Physical activity level and hypoglycemia in type 1 diabetes patients

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ABSTRACT

Introduction: The recommended management for individuals with type 1 diabetes (T1D) includes an intensive treatment with insulin therapy and the practice of regular exercise. However, this association is related with hypoglycemia episodes.

Objective: The aim of this study was to perform a cross-sectional evaluation of the association between the physical activity (PA) level and hypoglycemia episodes reported in patients with T1D.

Methods: Adult outpatients with T1D had their PA level assessed by the International Physical Activity Questionnaire (long form), considering the intensity of the physical activity (vigorous, moderate and/or walks) in daily activities, such as at work, means of transport, domestic activities and at leisure, and answered questions about self-care and hypoglycemia episodes.

Results: The study included 126 patients who presented the following characteristics: mean age of 35 (28-47) years old and 16 (11-24) years of diabetes duration, 55% women, HbA1c=9.3 ± 2.1%, and body mass index = 25.0 ± 4.2 kg/m². Very active patients had lower values of glucose and LDL-cholesterol when compared with the less active group. A greater proportion of active (48.1%) and very active patients (66.7%) reported practicing exercise regularly when compared with the less active subjects (13.3%; P=0.003). Less active patients had a three-fold chance of reporting hypoglycemia episodes when compared with very active patients (OR=3.49; CI 95%: 1.26-9.70; P=0.016).

Conclusions: Less active adults with T1D presented more hypoglycemia, probably due to the practice of informal moderate and/or vigorous activities without specific self-care.

Keywords: Exercise; self-care; blood glucose

Diabetes Mellitus (DM) is a metabolic disease characterized by hyperglycemia, resulting from defects in insulin action and/or secretion[1]. In Brazil, the prevalence of self-reported DM in the adult urban population is 6.3%[2]. Among the types of DM, type 1 DM (T1D) accounts for 10% of the cases in the population in general[3]. The treatment of individuals with T1D uses exogenous insulin, a healthy diet with carbohydrates from vegetables, fruits, whole grains, legumes and milk, besides frequently practicing, regular moderate-intensity aerobic exercise for at least 150 minutes a week[1,4].

Regular exercise improves cardiovascular performance, insulin sensitivity, and creates a feeling of well-being. Furthermore, the terms regular exercise and physical activity (PA) are often used synonymously, although they are not synonyms. PA is considered every bodily movement produced by the skeletal musculature, and that results in a greater expenditure of energy than the levels of rest[5] and it also presents biopsychosocial, cultural and behavioral components[6]. On the other hand, regular exercise is considered any PA that

practice of moderate and vigorous exercise or PA, at the same time as the PA questionnaire was applied. Asymptomatic hypoglycemia was defined as blood glucose values <3.9 mmol.L^{-1} with no symptoms. Moderate hypoglycemia was defined as an episode in which a patient felt confuse, adrift, slow and could not revert its hypoglycemia alone. A severe hypoglycemia was defined as an episode of hypoglycemia in which a patient required assistance from another person and needed glucagon or glucose injection[19].

Blood samples were collected after a 12-h fast. Plasma glucose was measured by the glucose oxidase method, glycated hemoglobin (HbA1c) by an ion-exchange HPLC procedure using a reference range of 4·8-6%[20], total cholesterol and triacylglycerol by specific enzymatic colorimetric methods and HDL-cholesterol by the homogeneous direct method. LDL-cholesterol was estimated using the Friedewald formula when triacylglycerol values <4.5 mmol/L[21]. All tests were performed at the Hospital de Clínicas de Porto Alegre Clinical Pathology Laboratory.

Statistical Analysis

For analysis the patients were grouped according to the classification of the PA level into three groups: less active, active or very active, based on the IPAQ classification. The data are described as mean ± standard deviation, median (interquartile interval), or number of cases for the total number of patients of the group (%). To compare the groups of patients, the ANOVA test and Kruskal-Wallis were applied for independent samples, or Chi-square, as described. P values <0.05 (two-sided) were considered as statistically significant. All analyses were performed using PASW 18.0 (SPSS, Inc.).

RESULTS

The study included 126 adults with T1D seen at the Endocrine Outpatient Clinic of HCPA during the period from October 2008 to March 2010 (age: 37.1±11.0 years old; diabetes duration: 16 (11-24) years; BMI: 25.0±4.2 Kg/m^2; male: 44.4%). The clinical, anthropometric, and laboratory characteristics according to the three levels of PA are shown in Table 1. A total of 15 patients (11.9%) were classified as less active, 81 patients (64.3%) as active, and 30 patients (23.8%) as very active. The very active patients presented lower values of LDL-cholesterol compared to less active patients (P=0.011), but without a statistical difference compared to the group of active patients (P=0.913). As to the HDL-cholesterol values, only the active patients presented higher values compared to the two groups of PA extremes, but with a borderline significance [very active and not very active; P=0.055].

