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Impact of physical activity on hypoglycaemia in patients with diabetes

ABSTRACT

Aim. Assessment of the effect of the physical activity level in diabetic patients on the occurrence of hypoglycaemia.

Material and methods. The survey was conducted in a group of 422 diabetic patients: 209 patients with type 1 diabetes mellitus (129 women, 80 men, mean age 30 ± 11 years, mean duration of diabetes 12 ± 8 years, HbA_{1c}: 7.5 ± 1.4%) and 213 patients with type 2 diabetes mellitus (119 women, 94 men, mean age 60 ± 12 years, mean duration of diabetes 10 ± 9 years, HbA_{1c}: 8 ± 1.5%). Patients filled in the questionnaire covering data on diabetes control and physical activity (based on the International Physical Activity Questionnaire — IPAQ).

Results. Overall the number of patients with hypoglycaemia was significantly higher in patients with high physical activity (65%) when compared to low activity (43%; $p < 0.01$). Patients with moderate activity did not differ from remaining groups. In type 1 diabetes mellitus number of episodes was significantly lower in low activity group (4%) when compared to high activity (61%; $p < 0.001$) and moderate activity (17%; $p < 0.001$). Also significant difference was found between high and moderate activity ($p < 0.001$). In type 2 diabetes mellitus the relation was similar. 23% patients with hypoglycaemia in high activity; 11% in moderate activity ($p < 0.005$) and 5% in low activity group ($p < 0.001$ *vs.* high and moderate activity respectively).

Conclusions. The incidence of hypoglycaemia increases along with increasing physical activity. This indicates the necessity of an increased education in patients planning physical activity. (Clin Diabetol 2018; 7, 2: 108–113)

Key words: diabetes, hypoglycaemia, physical activity

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Introduction

Physical activity (understood as an increase in energy expenditure of the body consequential to muscle contractions causing conscious body movements) is a fundamental factor that makes it possible to maintain a healthy lifestyle [1, 2].

As demonstrated in a WHO Report for 2002, physical inactivity is responsible for 15% of new cases of cancer, diabetes or cardiac diseases [3, 4]. Physical activity contributes to an improvement of general health, quality of life and diabetes course [5–7]. The positive effect of physical activity on the human body is mediated by a number of mechanisms. In general, physical activity improves glucose metabolism, participates in a reduction of adipose tissue, lowers blood pressure, reduces the levels of glycosylated haemoglobin (HbA_{1c}), and reduces body weight and waist circumference [3, 8, 9]. Those mechanisms are the main factors contributing to a reduction of incidence of cardiovascular heart disease or diabetes [3]. Nevertheless, glucose consumption during exercise via insulin-independent pathways may contribute to an increase in the number of hypoglycaemia episodes along with an increase in

the level of physical activity. The increase of the body's oxygen requirements during physical exercise leads to an increased consumption of glycogen and triglyceride reserves in skeletal muscles and free fatty acids and glucose originating from the liver. Glucose metabolism abnormalities existing in diabetes or excessive doses of insulin administered to the patient may inhibit physiological glucose mobilization, which will result in hypoglycaemia development. Episodes of hypoglycaemia related to physical activity occur mainly in patients with type 1 diabetes, and less commonly in patients with type 2 diabetes treated with sulphonylureas or insulin [3]. In patients with type 2 diabetes, physical exercise may also have a positive effect because it constitutes a basic element of the treatment.

The Polish Diabetes Association (PTD) recommends regular physical exercise undertaken at least twice or three times a week (at best daily), consisting of 5–10 minutes of initial exercises, the main part of physical activity, and cooling down activities at the end, in order to obtain an optimum result of diabetes treatment. Diabetic patients who take up physical activity should be aware of the increased risk of severe hypoglycaemia. The Polish Diabetes Association places special emphasis on feet care and selection of comfortable sports shoes (especially in patients with coexisting peripheral neuropathy and lowered pain threshold) because of the risk of foot injury during exercise [10].

