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SEGURANÇA GLICÊMICA DE UM TESTE AERÓBICO MÁXIMO EM PESSOAS COM DIABETES TIPO 1 E SUA CORRELAÇÃO COM PARÂMETROS DE SAÚDE

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Resumo:

Verificar a segurança glicêmica de um teste cardiorrespiratório máximo (V̇O2max) em pacientes com diabetes mellitus tipo 1 (DM1) e correlacionar os valores com parâmetros de controle metabólico como glicemia, hemoglobina glicada, tempo de diagnóstico (DT) e gordura (corporal[GC] e visceral[GV]). O estudo transversal avaliou dez DM1 (idade 24,9 ± 7,5 anos; tempo de diagnóstico 11,5 ± 7,4; índice de massa corporal 22 ± 2 kg/m2). Foram coletadas variáveis de controle glicêmico metabólico (antes e depois), hemoglobina glicada (HbA1c), tempo de diagnóstico e gordura total e visceral. O protocolo de teste máximo do CENESP foi utilizado na esteira com consumo máximo direto de oxigênio (V̇O2max). Teste de normalidade, teste t pareado e correlações ($p<0,05$) foram realizados. Nos resultados, glicemia pré 189 ± 67 mg/dL vs. pós 172 ± 66 mg/dL ($p = 0,140$). O V̇O2max com pontuação média regular para homens e mulheres (37,4 ± 6,6 ml.kg.min-1). Houve correlação negativa e quase perfeita com DT, GC e GV ($p = 0,028$; $p < 0,000$ e $p < 0,000$). Concluímos que é possível realizar um CENESP máximo com segurança glicêmica no DM1. No entanto, DT, GC e GV interferem negativamente na aptidão cardiorrespiratória e devem ser verificados antes do teste.

Palavras-chave: Diabetes Mellitus tipo 1; teste de esforço; ergoespirometria; glicemia.

Afiliação

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GLYCEMIC SAFETY OF A MAXIMUM AEROBIC TEST IN TYPE 1 DIABETICS AND THEIR CORRELATION WITH HEALTH PARAMETERS

Abstract:

To verify the glycemic safety of a maximal cardiorespiratory test (V̇O2max) in T1DM patients and correlate the maximum cardiorespiratory values with metabolic control parameters such as glycemia, glycated hemoglobin, time of diagnosis (TD), and fat (body [GC] and visceral [GV]). The cross-sectional study evaluated ten T1DM patients (age 24.9 ± 7.5 years; time of diagnosis 11.5 ± 7.4; body mass index 22 ± 2 kg/m^2). Metabolic glycemic control variables (before and after), glycated hemoglobin (HbA1c), time since diagnosis and total and visceral fat were collected. The CENESP maximum test protocol was used on the treadmill with direct maximal oxygen uptake (V̇O2max). Normality test, paired t-test and correlations ($p < 0.05$) were performed. In the results, blood glucose pre 189 ± 67 mg/dL vs. post 172 ± 66 mg/dL ($p = 0.140$). The V̇O2max with a regular average score for men and women (37.4 ± 6.6 ml.kg.min-1). There was a negative and almost perfect correlation with TD, GC and GV ($p = 0.028$, $p < 0.000$, and $p < 0.000$). We conclude that is possible to perform a CENESP maximal with glycemic safe in T1DM. However, TD, GC, and GV negatively interfere with cardiorespiratory fitness and should be verified before the test.

Key words: Type 1 Diabetes Mellitus; stress test; ergospirometry; glycemia

Introdução

Diabetes mellitus (DM) is caused by metabolic disorders in controlling glucose levels through the poor functioning of insulin secretion/action causing hyperglycemia[1,2]. Otherwise, if persist uncontrolled can induce secondary system complications (heart, nerves, blood vessels, kidneys, eyes, feet, etc.)[1,2]. Among the different types of diabetes, Type 1 Diabetes Mellitus (T1DM) is characterized by being a chronic metabolic dysfunction by the destruction of pancreatic β cells causing exogenous insulin dependence[1,3–5]. And, it is highlighted that starts generally in childhood, so the time of diagnosis and this non-controlled disease over time should be unhealthy[1,3].

