Subacute behavior of glucose and blood pressure of type 1 diabetic people after strength exercise session: Study protocol

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Abstract

Background: Type 1 Diabetes Mellitus (DM1) is characterized as a severe insulin deficiency resulting from the destruction of beta cells in the pancreas, associated with autoimmunity. The clinical picture of a patient with DM1 includes symptoms such as abnormal thirst, dry mouth, sudden weight loss, frequent urination, lack of energy, tiredness, constant hunger and blurred vision. Systemic arterial hypertension (SAH) is characterized by high levels of pressure in the arteries, being associated with risk factors for coronary artery disease; cerebrovascular accident (CVA); myocardial infarction; heart failure and kidney failure. Regular physical activity in these patients is associated with a reduced risk of future cardiovascular disease, better long-term glycemic control, better cardiovascular fitness, better quality of life, reduced daily insulin requirements and better weight control. Furthermore, it plays an important role in the primary and secondary prevention of diabetes cardiovascular disease, improving general health and well-being. Objective: The present study aims to evaluate the effects of strength training on glycemic parameters after an exercise session, in adult type 1 diabetic individuals, through a randomized controlled clinical trial. Methodology: The sample will be made up of 30 participants with DM1, made up of men and women based on the inclusion/exclusion criteria. Discussion: Practicing physical activity reduces the need for hypoglycemic drugs, also improves metabolic control and helps obese patients lose weight, reducing the risk of cardiovascular diseases and improving the quality of life of these patients. The practice of strength and aerobic training as a non-drug treatment is systematically found in the literature as a fundamental strategy for reducing systemic arterial hypertension and maintaining the cardiovascular system. Both resistance exercise and Pilates are effective for individuals with type 1 diabetes, improving metabolic and clinical control, especially when combined with adequate nutrition and amino acid supplementation. Physical activities reduce the need for hypoglycemic medications, help with weight loss and reduce the risk of cardiovascular diseases. Regular exercise, especially intermittent, significantly reduces the risk of acute hypoglycemia. Furthermore, it improves HDL and LDL levels, essential for reducing cardiovascular risks. Strength and aerobic training are essential for controlling high blood pressure and improving quality of life, with three weekly sessions being recommended for satisfactory results.

Keywords: Type 1 diabetes mellitus; strength training; subacute effect; physical exercise.

BACKGROUND

Type 1 Diabetes Mellitus (DMI) is a severe insulin deficiency resulting from destroying pancreatic beta cells associated with autoimmunity. It is most common in children and teenagers but can appear at any age. It presents clinically suddenly, often with a tendency to ketosis and ketoacidosis, requiring complete insulin therapy from diagnosis(1). It is also worth remembering that there are other classifications of diabetes,
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such as Type 2 Diabetes Mellitus (DM2), which is characterized by insulin resistance and partial deficiency in insulin secretion by pancreatic beta cells. It is commonly associated with obesity and aging, causing metabolic disorders in individuals. Despite being challenging, the phenotypic differentiation between DM1 and DM2 is essential, requiring a thorough assessment of anamnesis, physical examination, and laboratory tests.

Systemic arterial hypertension (SAH), also known as high blood pressure, is characterized by high levels of pressure in the arteries and is associated with risk factors for cerebrovascular accident (CVA), myocardial infarction; Coronary artery disease, heart failure, and kidney failure, these cases are further increasing cardiovascular mortality rates, being one of the diseases that kill the most in Brazil. In a survey carried out by DATASUS, there were around 1,312,663 deaths from cardiovascular diseases in 2017, and SAH was associated with 45% of these deaths.

