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Beneficial effects of low carbohydrate diet and sports in patients with type 1 diabetes

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Abstract. To reduce obesity and cardiovascular risk, a combination of low carbohydrate diet and sport is a good choice in otherwise healthy individuals. However, among patients with type 1 diabetes mellitus (T1DM), consuming a minimum of 130 g carbohydrates per day is recommended, and the desire to exercise decreased as well. We wanted to demonstrate that a low carbohydrate diet during physical activity in T1DM patients is safe with the right choice of insulin dosing and reduces the development of both short- and long-term complications. To this end, we collected data from T1DM patients on a normal and low carbohydrate diet using a questionnaire as well as measured blood glucose levels while exercising in healthy and T1DM patients. The main benefit of the diet was that it provided a safe exercise option with more stable blood glucose levels and lower bolus insulin requirements. Our data support that the emergence of new types of insulins, tissue glucose sensors, and pumps has provided the conditions for a freer, less complicated life for patients with T1DM, for which the combined use of a normal and low carbohydrate diet can be an important tool.

Keywords: diabetes, T1DM, low carb diet, physical activity, blood glucose level

Introduction

Being overweight and the concomitant type 2 diabetes mellitus (T2DM) is one of the most significant health problems today, which is almost epidemic (Kjaer et al. 2015). However, the incidence of type 1 diabetes mellitus (T1DM), which has a completely different mechanism, is also rising rapidly, especially among children (Haszon-Nagy 2019). This has tripled in the last 30 years, making T1DM the most common childhood chronic disease by now. However, these two basic types of diabetes mellitus (DM) are not mutually exclusive as overweight and the accompanying cardiovascular risk factors are much more common among T1DM diabetes patients than among healthy people, so they may also develop T2DM. This condition with the simultaneous diagnosis of T1DM and T2DM is called double diabetes mellitus (Minges et al. 2013).

A combination of diet and exercise is recommended to treat overweight and increased cardiovascular risk in healthy individuals. The question arose if a low carbohydrate diet (low carb diet, LCD) works well for non-DM individuals (Shai et al. 2008), why it should not work for DM patients as well, and why it should not be combined with exercise. One might think that what is healthy is good for everyone, which is partly true. However, there are obviously different needs for a developing youth body that is more prone to T1DM and an older, potentially obese adult who is more prone to T2DM. For the treatment of overweight and increased cardiovascular risk in healthy individuals many types of diets have spread, including fashionable, not necessarily evidence-based (e.g. paleolithic diet, ketogenic diet), as well as official recommendations (Skerrett, Willett 2010). Diets typically focus on weight loss, for which LCD is a possible choice. However, the American Diabetes Association (ADA) has been recommending LCD for DM patients only since 2019 (Kussin 2019). Until then, there was a general belief that with less than 130 g of carbohydrates a day, our brains are not functioning properly, and basic nutrient requirement is not fulfilled. However, the proven reduced insulin requirement and cardiovascular risk associated with lower carbohydrate intake ultimately convinced decision makers.

We must emphasize that it is always necessary to take individual needs into account, there is no "one-size-fits-all" rule. Low carb (and not low fat) can be considered as a uniform principle as an approach, but exact amounts and timing should be personalized. Based on literature data, a diet in which less than 26% of the total energy intake (in contrast to the normal 45–65%) comes from carbohydrates alone (<130 g carbohydrate/day for an average adult) can be considered low carb (Oh et al. 2022). It is important to emphasize that LCD is not the same as starvation ketogenic therapy (Westman et al. 2018), which was used in DM patients before the discovery of insulin. Nowadays, not only human insulin has appeared, but we also have long-term insulin analogues and insulin pumps that can meet the body's basic insulin needs. Thanks to them, we avoid the complete lack of insulin and the consequent ketoacidosis, which sooner or later became inevitable with the old ketogenic treatment. Less carbohydrate intake requires less insulin, which means less interference in the body's own metabolism, which we believe can lead to a greater degree of balance (Fig. 1). This could mean fewer acute complications in the short term and a reduction in the likelihood of chronic complications in the long term. Indeed, oscillating glucose levels seem to be more deleterious to our health than even a higher but steady glucose level (Ceriello et al. 2008; Sparks et al. 2021). Based upon latest observations, flattering our glucose curves seems to be a good choice (Inchauspé 2023).

Diet is just one tool for maintaining health, and the other is known to be beneficial exercise. Unfortunately, DM patients also lag behind their healthy counterparts in this area (Mottalib et al. 2017), in which fear of the most common acute complication (Burr et al. 2012), of low blood glucose (hypoglycaemia) is believed to play a role (Colberg et al. 2015). Sport should play a particularly important role in young people's lives and T1DM mainly affects them. The regulations of handling T1DM require attention to several things that deprive the patient of his/her freedom of movement and joy, and meanwhile the risk of hypoglycemia is continuously present.

We aimed to demonstrate that in T1DM patients, LCD is safe even during exercise with the right choice of insulin dosing and may reduce both short- and long-term complications.