Efficient treatment beyond insulin therapy to T1DM individuals is a lifestyle change as an appropriate nutrition balance (Academy Nutrition and Dietetics - AND) and adopting regular exercise (The American Diabetes Association - ADA) to aid in the management of glycemic control reducing, for example, glycated hemoglobin and fat after an exercise program[4,6]. However, exercising as non-diabetic in moderate to vigorous exercise there are hormones stimulation and glucose transporters to regulate energy metabolism (glucagon is increased and insulin reduced also with increased glucose production plus muscle glycogen stores and hepatic release) and is acutely continued after exercise, avoiding hypoglycemia[1,2]. Otherwise, in T1DM patients the use of exogenous insulin and the exercise intensity can cause hypoglycemia which is an important aspect to non-exercising and/or adhering to regular exercise programs because of this possibility to immediate and/or late acute hypoglycemia post exercising[6]. Thus, performing practice of physical exercises with safe glycemic control becomes essential, for that according to the ADA, when starting it is recommended to be in the range of 100 to 250 mg/dL[1,2,6].

Still, before beginning an aerobic exercise program, non-diabetics and diabetics need the prescription based on a cardiorespiratory assessment, which will enable the health professional to build a more accurate and effective planning exercise to promote health benefits. Therefore, assessment of the maximal oxygen uptake ($\dot{V}O2max$) allows knowing the maximum capacity of oxygen uptake, distribution, and metabolism for the organism[7]. This measurement can be evaluated directly by capturing and analyzing respiratory gases, or indirectly by applying tests added to the estimation/prediction calculations[7–9]. But even knowing that exercise testing is indicated for diabetics who want to start an exercise program[4] there seems to be no consensus on maximal testing as they may cause acute hypoglycemia in diabetics[2].

In addition, there is a lack of evidence in the literature evaluating metabolic signs of

exercise stress testing in insulin-dependent diabetics, according to recommendation[10], therefore, the verification of possible hypoglycemia (<100 mg/dL) should be monitored in effect to cardiorespiratory effort and applied insulin signaling[11]. Besides, the CENESP protocol has been used over the country due to the simple applicability (brief 2-3-minute warming with speed depending on their physical fitness, next 1km/h/minute until volunteer fatigue, recommended ~12-minute test). Thus, the purpose was to verify the glycemic safety of a V̇O2max test (proposed initially to non-diabetics) in T1DM patients and correlate the maximum oxygen uptake values obtained with metabolic control parameters such as glycemia, glycated hemoglobin, time of diagnosis, and fat.

Materiais e Métodos

Type of study, sample, and ethical aspects

This descriptive cross-sectional study had a sample of individuals with type 1 diabetes mellitus of male and female (aged 26.5 ± 8 years; 61.6 ± 7.7 kg, 169 ± 8.0 cm, and 21.5 ± 2.0 kg/m²) with previous experience in treadmill running. A power analysis (GPower Software, version 3.1.9) indicated that a sample of nine T1DM participants was needed to identify possible statistical pre to post-blood glucose differences considering large effect size value (0.6), 85% power, 5% level of significance, and two tails. The project was carried out by the Local Ethics Committee, number 1.560.045. The Informed Consent Form was used in accordance with the National Health Council resolution 466/12.

Techniques and protocols in Study Design

Initially, blood glucose control was assessed by blood analysis to check Glycated Hemoglobin (HbA1c) 1 hour before the maximal stress test in a certified biochemical laboratory to analyze blood glucose history[11,12]. Then, the participants were referred to the Human Performance Evaluation Laboratory for anthropometric and fat percentage measurements[13]. Measurements of body mass (kg) and height (cm) were obtained using a scale (Filizola®, Brazil), and a wooden stadiometer. Thus, the body mass index - BMI (kg/m²) was calculated. In addition to performing dual-emission X-ray densitometry (DXA) for more accurate Total and visceral body fat percentage (% G).

After, was performed capillary glucose by the glucometer, and reagent strips (Active AccuCheck, Roche, Brazil) collected before and immediately after the end of the maximum test. After analyzing the pre glycemia, the maximum protocol was performed. CENESP

protocol (Annex IV by Ordinance MET nº 221, Brazil) was in the COSMED T150 treadmill (Minnesota, Germany) to analyze the maximum oxygen uptake (V̇O2max) measured by COSMED QUARK CPET computerized metabolic analyzer. The respiratory variables were measured breath by breath and captured by Hans Rudolph Linc masks, model V2 (USA), and system calibration was performed according to the manufacturer's recommendations. The V̇O2max was accepted as the highest V̇O2 value found before the test was stopped. Based on its interruption, at least two of the following criteria: 1) If before the implement load, stabilization or decline in V̇O2 consumption occurred; 2) when the CO2/ V̇O2 ratio (R) equals or exceeds 1.15; 3) if the maximum heart rate ≥ 95% estimated by the age equation (220-age).