According to the International Diabetes Federation 2019, Brazil was the fifth country in terms of incidence of diabetes in the world, with 16.8 million adult patients (20 to 79 years old), second only to China, India, the United States, and Pakistan. The estimated incidence of the disease in 2030 will reach 21.5 million. Assessment of the secretory function of pancreatic beta cells with C-peptide measurement can help correctly classify diabetes, as patients with DM1 generally have a loss of insulin secretion capacity. Furthermore, DM1 is associated with risk factors such as heredity; having a family member with the condition slightly increases the risk of developing the disease. Environmental factors and exposure to some viral infections have also been associated with the risk of developing the disease. About 10% of all people with diabetes have type 1 diabetes. The clinical picture of a patient with DM1 includes symptoms such as abnormal thirst, dry mouth, sudden weight loss, frequent urination, lack of energy, tiredness, constant hunger, and blurred vision. Failure to treat this comorbidity can lead to numerous complications that include diabetic peripheral neuropathy, heart failure, diabetic retinopathy, kidney disease, dyslipidemia, infections, and liver disease, among others. Furthermore, it is essential to mention hypoglycemia as one of the main consequences of poor adherence to treatment, intense physical exercise, and poor diet.

The pharmacological treatment of DM1 includes insulin to control blood glucose levels in all patients. Different types of insulin depend on how quickly they work, when they peak, and how long they last. Insulin is commonly supplied with a syringe, insulin pen, or insulin pump. Patients requiring insulin must check their blood glucose levels regularly to inform insulin dosage. Blood glucose self-monitoring is the name given for measuring blood glucose levels by people with diabetes in their daily activities, whether at home, school, work, or elsewhere. People with T1D are advised to measure their blood glucose level at least four times daily.

Worldwide, diabetes has become a severe public health problem whose predictions are being surpassed with each new screening. For example, in 2000, the global estimate of adults living with diabetes was 151 million. In 2009, it had grown 88% to 285 million. In 2020, it is estimated that 9.3% of adults between the ages of 20 and 79 (a staggering 463 million people) live with diabetes. Additionally, 1.1 million children and adolescents under the age of 20 have type 1 diabetes. A decade ago, in 2010, the IDF’s global projection for diabetes in 2025 was 438 million. With another five years, this forecast has already
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been adjusted to 463 million\(^{(10)}\). According to the Brazilian Diabetes Society, in 2017, diabetes was in third place in the ranking of diseases with the highest morbidity and mortality rates in the country, with a higher rate among women. Despite this, there is a growing increase in cases among males\(^{(6)}\).

Exercise acts by increasing the entry of glucose into cells, using the translocation mechanism of the GLUT4 receptor, mainly responsible for the entry of glucose into the muscle cell. This mechanism helps insulin reduce glucose levels in the circulation\(^{(11)}\).

Regular physical activity in these patients, a beacon of hope, is associated with a reduced risk of future cardiovascular disease, better long-term glycemic control, better cardiovascular fitness, better quality of life, decreased daily insulin requirements and better weight control\(^{(7)}\). Furthermore, it plays an important role in the primary and secondary prevention of cardiovascular disease caused by diabetes, improving general health and well-being\(^{(12)}\).

The Brazilian Arterial Hypertension Guidelines recommend resistance physical exercise as a complementary component to aerobic training for the training of hypertensive patients. Resistance training has a more significant hypotensive effect when compared to aerobic exercise. Furthermore, different physical exercise programs affect the patient's blood pressure, observing a decrease of between 4 and 9 mmHg\(^{(13)}\).

Some variables, crucial to consider, must be analyzed before starting a training program, such as: intensity, duration of exercise, the individual's level of activity, the presence of disease complications and the clinical picture. Insulin dosages and/or carbohydrate replacement are some of the strategies that can be used to avoid exercise-related hypoglycemia. Another important factor is hydration during these activities and blood glucose monitoring carried out before, during and after exercise\(^{(14)}\). Therefore, this study aims to evaluate the acute effects of strength exercise on blood pressure and blood glucose in adult type 1 diabetic individuals after an exercise session through a randomized controlled clinical trial.

METHODS

Type of study: Randomized controlled clinical trial.