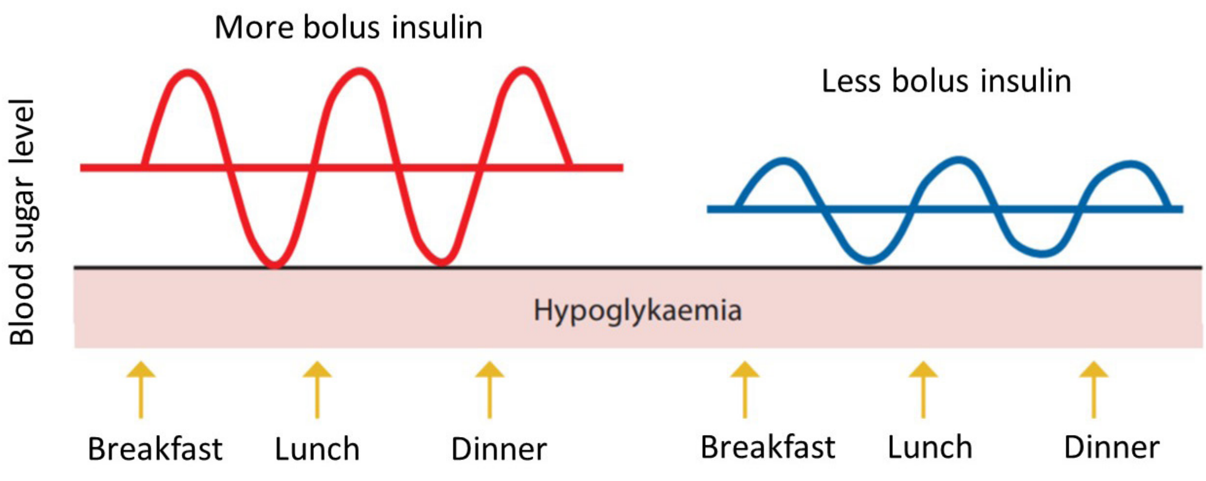

Fig. 1. The effect of the amount of bolus insulin on the fluctuation of blood glucose levels. Hypothetic drawing representing the flattering of the blood glucose curve after lower insulin doses

Materials and methods

Experiment 1. Questionnaire survey

Online data collection was performed based on the voluntary completion of pre-designed questionnaires, which were sent specifically to patients with T1DM. Aggregate data were stored anonymously, based on code, in an Excel file, from which individuals could not be identified. Two populations were included in the studies: those on a normal carbohydrate diet (daily carbohydrate intake: 186.0 ± 8.5 g; Semmelweis University, 1st Dept Pediatrics) and a group on a low carb diet (LCD, average daily carbohydrate intake: 45.8 ± 6.4 g; closed international LCD T1DM Facebook group). Our main question was how their blood glucose levels and their body mass index (BMI; calculated as weight (in kg)/height^2 (in m)) and laboratory parameters change during their physical activity, whether there is a correlation between the examined parameters (e. g. we hypothesized that the longer someone has been on LCD, the lower are their levels of harmful blood lipids and glycosylated hemoglobin (HbA1c)).

We surveyed what kind of sport the person was doing. Aerobic activities included basketball, football, physical education, running, biking, and walking, while anaerobic activities included weightlifting, wrestling, home gymnastics, and gym training. We also asked about the length and duration of a typical workout (finally, the data of the first 40 minutes were taken into account uniformly for everyone), blood glucose values measured before and during the workout, as well as carbohydrate consumption and insulin dosage related to the workout.

Finally, laboratory plasma values were asked: lipids (total cholesterol; low density lipoprotein (LDL), considered harmful; high density lipoprotein (HDL), protective), liver enzymes (alkaline phosphatase (ALP); gamma-glutamyl transferase (GGT); glutamate oxaloacetate aminotransferase (GOT); pyruvate aminotransferase (GPT)), total protein and albumin levels, which also reflect the synthetic activity of the liver, as well as creatinine values reflecting muscle activity and renal function.

Experiment 2. Blood glucose during training

To confirm previous, self-reported results, three healthy adults (two men and one woman) and three adults with T1DM (three men) were examined during a standard (40 minutes of running) aerobic exercise. To imitate LCD, the test was done at least four hours after the last meal in all individuals, without bolus insulin, but with basal insulin (Degludec) in T1DM patients. The average age was 29.6 ± 5.4 years and BMI was 21.4 ± 0.9 kg/m^2. The evolution of their blood glucose level was followed in every five minutes, in a blood sample taken from the fingertip (by DCont HUNOR measuring device; the sampling involved a stop for less than half a minute). There was no difference between the two examined groups in the average distance traveled (control: 6.59 ± 0.51 km; T1DM: 6.90 ± 0.30 km) and speed (control: 9.90 ± 0.33 km/h, T1DM: 9.86±0.57 km/h), as well as in the average heart rate measured by a wrist heart rate monitor (control: 137.5 ± 0.75/min; T1DM: 138.5 ± 0.75/min). That is, the load can be considered the same in both groups.