Similar recommendations are included in the guidelines of the European Association for the Study of Diabetes (EASD), emphasizing particular importance of physical activity in diabetes treatment. The studies referenced in the guidelines developed by the European Association for the Study of Diabetes in collaboration with the European Society of Cardiology demonstrate that regular aerobic exercise performed by patients with type 2 diabetes reduces HbA_{1c} by 0.6%. The European Association for the Study of Diabetes recommends minimum 150 minutes of physical activity per week preventively and to facilitate blood glucose level control in patients with type 2 diabetes [11–13].

The studies published so far investigated the effect of a single session of physical exercise on metabolic changes inducing an elevated risk of hypoglycaemia [14–16].

According to the literature, even 1 aerobic training session a week significantly improves insulin sensitivity of cells [1]. The objective of this present paper is to present the correlation between the level of physical activity performed by patients with diabetes of both types 1 and 2 and their incidence of hypoglycaemia.

Materials and methods

Data sources

The survey was conducted in 422 patients who attended a routine follow-up visit in diabetes consultation clinics in the Silesian region of Poland (including the towns of Zabrze, Gliwice, Tarnowskie Góry and Mikołów).

Study population

The survey population included 209 patients with type 1 diabetes mellitus (129 women, 80 men, age 30 ± 11 years, duration of diabetes 12 ± 8 years, HbA_{1c}: 7.5 ± 1.4%) and 213 patients with type 2 diabetes mellitus (119 women, 94 men, age 60 ± 12 years, duration of diabetes 10 ± 9 years, HbA_{1c}: 8 ± 1.5%) surveyed for 6 months (October 2015–March 2016).

The type of diabetes was diagnosed on the basis of the medical records and clinical data. In patients with type 1 diabetes, 51 were treated with continuous subcutaneous insulin infusion. Among patients with type 2 diabetes, 106 were treated with oral drugs and 107 with insulin.

The patients were asked to complete an anonymous 19-item questionnaire covering data on diabetes control, treatment, documented self-monitored glucose levels, severity of hypoglycaemia episodes in the past month and physical activity (based on the International Physical Activity Questionnaire — IPAQ) [17].

The Polish versions (short and long) of the International Physical Activity Questionnaire were developed in line with the guidelines of the IPAQ Scientific Committee by Biernat et al. [17]. The questionnaire is intended for persons aged 15 to 69 years. The short questionnaire used in the present survey contains 7 questions concerning all types of physical activity related to daily life, work and leisure. In the short version, all life domains are scored jointly, while in the types of physical activity, the number of days and time devoted to intensive and moderate physical activity and walking are scored separately. The questionnaire makes it also possible to determine the total time spent sitting. Physical activity expressed in MET-min/week is calculated by multiplying the number of days on which the specific exercise was performed by the MET value for the given exercise and by the mean number of minutes of performing this exercise daily. This enables easy classification of the respondents into one of three activity categories: low (below 600), moderate (600–1500 or 600–3000) or high (above 1500 or 3000 MET-min/week). The activities performed within the framework of professional work, at home, around home, while moving from place

Table 1. General characteristics of the survey patient groups. Data are numbers or means ± SD

	Total (n = 422)	Type 1 diabetes (n = 209)	Type 2 diabetes (n = 213)
Gender (M/F)	174/248	80/129	94/119
Age (years)	45 ± 19	30 ± 11	60 ± 12
BMI [kg/m^2]	27.3 ± 5.77	23.6 ± 3.97	30.9 ± 4.91
Diabetes duration (years)	11 ± 9	12 ± 8	11 ± 9
Fasting blood glucose (mean of 3 measurements) [mg/dl]	128 ± 32.1	124 ± 32.3	132 ± 31.6
Postprandial blood glucose (mean of 3 measurements) [mg/dl]	147 ± 34.5	146 ± 31.1	149 ± 37.6
HbA_{1c} (%)	7.52 ± 1.44	7.49 ± 1.41	7.54 ± 1.47

Table 2. Stratification of the survey group by the declared physical activity assessed by IPAQ. Data are presented as n (%)

Physical activity	Total (n = 422)	Type 1 diabetes (n = 209)	Type 2 diabetes (n = 213)
High	269 (64%)	146 (70%)	123 (57%)
Moderate	109 (26%)	48 (23%)	61 (29%)
Low	44 (10%)	15 (7%)	29 (14%)

to place and in the leisure time devoted to recreation, exercise and sports were taken into account. Information is collected on the time spent sitting and walking and the time devoted to movement activity — intensive and moderate. In both questionnaires (the short and long ones), only the activities that last for at least 10 minutes (uninterrupted) are taken into account [18].