The individuals classified as very active reported that they did more vigorous and moderate PA compared to active and less active patients as shown on Table 2. The frequency of reports of asymptomatic and symptomatic hypoglycemia in the last six months of evolution, and the presence of symptoms of hypoglycemia during PA are shown in Figure 1.

Table 1: Clinical characteristics, lifestyle, and laboratory characteristics of insulin-dependent type 1 diabetes mellitus patients, grouped according to the level of physical activity (n=126).

	Less active	Active	Very Active	P
N	15	81	30	-
Age (years)	40.9 ± 11.4	37.3 ± 11.0	34.4 ± 10.5	0.166[1]
Diabetes duration (years)	19 (14-26)	16 (11-21)	18.5 (13-25)	0.560[3]
Males	8 (53.3%)	30 (37.0%)	18 (60.0%)	0.074[2]
Whites	12 (80.0%)	69 (85.2%)	28 (93.3%)	0.394[2]
Current smokers	3 (20%)	11 (13.6%)	2 (6.7%)	0.462[2]
Alcoholic beverage intake (previous month)	3 (20%)	19 (23.5%)	12 (40%)	0.177[2]
Insulin therapy (IU)	52.1 ± 18.2	46.9 ± 19.3	44.9 ± 15.7	0.259[1]
Dietary counseling by registered nutritionist	8 (53.3%)	37 (45.7%)	18 (63%)	0.392[2]
Diet adherence (occasionally and/or always)	12 (80.0%)	60 (74.0%)	26 (86.7%)	0.213[2]
Fasting blood glucose (mmol/L)	12.8 (6.7-17.2)	10.2 (7.0-16.2)	7.1 (4.6-12.0)[a]	0.020[3]
HbA1c (%)	9.6 ± 2.0	9.5 ± 2.2	8.6 ± 1.6	0.108[1]
Total cholesterol (mmol/L)	10.4 ± 2.55	10.1 ± 2.3	9.9 ± 2.7	0.793[1]
HDL cholesterol (mmol/L)	2.8 ± 0.5[b]	3.4 ± 0.9[b]	3.1 ± 0.8	0.052[1]
LDL cholesterol (mmol/L)	7.2 ± 1.6[c]	5.4 ± 1.8	5.5 ± 2.1	0.036[1]
Triacylglycerols (mmol/L)	5.2 (3.9-6.5)	4.5 (3.3-6.9)	4.7 (3.3-2.5)	0.785[3]

Data presented as mean ± standard deviation; median (interquartile interval) or number for total of patients in group (%). [1]ANOVA test (LSD *post-hoc*); [2]Chi-square; [3]Kruskal-Wallis. [a]Very active people are different from less active and active ones; [b]Less active are different from the active ones; [c]Less active are different from active and very active patients.

Table 2: Median metabolic equivalents performed by patients in each domain of physical activity grouped according to the level of physical activity (n=126).

Metabolic equivalents (METs – minutes/week)	Physical activity level			P
	Less active (n=15)	Active (n=81)	Very active (n=30)	
Vigorous PA during work	0 (0-0)	0 (0-0)	720 (0-5,040)	0.01
Vigorous PA in leisure activities	0 (0-0)	0 (0-0)	240 (0-1,920)	0.01
Moderate PA during work	0 (0-0)	0 (0-1,470)	180 (0-4,440)	0.04
Moderate PA in the garden	0 (0-0)	80 (0-600)	360 (0-1,260)	0.01
Moderate PA in the house	0 (0-0)	810 (285-2,700)	615 (90-2,160)	0.01
Walking during work	0 (0-445)	0 (0-445)	495 (0-1,930.5)	0.01
Walking as mean of transportation	0 (0-495)	247.5 (66-478.5)	577.5 (0-1,188)	0.04