Statistical analysis

The data were given as mean±SEM (standard error of mean). The analysis was performed by StatSoft 15.0 software (TIBCO, USA). A t-test was used to compare two samples, two-way ANOVA analysis was used to compare the four groups (factors: normal or low carbohydrate diet, type of training) and repeated-measures ANOVA was performed for blood glucose parameters during training. Fisher's LSD test was used for posthoc comparisons. The correlation between the parameters was examined using the Pearson test. A value of $p < 0.05$ was considered significant.

Results

Experiment 1. Questionaire survey

In this study T1DM patients with a normal diet and LCD were included.

General parameters

The age of the LCD T1DM group was significantly higher compared to the group on the normal carbohydrate diet (normal: 15.1 ± 0.5 years; LCD: 37.9 ± 3.2 years; $p < 0.01$), but no difference was found between those performing aerobic or anaerobic work ($p = 0.50$) (Table 1). Nevertheless, the height, weight, and BMI of the examined individuals did not show significant differences according to either diet or type of training ($p > 0.05$).

Although larger body sizes would normally be expected in men, strangely, we found no difference in height and weight between the sexes (Table 1). BMI, on the other hand, was higher among women (males: 20.8 ± 0.7 kg/m^2; females: 24.8 ± 1.3 kg/m^2, $p = 0.01$), which was more pronounced in the younger age group consuming normal carbohydrates (normal carbohydrate group male-female difference: $p = 0.019$, low carbohydrate group male-female difference: $p = 0.26$).

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Table 1. General parameters of T1DM patients who consumed normal or low carbohydrate diets (Experiment 1)

	Normal diet		Low carb diet	
Training type	**aerob**	**anaerob**	**aerob**	**anaerob**
Number of participants	19	7	11	10
Ratio of man/woman	61.11	60.00	45.45	44.44
Age	15.08 ± 0.57	15.14 ± 1.37	39.91 ± 4.99	35.56 ± 4.09
Height (cm)	165.21 ± 2.93	162.86 ± 8.18	165.05 ± 6.13	170.00 ± 2.20
Body weight (kg)	60.38 ± 4.46	56.61 ± 6.87	65.65 ± 5.20	69.72 ± 2.69
BMI	21.86 ± 1.43	20.82 ± 1.34	23.66 ± 1.44	24.13 ± 0.84

Note: In the normal diet group more men than women were involved, while in the low carb diet group it was the other way round. The average age of the low carb diet group was higher than in the normal diet group. Analyzed by two way ANOVA. Abbreviation: BMI—body mass index, calculated as weight (in kg) / height^2 (in m).

Carbohydrate metabolism

We found higher basal insulin requirements in women than in men (approximately 1.4-fold, men: 15.078 ± 1.400unit/day, women: 21.205 ± 3.051unit/day; $p = 0.036$) and—in women only—a positive correlation was found between the amount of daily basal insulin requirement and body weight (correlation: $p < 0.05$) and BMI index (correlation: $p < 0.05$) (Table 2). Body weight and BMI parameters showed no correlation with either duration of diabetes mellitus or LCD, or interestingly, with daily carbohydrate intake and HbA1c levels.

Table 2. Correlation between general body parameters (height, weight, BMI) and typical carbohydrate parameters of the T1DM patients (Experiment 1)

	correlation	**r**	**p**
duration of DM	Height	0.18	0.23
	Weight	0.21	0.16
	BMI	0.19	0.22
basis insulin / day	Height	0.08	0.61
	Weight	0.34	0.02
	BMI	0.45	0.002
carbohydrate / day	Height	0.08	0.59
	Weight	–0.18	0.23
	BMI	–0.28	0.06
duration of LCD	Height	0.18	0.45
	Weight	0.15	0.52
	BMI	0.05	0.83
HbA1c	Height	–0.01	0.93
	Weight	0.004	0.98
	BMI	0.04	0.78

Note: Significant correlations are marked as bold. Analyzed by Pearson test. Abbreviations: BMI: body mass index, DM: diabetes mellitus, LCD: low carb diet.

However, insulin sensitivity is believed to be best inferred from basal insulin requirement per kilogram body weight and the bolus insulin values necessary for 10 g of carbohydrate (Table 3). Examining these, the gender difference disappeared in basal insulin values ($p = 0.103$), but those on LCD had approximately 15% less basal insulin requirements than those on a normal carbohydrate diet ($p = 0.028$). Accordingly, the amount of bolus insulin required for 10 g of carbohydrate was also significantly lower among those on LCD (by about 37%, $p = 0.042$). The longer the diabetes mellitus existed, the more basal insulin was needed ($r = 0.576$, $p = 0.008$) and the amount of bolus required for 10 g of carbohydrates also increased ($r = 0.646$, $p = 0.002$).