The CENESP protocol was performed for two categories: 1) individuals who were inappropriately active A warmed up at 5km/h for 3 minutes, whereupon there was an increase of 1km/h every minute to the maximum limit of the volunteer. 2) for the inadequate active individuals B (analyzing by self-reported weekly physical activity practice - time), the warm-up was started at a speed of 3km/h following the same temporal and incremental order as the previous protocol, following the recommendations by warming with speed depending from their physical fitness, adapting to diabetic patients according to the main guidelines[11]. The categories were designed to ensure that all volunteers completed the test within its validity according to their physical aptitude. Thus, the test was considered valid with an average duration of 8 to 12 minutes, according to recommendations[13].

The subjects used insulin at least 1.5 - 2 hours before the test with their last pre-test feeding, reducing 30-50% of the usual dosage according to the recommendations[4]. Physical tests were performed at the Human Performance Assessment Laboratory, in an environment with a temperature (22 ± 2 °C) and controlled relative humidity (40-60%) according to recommendations[10,14].

Statistical analysis

Data were tabulated and analyzed in the Microsoft Excel spreadsheet (Windows® Office, 2013, USA) using descriptive statistics (mean ± standard deviation - SD). Data were transferred to Graph Pad software (version 3.1) and used to verify pre and post-glycemic hold by Student's t-test for paired samples. For correlation of maximal oxygen uptake and metabolic control parameters, Pearson test was used considering the following scores: 0-0.19 poor; 0.2-0.39 mild; 0.4-0.59 moderate; 0.6-0.79 high and 0.8-1.0 almost perfect correlation. The effect size was calculated to glycemia. Significance was set at $p < 0.05$ for all tests.

Results

Table 1 shows the main characteristics of the T1DM participants (mean ± standard deviation).

Table 1. The T1DM patient's characteristics (n = 10).

Diabetics characteristics	*mean ± standard deviation*
%G (DXA)	24.4 ± 6.1
Diagnostic Time (years)	8.6 ± 1.4
Glycated Hemoglobin (%)	11.5 ± 7.4
Insulin - Basal (IU)/day	26 ± 7.0
Insulin – ultra-fast (UI)/day	21 ± 10.0
Pre capillary glucose (mg/dL)	189.5 ± 67.1
Post capillary glucose (mg/dL)	172.7 ± 66.8
HR_{max} (bpm)	186.1 ± 11.14
$\dot{V}O_{2max}$ (ml.kg.min^{-1})	37.4 ± 6.6

DXA - Dual-emission X-ray densitometry; HR_{max} – maximal reached heart rate; $\dot{V}O_{2max}$ – Maximal Consumption Oxygen reached in CENESP test; %- percentage; IU –Insulin units.

Individuals did not show a significant difference between pre and post-blood glucose levels (p=0.140) intervention and did not report late/nocturnal hypoglycemia. Also, the effect size was 0.57 (moderate) to glycemia, presenting important safety. A correlation matrix was performed to identify possible relationships of metabolic control parameters of the T1DM individuals with the maximal oxygen uptake responses. Significant correlations were found with the time of diagnosis (high negative correlation; -0.685), with %G (almost perfect negative correlation; -0.897) and visceral %G (almost perfect negative correlation; -0.859) (Table 2).

Table 2. Correlations with oxygen consumption of T1DM patients.

$\dot{V}O_2$ vs.	**TD**	**Gbefore**	**Gafter**	**%G**	**%Gvisceral**	**Hba1C**
r	-0.685	0.454	0.149	-0.897	-0.859	-0.266
p	0.028*	0.187	0.679	<0.001*	<0.001*	0.456

$\dot{V}O_2$: Maximum oxygen consumption; TD: Time of diagnosis; G: Blood capillary glycemia; %G: fat percentage; %G Visceral: Percentage of visceral (trunk) fat; Hba1C: Glycated Hemoglobin; *r*: correlation value.

Discussão

To the author's knowledge, this is the first study to evaluate performance adaptations associated with the correlation of verifying the glycemic safety of a V̇O2max test in T1DM and its metabolic control parameters, such as glycemia, glycated hemoglobin, time of diagnosis, and fat. The most important results of this document indicate: a) this maximal stress test protocol has glycemic safety without statistical difference between pre and post blood glucose levels (p=0. 140), and b) it is important to consider the time of diagnosis and total and visceral body fat, which is negatively related to maximal oxygen uptake (-0.685, -0.897 and -0.859, respectively, $p<0.05$).

The treadmill test was chosen because of its practical applicability and approximation of reality, since the walking activity is more similar to the basic skills inherent to humans, not requiring very specific skills, besides the muscles that are recruited to maintain the activity. Thus, it was used with recreational athletes, but can also be used with non-athletes[7]. There are studies that use ergospirometry as a preliminary test for subsequent experiments with diabetics, but mostly in the leg cycle ergometer and not treadmill[15,16].