Data presented as median (interquartile interval) in minutes/week. Kruskal-Wallis. PA: Physical activity.
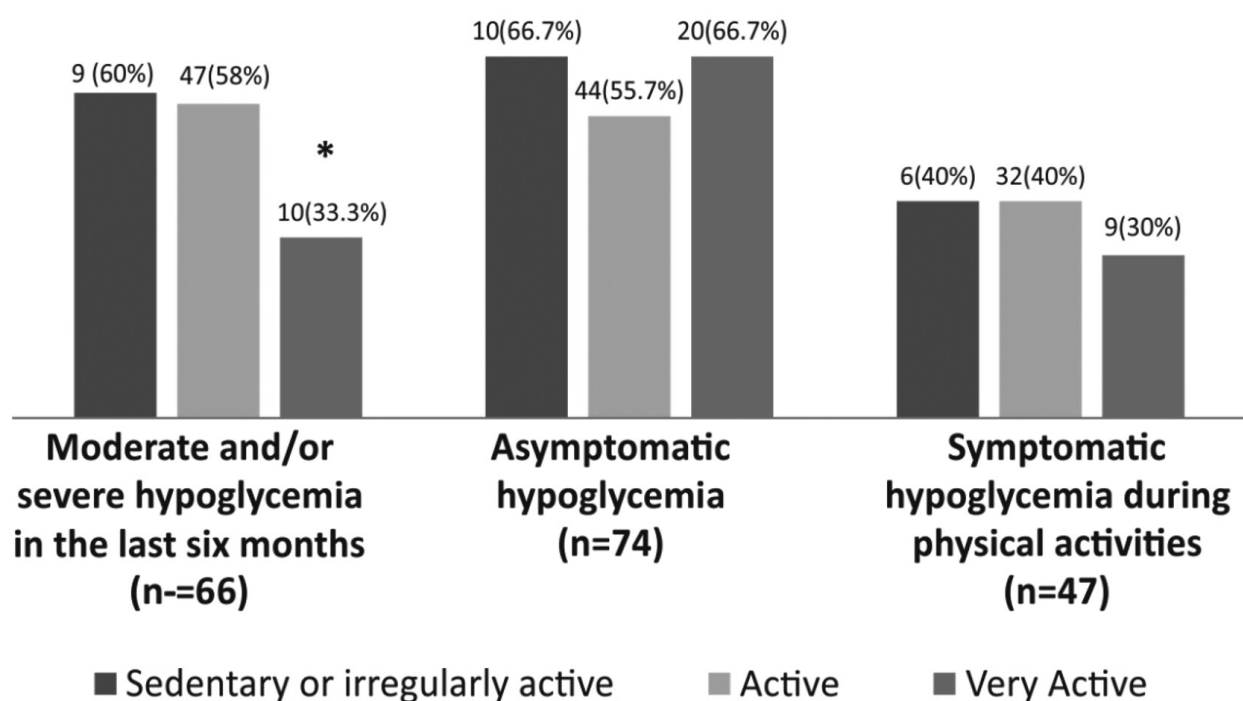
Figure 1: Frequency of hypoglycemia report in patients with type 1 Diabetes Mellitus according to Physical Activity Level proposed by the long version of the International Physical Activity Questionnaire (n = 126). *P = 0.056 (Chi-square test).

A greater proportion of active patients (48.1%) and very active patients (66.7%) reported that they practiced exercise regularly compared to the less active group (13.3%; p=0.003). When we analyzed the frequency of programed regular exercise of the patients, only 61 patients (48.4%) reported that they practiced regularly. Also, 22 of the 61 patients reported that they received specific orientation about self-care (insulin, diet, capillary blood glucose monitoring) to practice regular exercise, and that these orientations were given by a physician to 36.4% of the patients, by a registered nutritionist to 45.4% of the patients,

and by both professionals to 13.6% of the patients. One patient reported having received guidance from another health care professional. The proportion of patients who reported receiving specific guidance for the practice of regular exercise was not different among the patients with or without complaints of episodes of hypoglycemia in regular exercise: 9 (40.9%) vs. 13 (59.1%); p=0.792.

Of the 61 patients who practice exercise regularly, only 28 patients reported taking some kind of care before, during or after regular exercise. The most cited results were careful with food (25%), followed

by being careful with food associated with monitoring of the capillary blood glucose (21.4%). Besides, care with stretching and/or warm ups (10.7%), only stretching (17.9%), monitoring capillary blood glucose alone (14.3%), monitoring associated with stretching (3.6%), presence of prior symptoms (3.6%), stretching associated with food (3.6%) were also reported.

Multiple regression models was performed with at least one report of moderate and/or severe hypoglycemia in the last six months as dependent variable and PA level as independent variable adjusted for variables of biological importance, such as blood glucose values and report of following diet. The less active patients presented three times more chance of reporting episodes of hypoglycemia compared to very active patients (OR=3.49; CI 95% 1.26-9.70; p=0.016). There were no differences between very active patients vs. active patients and between less active and active patients.