A more stable glucose metabolism was expected in the LCD group (Fig. 1). This was confirmed by the fewer hypoglycaemic episodes detected in LCD compared to normal diet group over 30 days (normal: 10.5 ± 1.9, LCD group: 3.9 ± 1.1; $p = 0.018$) and lower HbA1c levels reflecting long-term blood glucose levels (approximately 28% lower values in the LCD group; $p < 0.001$) (Table 3). Indeed, the higher the daily carbohydrate intake was, the higher HbA1c level was detected ($r = 0.445$, $p = 0.002$). The gender had no effect on these parameters.

Acute effect: changes in blood glucose levels during exercise

Based on the questionnaires, a typical 40-min physical activity led to lower blood glucose values in the LCD group than in the normal diet group (based on 0, 15, and 30-min values in the analysis; $p < 0.05$), which was mainly observable in the initial values (Fisher posthoc test: $p = 0.021$) (Fig. 2).

Because the nature of the physical work performed (aerobic or anaerobic) did not affect the measured blood glucose levels ($p = 0.59$), we merged these two groups and compared those on a normal diet and LCD only. Diet significantly affected the time course of blood glucose levels (diet x time interaction: $p < 0.05$). Blood glucose levels gradually decreased during sports in those on a normal diet, whereas no such change was observed in the LCD group. If we looked at the change in blood glucose level during the 40 min physical activity (comparing 0 and 40 min values) those on LCD had a much smaller decrease in blood glucose levels (–0.16 ± 0.28 mmol/l) than those on a normal diet (–2.36 ± 0.47 mmol/l) ($p < 0.01$). Comparing the standard deviations of the two groups, we found that the values of those on the normal diet showed greater variability than those on the LCD ($p < 0.01$) (Fig. 2).

The change in blood glucose during exercise (between 0 and 40 min) negatively correlated with the amount of carbohydrate consumed per day ($r = -0.689$, $p = 0.002$), but did not depend on the amount of basal insulin ($r = -0.077$, $p = 0.769$).

Long-term effect: laboratory results

Since acute physical activity is not expected to affect laboratory values in the long run, but a long-term LCD does, we focused on the latter effect here and compared two groups (Fig. 3).

Table 3. Questionnaire-based evaluation of carbohydrate metabolism parameters in T1DM patients (Experiment 1)

	Man		**Woman**	
	normal diet	**LCD**	**normal diet**	**LCD**
basis insulin (n)	17.700 ± 1.615 (14)	11.000 ± 1.944 (9)	21.938 ± 3.804 (8)	20.673 ± 4.638 (11)
basis insulin/bwkg	0.329 ± 0.034	0.167 ± 0.026	0.348 ± 0.039	0.301 ± 0.065
bolus insulin necessary to 10 g carbohydrate	1.971 ± 0.350	1.333 ± 0.166	2.300 ± 0.744	1.236 ± 0.257
number of hypoglycaemic episodes / month	11.357 ± 2.808	4.444 ± 2.180	9.812 ± 3.789	3.545 ± 1.163
HbA1c	7.892 ± 0.373	5.611 ± 0.256	8.600 ± 0.613	5.900 ± 0.292

Note: The basis insulin per body weight as well as bolus insulin per 10 g carbohydrate requirements were significantly lower in the LCD than in normal diet group. Moreover, the number of hypoglycaemic episodes as well as the HbA1c levels were lower in this group, too. Note that if men and women are combined, then in the LCD group a number of participants was lower than in the group with a normal diet. Analyzed by two way ANOVA. Abbreviation: LCD: low carb diet.

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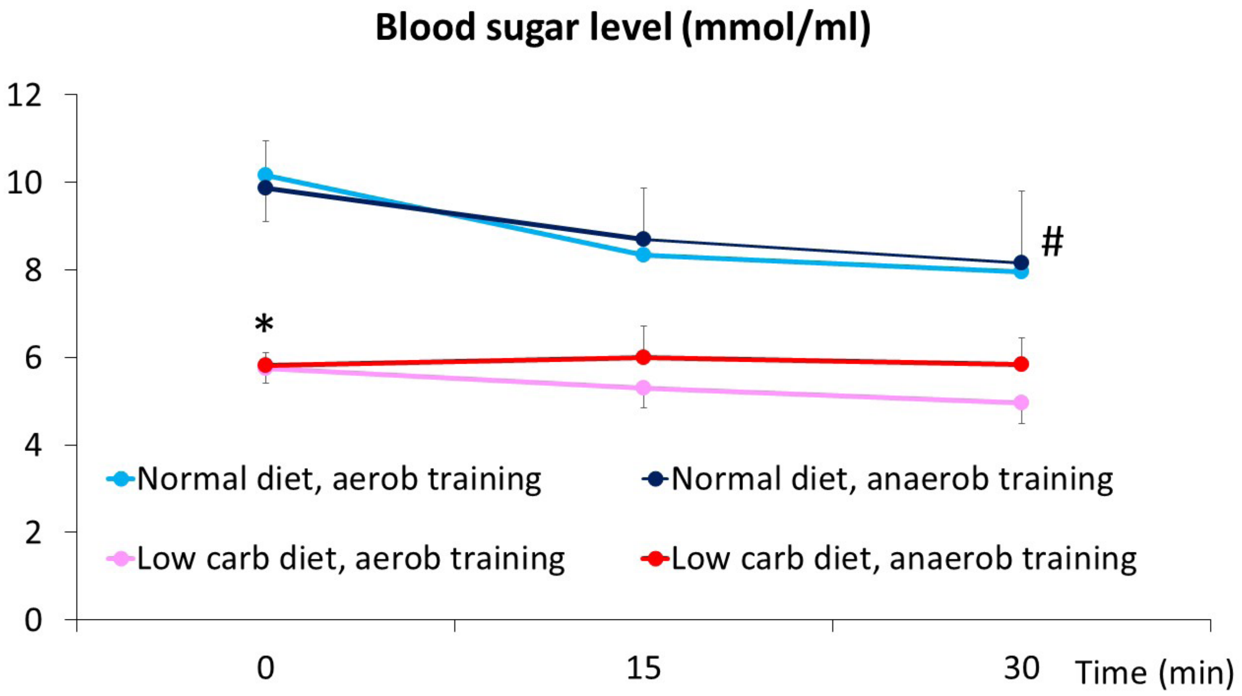