Sample: The sample will consist of 30 patients, of both genders, with a clinical diagnosis of DM1.

Inclusion criteria:
- Diagnosis of DM1, according to guidelines from the American Diabetes Association\(^{11}\).
- Age between 25 and 55 years old;
- Regular treatment and minimum frequency every three months; Use of insulin;
- Signing of the Free and Informed Consent Form (TCLE).

Exclusion criteria:
- Feverish state and/or infectious disease;
- Obesity class II or more – BMI (body mass index) ≥ 35 kg/m\(^2\);
- Class III or IV heart failure; Recent cardiovascular event (last 3 months);
- Chronic renal failure; Severe liver disease; Active smoking;
- Orthopedic limitations or any physical or mental limitation that prevents you from performing the exercises.
Study design

The sample will consist of 30 participants with DM1, selected from a Diabetics Association in the city of Anápolis GO through direct contact with the association (APPENDIX I), consisting of men and women, according to the recruitment order, and based on the inclusion/exclusion criteria. Because we did not find a similar study (Type 1 Diabetes Mellitus - DM1) previously published, the “Intention to treat” principle adopted the convenience sampling criterion. The sample (n=30), after inclusion in the study, will be randomized into two groups with an equal number of participants, Experimental Protocol - EP (n=15) and Control Protocol - CP (n=15). After completing the protocol, blood glucose will be collected after 24 hours, and participants will perform the crossover protocol (participants who performed the EP will now perform the CP, and those who started the CP will perform the EP, characterizing the Crossed design of the study). To carry out this study, a bibliographical survey was carried out in different databases to obtain basic information for elaborating the central hypothesis. The research will be suspended in case of non-compliance with the project and lack of responsibility and serenity with the research. If the target population does not adhere to activities and others that make it impossible to create a statistically viable sample, it will be possible to re-discuss the project outline, suspend it, or even close it.

The randomization technique for participating in the protocols will be used using a computer program (www.randomizer.org) containing the coded distribution. Allocation confidentiality will be guaranteed by a randomization list located in a remote location, preventing the researcher from identifying which intervention each patient will initiate. The sequence of numbers will be generated by a researcher “blind” to the study after selecting patients according to the inclusion and exclusion criteria. The sequence of digits for randomization will be kept confidential until the exact moment the experiments begin. The research consists of signing the informed consent form and conducting a clinical evaluation to analyze the inclusion/exclusion criteria. Patients will be randomized into two protocols, with an equal number of participants: PE and PC. Afterward, they will perform the one maximum repetition test (1RM) to define the load to be used in the PE. After 72 hours, the study protocols will be carried out. Capillary blood glucose and clinical BP measurements will be taken before each session, immediately after, and at intervals of 15 minutes up to 60 minutes after the end of the protocols. After 24 hours, blood glucose and blood pressure will be collected in individuals who underwent PE and allocated to PE and vice versa, characterizing the crossover design.

Anthropometric Assessment

The BMI assessment, a crucial part of this study, will be conducted with precision. We will use a stadiometer graduated in centimeters and with an accuracy of 1 mm, Sanny (american medical do brasil ltda-São Bernardo do Campo, São Paulo, Brasil), for height identification. For body mass, we will rely on an electronic scale, with an accuracy of 0.05 kg, made by Welmy (Welmy - industry and commerce - Santa Barbara do Oeste, São Paulo, Brazil). The BMI classification will adhere to the standards set by the World Health Organization (1995).

The measures
Measurements of the primary (capillary blood glucose) and secondary (clinical BP) outcomes will be performed at six moments. Patients will arrive at the gym to carry out the protocols and will rest in a seated position for 10 minutes to carry out the Pre-Protocol measurement (M1); they will carry out the protocols immediately after finishing the protocols (M2); And in 15 minutes (M3); 30 (M4); 45 (M5) and 60 (M6), post protocols, measurements will also be taken to measure capillary blood glucose; After 24 hours of measurement M1 (pre-protocol), a new collection will be carried out (M7).