Otherwise, our test was performed in a treadmill into a laboratory environment in a temperature-controlled environment, since diabetes was associated with deficiencies in its regulation, where heat stress can be a challenge for homeostasis, especially for the cardiovascular system and blood glucose. Cardiovascular adjustments are fundamental for temperature regulation during the heat and cold exposure, so blood should be redistributed to the periphery (vasodilation) and to the nucleus (vasoconstriction) respectively, to maintain stable core temperature and therefore thermal equilibrium, and it is preferable that the exercise or test be performed under milder temperatures [8,14].

Thus, the capillary blood glucose test after the stress test had a value of 172.7 ± 66.8 mg/dL (min; 74 mg/dL and max: 315 mg/dL), which did not provide hypoglycemia values, although it increased only one for hyperglycemia values [1,3]. This can be explained by some evidence found that aerobic exercises performed with glycemic rates considered normal in T1DM, have substrate oxidation similar to that of healthy individuals, changing to lipid oxidation[15,17].

Whereas individuals who exercised with higher than recommended blood glucose levels had predominantly carbohydrate oxidation metabolism, contesting the premise that muscle glycogen would be preserved, showing that exercise under higher insulin concentrations increases the use of glucose but does not spare the breakdown of muscle glycogen[17]. Metabolic

processes during exercise in insulin-dependent diabetic patients should be better analyzed and the recommendations for prescribing physical activity could be refined. However, quantitative data on the exercise fuel metabolism of patients with type 1 diabetes are scarce to date[15].

During one of the interventions, the use of two honey sachets (5-10g carbohydrate) by a single volunteer was necessary to measure above 100 mg/dL before the maximum test (min: 107 mg/dL and max: 300 mg/dL). Considering that each sachet increases plasma glycemia by 10-15 mg/dL (unpublished data) reinforces the view that exercise, carbohydrate consumption, and insulin dosage must be strictly balanced, with modified insulin therapy in anticipation of the year[4,9]. Insulin use by type-1 diabetic patients may be substantially reduced depending on exercise intensity and duration up to 12 hours after exercise[8].

In the literature, the impact of glycemic control on functional capacity during cardio-pulmonary exercise testing in people with type 1 diabetes. They found that poor glycemic control is related to the less economical use of oxygen at submaximal work rates and an earlier time to exhaustion during cardio-pulmonary exercise testing (r=0.47; p=0.03)[18]. Similar to our results, showing $\dot{V}O_{2max}$ as negatively correlated with time since diagnosis (r= -0.685; p=0.028) and total fat (r= -0.897; p<0.000) and visceral fat (r= -0.859; p<0.000) and, with HbA1C (r= -0.266; p=0.458) although non-statistical significant.

Therefore, our results are according to Cortez et al.[19] presenting that longer diagnosis time can elevate the chance of having complications with the management of diabetes. Consequently, the reduction in cardiorespiratory capacity as well as the increase in body and visceral fat, which are important variables for overall metabolic control[20]. Tagougui et al.[21] support the idea after 11 vs. 12 T1DM patients performed an exhaustive incremental exercise to determine VO_{2max}. They found poorly controlled patients displayed lower VO_{2max} and blunted muscle deoxyhemoglobin increase.

The limitations of the study were: a) higher sample size could be performed although the pre-post effect size was considered over than 0.5 (large, *d Cohen*= 0.57) and considerable actual power (0.86); b) A single $\dot{V}O_{2max}$ test were used. Otherwise, in clinical practice, this maximal test does not promote hypoglycemia and the professionals should verify the % fat and diagnostic time in order to initiate the warming-time of this test at lower speeds, knowing that the $\dot{V}O_{2max}$ of type 1 diabetic patient with high body fat and diagnostic time will be possibly lower than those with less fat and diagnostic time.

From a practical application, maintaining performance during the test, always performing glycemic control in stages while performing it is essential for the safety of the

athlete or patient. Finding a hypoglycemia flag is a priority that leads to the maximum cardiopulmonary effort. However, within our findings, the CENESP protocol provides these two safeguards, both in terms of metabolism and blood.

Finally, knowing that glycemic safety and health-related physical aspects (e.g. body composition and cardiorespiratory fitness) are important to verify in healthy[8,9,13,22,23], diabetics and also in type 1 diabetics[1,2,18, 21, 24,25,26], further studies are needed to determine the glycemic safety of several cardiorespiratory fitness tests, as well as the association of metabolic control variables in type 1 diabetics.

Conclusão

The CENESP exhaustive incremental and maximal test in type 1 diabetics is a glycemic safe test, avoiding hypoglycemia. However, cardiorespiratory fitness was negatively related to the time of diagnosis and total visceral and body fat, which could indicate poorly controlled diabetes management over the years.

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