Fig. 2. Effect of physical activity on blood glucose levels. Data were collected by a self-reporting questionnaire. The low carb diet group reported lower blood glucose level before and during the exercise. N = 7–19. Analyzed by repeated measure ANOVA. *— $p < 0.05$ significant difference between the group consuming normal and low carbohydrates (Fisher LSD posthoc test on main diet x time interaction), #— $p < 0.05$ significant difference the 0 and 30-minute values of the group consuming normal carbohydrates (Fisher LSD posthoc test on main diet x time interaction)

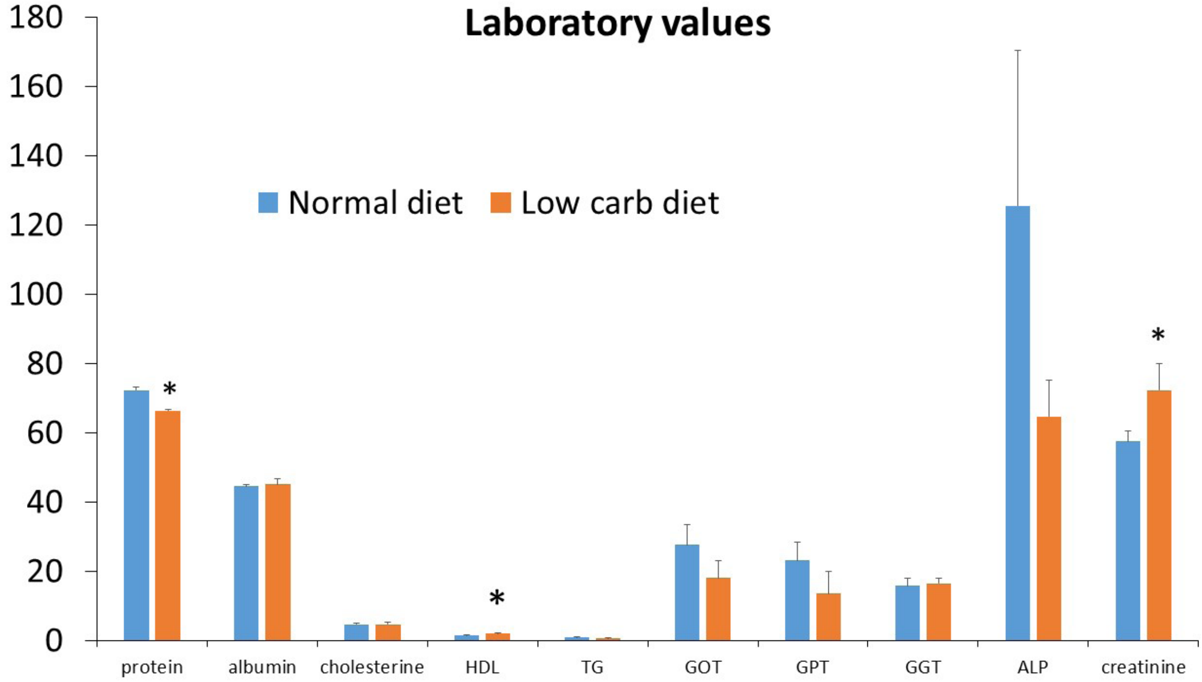

Fig. 3. Laboratory values in T1DM patients consumed normal or low carbohydrate diets. Analyzed by t-test. Abbreviation and units: albumin: g/L; ALP: alkaline phosphatase, U/L; cholesterine: mmol/L; creatinine: μmol/L; GGT: gamma-glutamyl transferase, U/L; GOT: glutamate oxaloacetate aminotransferase, U/L; GPT: pyruvate aminotransferase, U/L; HDL: high density lipoprotein, mmol/L; LDL: low density lipoprotein, mmol/L; protein: g/L. N = 8–20. *—$p < 0.05$ significant difference with t-test

We found significant differences in three parameters (although the measured values still fell in the physiological range). Those on LCD had (1) lower total protein (but not albumin) levels and (2) higher creatinine and (3) HDL cholesterol (so-called "good" cholesterol) levels without significant difference in total cholesterol levels. There was a negative correlation between the duration of DM and albumin concentration ($p < 0.05$) (Table 4). Height, body weight, and BMI data, as well as duration of diabetes mellitus (excluding albumin), were not significantly correlated with any of the laboratory parameters. However, HbA1c levels showed a positive correlation with GPT and GGT.