DISCUSSION

In the present study, less active patients with T1D had a three-fold greater chance of reporting episodes of hypoglycemia compared to very active patients. The patients were classified by IPAQ as active and very active, mainly by the moderate and vigorous PA performed in the work environment and the walks to get around (as a means of transport).

No Brazilian studies were found to evaluate the PA level and its relationship with hypoglycemia in patients with T1D, only studies conducted with young Finns[22] and Italians[11]. The heterogeneity between international[10,11,22-24] and national studies[25] is also outstanding regarding the methods used to evaluate the PA level of populations, making it difficult to have an adequate comparison between the existing evidence. The evaluation of PA level by IPAQ in different populations worldwide has been suggested by the World Health Organization since 2001, precisely to allow comparisons between the populations[26].

The less active patients presented a three-fold greater chance of reporting hypoglycemia compared to the very active patients. Patients that are more active are probably those that are more compliant with all other issues concerning diabetes self-care. Taking into account that regular exercise improves sensitivity to the action of insulin[27], possibly the less active individuals do not know the reaction of their own metabolism to PA, and they did not practice enough exercise to have the benefit in the metabolic control. The ADA recommend that adults with diabetes should be advised to perform at least 150 minutes/week of moderate-intensity aerobic physical activity (50-70% of maximum heart rate), spread over at least 3 days/week with no more than 2 consecutive days without exercise[4]. There are also considerable data for the health benefits (e.g., increased cardiovascular fitness, muscle strength, improved insulin sensitivity, etc.) of regular exercise for those with type 1 diabetes[4]. On the other hand, good fitness level individuals tend to exercise at greater work thresholds and present better insulin sensitivity, which have been already associated with exercise-associated hypoglycemia in patients with Type 1 diabetes[28]. The strategies to prevent episodes of hypoglycemia related to the practice of PA recommended by the ADA[1] are self-monitoring of blood glucose before, during and after regular exercise to adjust the diet and insulin doses used habitually. In this study, care with food was the most prevalent self-care behavior among the patients who practiced regular exercise, followed by the association of care with food and capillary blood glucose. The regular practice of exercise allows a better management of this issue by the patient with diabetes guided by their health team, since the factors that have been related to the glycemic response during the regular exercise are: the metabolic control of the patient itself, the type and intensity of the activity performed, the amount of insulin applied before the regular exercise, the time when exercise is done, besides the phase of the menstrual cycle in women[29]. Further, a cross-sectional study of 103 patients with T1D observed that one of the main causes that prevent the practice of regular exercise was the fear that hypoglycemia episodes would occur[29].

Patients who were less active presented higher values of plasma glucose and LDL cholesterol compared to very active patients. However, since Hba1c was similar among groups, this could be caused by chance. Some authors[11,22] observed a better glycemic control in more active patients. Patients with T1D who irregularly practiced 60 minutes of PA a week[11], or patients classified as sedentary[22], presented worse glycemic control (evaluated by HbA1c), when compared to the more active patients. In fact, lifestyle modifications - healthy diet and regular practice of PA - associated with the regular use of insulin are recommendations to obtain and maintain a better metabolic control of DM[6]. The practice of regular exercise improves glycemic control and the lipid profile in individuals with and without DM[30,31].

The active and very active patients in this study were classified thus due to the PA performed during work and as a means of transportation and not by regular exercise. Similar results were observed by other authors in cross-sectional studies with patients without DM[32,33]. Regarding this, a more comprehensive

evaluation of the PA level seems to be important for the health professional team in order to advise on self-care during routine physical activity, and not only in formal exercise.

Limitations inherent to the instrument used to evaluate the PA level, sample size, and evaluation of the outcome (hypoglycemia) of the reports and not from capillary measurements needs to be considered in the preliminary analysis of the results presented. However, the use of self-reported hypoglycemia is a conservative bias, since the patients may have autonomous neuropathy and not perceive the hypoglycemia associated or not with the practice of PA.

Based on the presented results, patients with T1D were classified mostly as active, but due to the practice of moderate and/or vigorous PA during work and as a mean of transport, and not due to the practice of regular exercise. The very active T1D patients may have three times less chance of reporting episodes of hypoglycemia compared to the T1D who exercise less or do it irregularly. And only one-third of those who practiced regular exercise, independent of the level of PA by IPAQ, perform self-care measures for the prevention of PA-related hypoglycemia. These findings show that the T1D patients need special attention and better information from their health professionals about PA and hypoglycemia prevention.

Acknowledgements

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