**Blood glucose**

Capillary blood glucose will be measured using the Accu-Chek go brand and model, Roche Group, Germany, which allows the glucose level to be checked directly by aspiration of capillary blood using the reagent strip. To this end, the researcher will measure blood glucose on the index fingers, who will be adequately equipped with the appropriate personal protective equipment: lab coat, gloves, and glasses. The finger to be collected will be cleaned using cotton wool with 70% alcohol. Afterward, there will be lancing with a single-use disposable lancet of the same brand, which will be immediately discarded in the trash to dispose of sharps (discard pack). Then, the researcher will apply light pressure on the lanced finger until a drop of blood comes out and will bring the reagent strip into contact with the reagent strip to aspirate the blood, where a chemical reaction and analysis of the glucometer will occur, which will generate the value glycemia in mg-dL. The tape and cotton will then be disposed of in specific waste bins.

**Blood pressure**

The clinical assessment of BP will occur following the regulations of the Seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure\(^4\) with the individual seated, using a semi-automatic device brand and model Omron HEM 742 (cirurgica Rio de Janeiro LTDA - Rio de Janeiro, Rio de Janeiro, Brazil). BP will initially be measured in pre-study evaluations in both arms, adopting the side with the highest value for research purposes. Two measurements will be taken at each time of the study, 2 minutes apart, and their average will be taken.

**Intervention Session**

The training and control session, a pivotal part of our study, will be held at the Bluefit Academy. The academy is conveniently located at Anápolis (GO), Brazil. Both groups will receive comprehensive nutritional guidance, including instructions on healthy nutrition and other recommendations, prior to the study. This detailed information will help all stakeholders feel prepared and informed.

**Experimental Protocol**

The EP will be held at the Bluefit Academy, where all the equipment for the strength exercise session is presented. After the patients arrive, they will rest in a calm and comfortable place, sitting for 10 minutes to measure blood glucose and blood pressure. They will then perform the EP, consisting of 5 minutes of joint warm-up on three machines, 15 repetitions at 50%1RM. Then they will perform the central part, which will consist of 6 different exercises: front pull; bench press on the machine; biceps curl; leg press on the machine; knee extension sitting on the machine (extension chair); calf press, divided into
three series consisting of 8-10 repetitions with 2-minute breaks between series and exercises. All participants will be discouraged from using the Valsalva maneuver.

After the end of the protocol, patients will be transferred to a quiet place, where their blood glucose and blood pressure will be measured immediately in a sitting position. They will remain seated in the same place for 60 minutes to successively record blood glucose and blood pressure, at 15-minute intervals.

Control Protocol
The CP will also be carried out in the gym where the PE was carried out, and participants will not perform any physical exercise for a period similar to the PE, around 45 minutes. During the CP, individuals can stand, sit, talk, and hydrate, but exercise and food intake will be prohibited. At the end of the 45 minutes, patients will sit down for successive blood glucose and blood pressure measurements at 15-minute intervals.

Analysis and Statistics
The collected data will be tabulated in the Microsoft Excel program and analyzed using the Statistical Package of Social Science – SPSS, version 19.0 (Chicago, IL, USA). The Shapiro-Will test will be used to verify whether the numerical data presented a normal distribution. The Student’s T Test will be used for paired samples in intragroup assessments, comparing pre- and post-protocol moments, for each of the outcomes analyzed: BP and blood glucose. For intergroup assessments of the pre, immediately after, 15’, 30’, 45’ and 60min post moments, analysis of variance (ANOVA) will be used followed by Bonferroni post-hoc. The Wilcoxon test will be used for data that do not present a normal distribution. All analyzes will be carried out by intention to treat and the significance level adopted will be p<0.05.