Experiment 2

Pre-running blood glucose values measured after a minimum of 4 h of fasting did not show a difference between the two groups (control and T1DM; Fig. 4). Running did not lead to temporal fluctuations and the fact of diabetes mellitus did not affect the time course. However, we found a significant difference between the two groups during sports: the T1DM group had higher blood glucose values ($p < 0.01$).

Table 4. Correlation of laboratory parameters with characteristic parameters of diabetes (Experiment 1)

		Duration of DM	**Basis insulin / day**	**Carbohydrate / day**	**HbA1c**
total protein	r	–0.08	0.88	0.94	0.19
	p	0.95	0.31	0.22	0.88
albumin	r	–1.00	–0.42	0.39	–0.97
	p	0.02	0.72	0.75	0.15
total cholesterine	r	0.52	–0.57	–0.99	0.28
	p	0.65	0.61	0.08	0.82
HDL	r	–0.56	–0.98	-0.53	–0.76
	p	0.62	0.11	0.65	0.45
TG	r	0.99	0.54	–0.26	0.99
	p	0.10	0.64	0.83	0.07
GOT	r	0.87	0.80	0.09	0.97
	p	0.32	0.41	0.95	0.15
GPT	r	0.95	0.66	–0.12	1.00
	p	0.19	0.54	0.93	0.02
GGT	r	0.94	0.69	–0.08	1.00
	p	0.22	0.52	0.95	0.05
ALP	r	–0.62	0.47	0.97	–0.39
	p	0.58	0.69	0.15	0.75
creatinine	r	0.30	–0.75	–0.99	0.04
	p	0.81	0.46	0.08	0.98

Note: Significant correlations are marked as bold. Analyzed by Pearson test. Abbreviation: ALP: alkaline phosphatase; GGT: gamma-glutamyl transferase; GOT: glutamate oxaloacetate aminotransferase; GPT: pyruvate aminotransferase; HDL: high density lipoprotein; LDL: low density lipoprotein.

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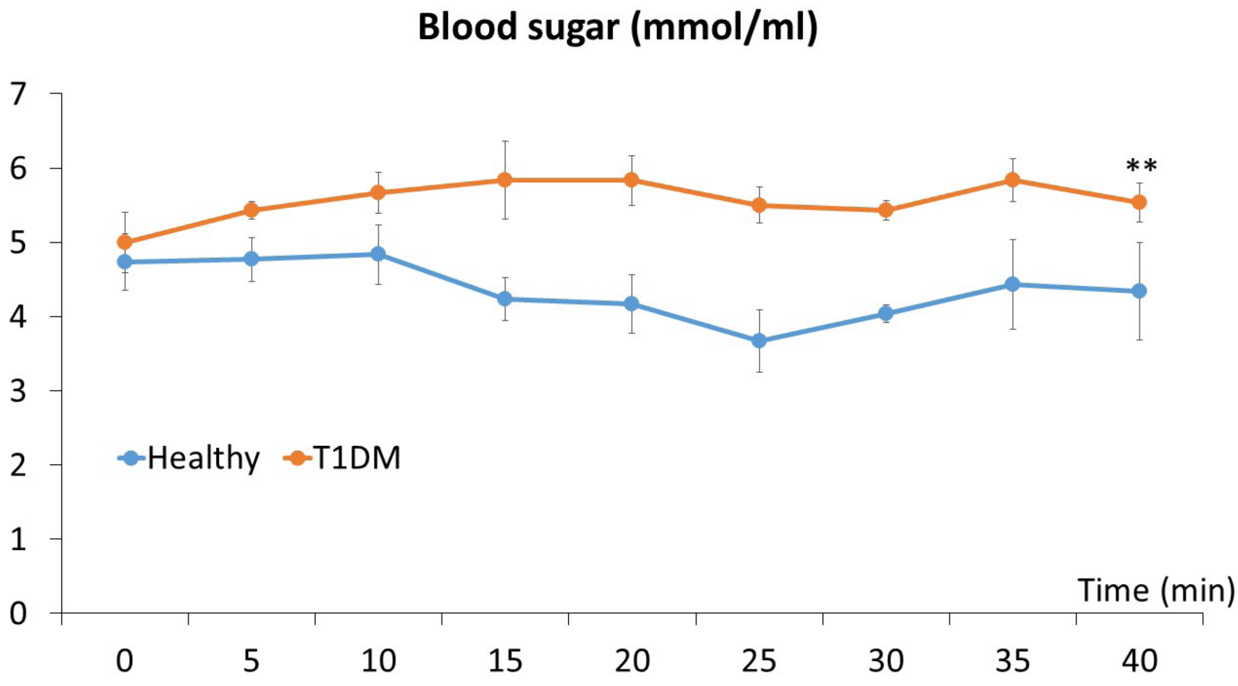