Hypoglycaemia was defined as the occurrence of adrenergic symptoms or neuroglycopenia symptoms resolving after carbohydrate intake. Two types of hypoglycaemia were differentiated — mild hypoglycaemia, in which the patient was able to self-ingest carbohydrates, and severe hypoglycaemia, when assistance of a third party was necessary [19].

Statistical analyses

The data obtained were processed with the use of Statistica 12.0. Univariate analysis of variance (ANOVA) and the Pearson's Chi-square Test for Independence were used for inter-group comparisons.

Results

Patient characteristics

422 patients took part in the survey, 209 of whom had type 1 diabetes and 213 had type 2 diabetes. The characteristics of the surveyed groups studied are presented in Table 1.

International Physical Activity Questionnaire

On the basis of the answers provided by the patients in the IPAQ (International Physical Activity Questionnaire), 64% (n = 269) of the respondents were classified in the group with a high level of physical activity, 26% (n = 109) were classified in the group with a moderate level of physical activity and 10% (n = 44) were classified in the group with a low level of physical activity (Tab. 2).

Hypoglycaemia episodes as the function of physical activity

Table 3 presents the number of patients with mild hypoglycaemia episodes in function of their physical activity. In the whole group of patients the incidence of hypoglycaemia was significantly higher in the high physical activity level subgroup when compared to moderate physical activity level and low activity level subgroups respectively ($p < 0.01$ for both comparisons).

Among patients with type 1 diabetes the incidence of hypoglycaemia was significantly higher in the high physical activity subgroup when compared to moderate physical activity and low physical activity subgroups respectively ($p < 0.001$ for both comparisons). Also the incidence of hypoglycaemia was significantly higher in the subgroup with moderate when compared to low physical activity level ($p < 0.001$).

In patients suffering from type 2 diabetes the incidence of hypoglycaemia was significantly higher in subgroup of patients with high physical activity level when compared to moderate and low activity level ($p < 0.001$ and 0.005, respectively). Also comparison between moderate and low physical activity showed significant difference ($p < 0.001$).

Table 3. Number of patients experiencing mild hypoglycaemia in the past month, in function of the declared physical activity assessed by the IPAQ. Data are presented as n (%)

Physical activity level	Number of patients with mild hypoglycaemia episodes		
	Total (n = 422)	Type 1 diabetes (n = 209)	Type 2 diabetes (n = 213)
High (n = 269)	175 (65%)*	$^{++}$127 (61%)**	$^{+}$48 (23%)**
Moderate (n = 109)	62 (57%)	39 (17%)**	23 (11%)**
Low (n = 44)	19 (43%)	9 (4%)	10 (5%)

*p < 0.01 *vs.* low physical activity level; **p < 0.001 *vs.* low physical activity level; $^{+}$p < 0.005 *vs.* moderate physical activity level; $^{++}$p < 0.001 *vs.* moderate physical activity level

Table 4. Number of patients experiencing severe hypoglycaemia in the past month, in function of the declared physical activity assessed by the IPAQ. Data are presented as n (%)

Activity level	Number of patients with severe hypoglycaemia episodes		
	Total	Type 1 diabetes	Type 2 diabetes
High (n = 269)	33 (12%)	24 (16%)	9 (7%)
Moderate (n = 109)	6 (6%)	3 (6%)	1 (2%)
Low (n = 44)	2 (5%)	0 (0%)	1 (3%)

In type 1 diabetes, a higher level of physical activity increased also the incidence of severe hypoglycaemia but small amount of episodes does not allow to perform statistical analysis (Tab. 4).

Discussion

One of the elements of diabetes treatment is normalization of glucose levels, which protects the patient from the consequences of chronic hyperglycaemia. As evidenced in the UK Prospective Diabetes Study (UKPDS), long-term maintenance of normal blood glucose levels may decrease the risk of diabetic complications [20].

