during the maximum effect of in-

sulin. Thus, performing high intensity exercise at different times

after insulin bolus should also be safe, however might be related to

higher risk of hyperglycemia.

We found that glucose levels after 6 h were significantly higher

than at the end of the exercise test and the beginning of the obser-

vation. While hyperglycemia after intense physical exercise has pre-

viously been described in numerous publications evaluating the

effect of aerobic, anaerobic, and combined training for diabetes

control [10, 30], no observation lasting 6 h has been conducted so

far after high intensity exercise. Yardley et al. showed greater in-

creases in glucose throughout 6-h recovery in type 1 diabetic pa-

tients using MDI compared to CSII [33], however after standar-

dized aerobic exercise. Hyperglycemia may be a cause of failure to

improve the control of T1D in people who are physically active. In-

deed, the occurrence of hyperglycemia during sport makes it diffi-
cult to demonstrate the beneficial effects of exercise on diabetes control. Physical exercise at high intensity induces significant production of catecholamines, which in turn promote, increase blood glucose levels. This situation is especially evident in patients with T1D with chronic poor control of glycemia and may lead to the development of diabetic ketoacidosis. Intensified ketosis in healthy subjects is a physiological phenomenon, while occurrence of this process in patients with T1D requires control. Based on previous publications, it was assumed that very intense exercise (> 90 % VO2max) could lead to decompensation of diabetes and ketoacidosis [9, 12]. However, we found that high-intensity physical exhaustion caused no greater risk of diabetic ketoacidosis. The concentrations of ketones assessed in the capillary blood were in the normal range at the end of the exercise test and after 6 h of observation. We measured ketones in the capillary blood in this study, as this allows for quicker identification of metabolic disorders than the determination of ketones in the urine [24]. Therefore, our results confirm that, with proper treatment of T1D, the exercise at high intensity does not cause decompensation of diabetes and the occurrence of diabetic ketoacidosis.

Despite this, we also found that, ketone concentration after 6 h was significantly higher in MDI patients compared to those with CSII. For patients using pen-type injectors, a subcutaneous deposit of intermediate-acting insulin (NPH) or long-acting insulin analogue is formed, and physical activity causing enhanced blood flow can increase the absorption of insulin from the subcutaneous tissue [29]. Faster absorption of insulin could explain the lower glucose levels observed in the MDI group at the beginning of the test and the lower insulin concentrations 6 h after the test. Therefore, a lower concentration of insulin after 6 h may result in a higher con-
centration of ketones in the capillary blood. Although, Campbell et al. showed that reduction of prandial insulin and basal insulin dose prior to exercise did not cause an increase in the concentration of beta-hydroxybutyric acid compared to patients who did not reduce insulin dose [7]. Although, their study concerned exercise of moderate intensity with concentrations of lactic acid of 3.40 ± 0.66 mmol/L and 3.27 ± 0.58 mmol/L in the 2 examined groups [7]. Furthermore, in a publication of Jankovec et al., the presence of ketosis was primarily associated with disconnection of the insulin pump for too long a period of time during physical activity, but this aspect was not considered in the context of exercise intensity [14].

In intense exercise, unlike at lesser intensities, glucose is the exclusive muscle fuel. Typically, increments in lactate production markedly exceed those in uptake, resulting in blood lactate concentrations increasing from 10- to 20-fold [19]. We have determined that lactate concentration assessed immediately after exercise test was significantly higher in the group treated with MDI. We are aware of the fact that the study is limited by the lack of maximal aerobic capacity assessment. However, the difference in lactate concentration occurred despite the fact that the distance and time of exercise test did not differ between groups CSII and MDI. Moreover, the incidence of lactate concentrations outside the normal range did not differ between the groups and after 6 h of observation, lactate concentrations in both groups were within the normal range. Indeed, the proper preparation for the exercise in the study group resulted in reduction of the risk of lactic acidosis to minimum. In this situation, the biochemical processes associated with lactate production and metabolism that occur in subjects with T1D during and after high intensity exercise, as in the study of Adolffson et al., were comparable to healthy controls [3].

There are currently no reliable data assessing the effects of administration of insulin using pens and personal insulin pumps on sporting results. In a German study on 20 professional athletes with T1D, 8 were treated with MDI and 12 using CSII. The authors, however, did not compare the results of these professional athletes depending on the type of treatment [22]. Moreover, Tagougui et al. showed that efficiency of exercise, as measured by VO2max, was lower in patients with T1D when their HbA1C was higher than 8 %; but if HbA1C was < 7 %, the VO2max did not differ between people with diabetes and healthy controls [27]. This study assessed the distance covered on a treadmill and duration of exercise but did not examine differences among groups treated with MDI or CSII. In the current study, we have shown the metabolic advantage of the treatment with continuous subcutaneous insulin infusion. Moreover, these results are of particular value as the MDI and CSII groups did not differ in age and metabolic control of diabetes.

In order to assess the safety of high intensity physical exertion, we determined the risk of occurrence of single endpoints and one composite endpoint (hypoglycemia < 70 mg/dL and/or hyperglycemia > 300 mg/dL and/or lactate > 2.2 mmol/L and/or ketones ≥ 0.6 mmol/L). The risk of the composite endpoint was almost 4-fold higher in patients treated with conventional pen-type injectors. Similarly, Yardley et al. showed among individuals performing regular moderate-to-heavy intensity aerobic exercise that use of CSII helped to limit post-exercise hyperglycemia compared with MDI therapy [33]. Moreover, CSII was not associated with an increased risk for post-exercise late-onset hypoglycemia in these patients [33]. The advantage of this type of insulin therapy stems mainly from the possibility of changing the dosage of insulin using temporary basal rate reduction, suspending the pump during the training, or making minor adjustments (smaller than 1 unit of insulin). Therefore, CSII limits the amount of hypoglycemia, particularly that occurring in the later stages, in patients with T1D during maximum exercise [2].

In conclusion, the planned high intensity physical effort in the 90th minute after insulin bolus preceding a meal in males with well-controlled T1D is metabolically safe. Mean glucose levels remain within normal ranges with little risk of hypoglycemia. The upward trend in blood glucose after a high intensity exercise may suggest that a reduction of insulin dose is not required for this type of activity. The study confirms that people with T1D can actively play sports and make physical efforts at high intensity. However, patients must have properly treated diabetes, a lack of contraindications, and appropriate adjustment of insulin therapy before exercise. Furthermore, treatment with CSII may have an advantage over MDI in physically active people.

Acknowledgements

This study was supported by the scientific grant of Diabetes Poland.

Conflict of interest

The authors declare no conflicts of interest.

References