Fig. 4. Evolution of blood glucose levels during 40 minutes of running in healthy and T1DM people 4 hours after the last meal. N = 3. Analyzed by repeated measure ANOVA. **—$p < 0.01$ higher blood glucose values were observed in patients with diabetes mellitus

Discussion

Our studies demonstrated that LCD in T1DM patients reduced the risk of developing acute complications (hypoglycemia). In addition, we observed favorable changes in several parameters that can lead to chronic complications (HbA1c, blood lipids). The main benefit of the diet was that it provided a safe sport opportunity, which was also supported by a 2019 summary report (Scott et al. 2019). This might be because hypoglycemia is not caused by exercise but by bolus insulin. LCD is accompanied by fewer bolus insulin requirements, leading to more stable blood glucose values (Fig. 1). Therefore, lower HbA1c values can be achieved.

Despite younger age, the T1DM normal diet group had similar height and weight to the older LCD group (Table 1). It is likely that in the 15-year-old age group, the anabolic effect of insulin resulted in an early increase in body size. Indeed, some studies have reported that T1DM populations, especially those with early onset, are higher than healthy pediatric populations, yet their adult height is normal (Santi et al. 2019). A possible background mechanism might be that insulin directly acts on insulin-like growth factor-1 receptors promoting body growth.

Our data on higher BMI values in women than men confirmed previous results in 197 T1DM patients (Szadkowska et al. 2015). The authors of the study found that all body fat mass parameters studied were higher in DM women than in controls, whereas in men only the relative fat mass of the lower extremities increased with T1DM. One possible explanation is that – according to a study of more than 1,400 people — insulin sensitivity of fat and muscle tissue in women is more affected by T1DM than in men (Millstein et al. 2018). It cannot be ruled out that the aromatase-stimulating effect of insulin promotes the conversion of androgens to estrogens. This mechanism may also play a role in the development of more frequent insulin resistance and polycystic ovary syndrome in women (Millstein et al. 2018). In support, we confirmed that women had higher basal insulin requirement than men and their insulin requirements correlated positively with their body weight and BMI.

The insulin sensitivity was better in LCD than in normal diet group based upon both the basal insulin requirement per kilogram body weight and the bolus insulin values necessary for 10 g of carbohydrate consumption (Table 2). Similar to our results, a 12-week LCD (< 50g/day) improved insulin sensitivity and body composition in healthy individuals (LaFountain et al. 2019). This may be explained by a hepatic-peripheral distribution ratio of exogenous insulin. Physiologically, insulin first reaches the periphery through the portal circulation, touching the liver. However, individuals treated with subcutaneous insulin will have a much higher ratio of peripheral to hepatic insulin than healthy individuals. A similar condition has been observed in T2DM, which explains the metabolic disturbances in patients with T1DM and the phenomenon of dual diabetes mellitus mentioned in the introduction, which may lead to the relatively rapid development of insulin resistance in T1DM patients. This is also supported by the fact that the longer diabetes mellitus existed, the more basal insulin was required, and the amount of bolus required for 10 g of carbohydrate also increased. However, we cannot close out the confounding effect of age, as there is insulin resistance in puberty and the group on a normal carbohydrate diet belonged to that age group in contrast to the LCD group.

Our data — in accordance with the literature — support more stable blood glucose values during sports in those on LCD than normal diet (Scott et al. 2019). It may be due to the fact that the body is in a starvation-like state and bolus insulin is also missing. Under aerobic conditions, red muscle fibers burn fatty acids, white muscle fibers form lactate, while under anaerobic conditions, both types of muscle fibers produce lactate, which is converted to glucose in gluconeogenesis using energy from fatty acids in the liver, ensuring constant blood glucose level. Ultimately, in both aerobic and anaerobic cases, energy comes from lipids. This phenomenon is supported by the fact that there was no difference in the course of blood glucose levels measured during aerobic or anaerobic movements. In contrast, higher baseline blood glucose levels were detected in the group consuming normal amounts of carbohydrates, so muscle instead of fatty acid oxidized excess glucose circulating in the blood. Additionally, the bolus insulin was also applied in the normal diet group, which may have acted even when the muscle has already removed the excess glucose and switched to burning fatty acids. This is probably why blood glucose levels dropped further in this group until hypoglycaemia. This can, of course, be avoided by reducing insulin doses appropriately or by taking in extra carbohydrates, but this balance is always difficult to strike accurately. This is also shown by the greater variance in blood glucose values in the normal carbohydrate group and the higher incidence of hypoglycemic episodes. Unfortunately, even in this case, we cannot rule out the confounding effect of the younger age in normal diet group (see larger hormone fluctuations during puberty).