However, a pivotal clinical trial — The Diabetes Control and Complications Trial (DCCT) — conducted in 1984–1993 demonstrated that the most meaningful side effect of intensification of antihyperglycaemic treatment was an increased risk of hypoglycaemia, including severe episodes requiring assistance of a third party. In Diabetes Control and Complications Trial, 65% of patients in the group receiving intensified treatment *vs.* 35% of patients in the group receiving conventional treatment experienced at least one episode of severe hypoglycaemia in the course of the study [21]. While trying to answer the question on how else hypoglycaemia constitutes a barrier to attain glycaemic goals, we evidenced that undertaking physical activity by patients was associated with an increased risk of hypoglycaemia.

The survey was performed in consecutive patients coming to the consultation clinic, and thus it can be assumed that the results obtained can be representative for the overall incidence of the investigated phenomenon in adult patients.

For the assessment of hypoglycaemia incidence, a classification based on clinical data similar to those used in most of the studies, and thus it seems that in this survey the probability of overestimating hypoglycaemia incidence is negligible [22–25].

In the collected and analyzed data, mild hypoglycaemia episodes were clearly predominant (61% of patients surveyed). Most commonly, those episodes were observed in patients with type 1 diabetes (84%) and were correlated with the level of physical activity, followed by patients with type 2 diabetes treated with insulin (57%), metformin (22%) and sulphonylureas (8%).

Severe hypoglycaemia episodes occur much less commonly (10% of the surveyed population); the distribution of their incidence is similar — they are most common in patients with type 1 diabetes (13%), followed by patients with type 2 diabetes treated with insulin (11%), metformin (2%) and sulphonylureas (0%) [26]. The respondents were also asked about the number of mild and severe hypoglycaemia episodes in the past year. Unfortunately, the patients were unable to determine the number of episodes in such a long time period, and thus those data were not taken into account in view of inadequate accuracy of the responses.

Similar results were obtained by Alveres-Guisasola et al. in the RECAP study [27], where hypoglycaemia episodes were found in 38% of patients, including severe ones in 5%, and by Tłuczykont et al. — hypoglycaemia

affected 41% of patients, and mild hypoglycaemia occurred in 31% of the total number of patients and severe in 9%. Most commonly, mild hypoglycaemia episodes were experienced by insulin-treated patients with both type 1 (45%) and type 2 diabetes (52%) [19].

Indeed, as evidenced by Bodmer et al., the highest risk of hypoglycaemia is present during insulin treatment (14.9%) [28]. As to the risk of oral drugs, it was 1% and 2.86%, for metformin and sulphonylureas respectively.

In a study of Pilemann-Lyberg et al., 76% of patients treated with sulphonylureas experienced hypoglycaemia episodes. The investigators suggested that those medicines may have to be used with caution in elderly patients, in patients with renal, hepatic or cardiovascular diseases and in patients with an acute infection, and also in malnourished patients. They also suggested that the control of glucose levels in those patients should be less strict to avoid severe complications of hypoglycaemia [29]. On the other hand, no episodes of severe hypoglycaemia in patients receiving SU were found in the present survey, which may be due to the small size of the surveyed group (n = 24).

There are various methods used to measure physical activity. Direct methods with accelerometers are being used in addition to questionnaire studies, among which IPAQ questionnaire is the most popular one. The question arises, will questionnaire methods assess the actual level of physical activity. Mynarski et al. compared the physical exercise assessment in diabetic patients . They used the IPAQ questionnaire and Caltrac accelerometer among 31 patients with type 2 diabetes treated with insulin. Their results showed, that the questionnaire study does allow the assessment of physical activity and is equivalent to direct methods [30].

The effect of physical exercise on the severity and risk of hypoglycaemia was a subject of few literature reports only [31–33].

Nevertheless, an effect of a cycle of exercises recommended to patients was analyzed in those reports. No analyses of correlations between daily physical activity and hypoglycaemia severity in the everyday practice setting were found in the existing publications.

Conclusions

The incidence of hypoglycaemia depends on the type of diabetes and is the highest in patients with type 1 and insulin-treated type 2. The incidence of hypoglycaemia increases along with increasing physical activity.

Statement of competing interests

The authors declare that they have no conflict of interest.

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