EXPECTED RESULTS
The present project presented some limitations due to the process of executing the data collection stage. Based on the articles in this review, exercise benefits both people with type 1 and type 2 diabetes mellitus. However, it is necessary and fundamental to motivate the patient to exercise and maintain the reduction of acute hypoglycemia along with blood pressure control.

DISCUSSION
Both resistance exercise and Pilates have been proven to empower individuals with type 1 diabetes, aiding in their metabolic and clinical control. The effects of these activities, when combined with adequate nutrition and amino acid supplementation, not only reduce the risk of secondary diseases but also preserve vital functions in these patients, instilling a sense of control and hope. Engaging in physical activity not only reduces the need for hypoglycemic drugs and improves metabolic control but also aids in weight loss for obese patients. This reduction in weight significantly reduces the risk of cardiovascular diseases, thereby improving the quality of life of these patients. These positive outcomes should encourage healthcare professionals and researchers. Another study presented similar results, finding that there were improvements in glycemic control, regardless of the type of physical exercise.
Regular physical exercise, particularly intermittent exercise, significantly reduces the risk of acute hypoglycemia. The forecast shows a glycemic drop between 36 + 14.4 mg/dl to 90 + 9 mg/dl, with percentage values between 18.18% and 54.05% induced by physical exercise. This data should reassure healthcare professionals and individuals with type 1 diabetes about the effectiveness of physical exercise in managing their condition\(^\text{(18)}\). A study concluded that physical exercise can change blood fat levels, increasing levels of “high-density lipoprotein” (HDL) and reducing total cholesterol levels, improving the level of “low-density lipoprotein” (LDL). It is extremely important for people with diabetes due to the high risk of cardiovascular diseases. This is justified by the fact that physical exercise uses a quantity of glucose used in cells, reducing its concentration in the blood\(^\text{(19)}\).

The literature systematically finds strength and aerobic training as a non-drug treatment as a fundamental strategy for reducing systemic arterial hypertension and maintaining the cardiovascular system, as well as controlling the percentage of fat and other physical functions, whether acutely or chronically\(^\text{(20)}\). All studies that proposed some type of physical activity as a form of intervention, whether aerobic exercise or resistance training, showed that carrying out at least three weekly sessions was sufficient to achieve satisfactory results for BP control\(^\text{(21)}\).

Resistance training is a fundamental factor in controlling systemic blood pressure as much as the use of antihypertensive drugs. Therefore, strength exercises must be included in a plan to increase the possibility of controlling blood pressure levels, as they are a non-pharmacological strategy\(^\text{(22)}\). Exercise applied effectively provides older people with effective treatment against increased blood pressure, including improving quality of life. He also concluded that, as it is not a non-pharmacological treatment, exercise, in turn, can stabilize both diastolic and systolic pressure\(^\text{(23)}\).

Regarding the type of physical activity practiced, aerobic training has been strongly recommended to reduce blood pressure, potentially improving peripheral vascular resistance, such as central arterial compliance. High-intensity interval training, popularly known as HIIT, is equal to or superior to moderate-intensity continuous training and is considered efficient as an aerobic modality. Furthermore, patients have a significant adherence rate to HIIT. No differences were found between HIIT and MICT in reducing diastolic or systolic blood pressure in hypertensive and pre-hypertensive individuals. However, in the nighttime measurement of diastolic blood pressure, there was a vital reduction when HIIT was practiced\(^\text{(24)}\).

**Final considerations**

It is concluded that regular physical activity is considered a preventive approach and a type of first-line non-pharmacological treatment for diabetes and high blood pressure. In short, it is noted that, regardless of the type of physical exercise practiced, there is a reduction in cardiovascular risk, blood pressure values, and glycemic values, in addition to avoiding decompensation of comorbidities. Clearly, there are still gaps in knowledge, and more studies are needed that involve working with trained or untrained individuals to verify hypotensive effects on them, in addition to pharmacological or nutritional monitoring of the individuals.
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