The data from the acute measurement (Experiment 2) were consistent with the findings of the questionnaire (Experiment 1). In this case, exercise was carried out in both healthy and T1DM-treated subjects in fasted (LCD-like) conditions. The absence of extra carbohydrate intake did not require extra bolus insulin administration before exercise. The lack of bolus insulin and the appropriately adjusted amount of long-acting insulin analog adequately stabilized glucose levels even in T1DM patients. Therefore, there was no significant change in blood glucose during exercise in either group. This also supports the first experiment that physical activity in the absence of a bolus insulin does not lead to a significant reduction in blood glucose levels. This is due to the activation of the counterregulatory processes that may have contributed to the maintenance of blood glucose levels e. g. by enhancing gluconeogenesis (glucagon, adrenaline, growth hormone, glucocorticoids, thyroid hormones, etc.) (Wilcox 2005). Moreover, during exercise, we observed higher blood glucose values in DM patients. This is also due to the aforementioned activation of the gluconeogenesis, and presumably the retained insulin-producing ability of healthy subjects, which allowed for more precise regulation. This is consistent with the fact that in the first experiment there was no association between the amount of injected basal insulin and the decrease in blood glucose. Thus, we might conclude that basal insulin at the appropriate dose has no hypoglycemic effect during exercise and the presence of insulin protects against ketoacidosis. In fact, a tenth of the insulin dose required for blood glucose control is sufficient to limit ketone body synthesis.

From the reported changes in laboratory values, the decrease in total protein levels in LCD group compared to the normal diet T1DM group could be explained by the fact that in this case the body basically uses protein breakdown to maintain blood glucose levels. Most of the proteins come from the muscles, and their degradation can lead to higher creatinine levels as well in the LCD. However, we cannot rule out, that — because of fear of hypoglycemia — members of the normal carbohydrate-consuming group exercised less, resulting in less microinjury in their muscles, manifested in their lower creatinine levels. Because albumin synthesis is stimulated by insulin (Chen et al. 2016), its rise over time, during disease progress, could be expected due to increasing insulin demand. However, instead of the expected positive correlation, a negative correlation was observed between disease duration and measurable albumin concentration. A possible explanation is that insulin resistance increased to a greater extent than insulin levels, thus, ultimately reducing the effect of insulin.

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As for the lipid levels, HDL transports lipids back from the periphery to the liver, the so-called reverse cholesterol transport, thereby protecting — among other things — our blood vessels. During LCD, decreased insulin intake also results in lower cholesterol synthesis, which may necessitate the mobilization of peripheral "reserves," leading to an increase in HDL-associated reverse cholesterol transport. It is expected that the levels of other lipoproteins (e. g. LDL) that transport lipids from the liver to the periphery will decrease and therefore the level of total cholesterol in the blood will remain unchanged.

Interestingly, the value of HbA1c showed a positive correlation with GPT and GGT parameters. Elevated HbA1c indicates persistently poor carbohydrate metabolism, which may be characterized by elevated levels of GPT (Abe et al. 2009) and GGT. This typically occurs with increased hepatic lipid accumulation and insulin resistance (Thamer et al. 2005). However, age may also play a role here, as HbA1c is known to be the highest in puberty.

Our study has several limitations. First of all, the first dataset was based upon an online questionnaire and there was a high age difference between the two dietary groups. The reported sports were rather heterogenous, and the small number of items per group all limit the correctness of our conclusions to be drawn. Therefore, further research is needed on this topic.

Nevertheless, in T1DM patients during current sport recommendations tend to recommend extra carbohydrate intake and a combinational hormone therapy (insulin + glucagon) to prevent hypoglycemia (Basu et al. 2014). In contrast, our results support the safety of LCD with less short and long term negative consequences. Moreover, a diet may be beneficial for common comorbidities as well. For example, it can help to maintain a gluten-free diet, as the main carbohydrate sources mostly contain gluten. However, the combined use of a normal diet and LCD can better tailor the treatment of diabetes mellitus. Among others, concomitant use of the two diets may help to slow the progression of T1DM, prolonging the "honeymoon" (Tóth-Heyn 2018). Nevertheless, LCD definitely has a place among the therapeutic options for T1DM. This flexible therapy is possible due to new types of insulins, tissue glucose sensors, and pumps, providing the conditions for a freer, more uncomplicated life for those with T1DM as well. A proper diet combined with physical activity can have many other beneficial effects, e.g, reducing the cardiovascular risk and the development of tumors (Boér 2021).

Conflict of Interest

The authors declare that there is no conflict of interest, either existing or potential.

Author Contributions

a. Zelena Zalán—planning and conducting the experiments, data collection, writing the first draft;

b. Zelena Dóra—data analysis, visualization of the data, writing;

c. Körner Anna—supervising the work, data collection, interpreting the data.

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