Case Report

A Case Report on Exercise and Type II Diabetes Mellitus: Can We Still Be Amazed?

Um relato de caso sobre exercício físico e Diabetes Mellitus Tipo II: ainda podemos nos surpreender?

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ABSTRACT | INTRODUCTION: Diabetes mellitus type 2 (DM2) is an independent risk factor for the development of cardiovascular diseases. Physical exercise is an adjuvant and effective therapy in the control of DM2, as it prevents functional decline, cardiovascular complications and improves quality of life. **OBJECTIVE:** To present the repercussions of a cardiovascular and metabolic rehabilitation program on glycemic control and functional capacity in a patient with DM2 and class III heart failure. **METHODS:** This is a case report that involved a 63-year-old woman, irregularly active, eutrophic, sarcopenic, hypertensive and with DM2 on insulin (NPH and ultra-fast) for 6 years, diagnosed with heart failure (HF) functional class III. Joins a supervised cardiovascular and metabolic rehabilitation program. Performs lipid profile, glycated hemoglobin, 6-minute walk test (6MWT), fasting glucose. During the session, capillary blood glucose, blood pressure (BP) and electrocardiographic tracing were monitored. The protocol consisted of stretching, neuromuscular exercises and a treadmill performed with a load of 12-14 on the Borg scale. The program lasted 16 weeks, being carried out twice a week totaling 80 min per session. **RESULTS:** There was an increase of 128.57% in the 6MWT (350 vs 800m). The glycated hemoglobin values before and after the training program were 12% -vs-7.5%; fasting blood glucose 346mg / dL-vs-105mg / dL; total cholesterol 158mg / dL-vs-108mg / dL; low-density lipoprotein (LDL) 95mg / dL-vs-58mg / dL; high density lipoprotein (HDL) 31mg / dL-vs-41mg / dL; triglycerides 115mg / dL-vs-97mg / dL and PA 185x95mmHg vs 139x85mmHg. At the end of the program, the use of subcutaneous insulin was withdrawn. **CONCLUSION:** The program proved to be adequate in improving submaximal functional capacity and in controlling plasma glycemic and lipid levels.

KEYWORDS: Metabolic syndrome. Cardiac rehabilitation. Blood glucose. Quality of life.

RESUMO | INTRODUÇÃO: O Diabetes mellitus tipo 2(DM2) é fator de risco independente para o desenvolvimento de doenças cardiovasculares. O exercício físico é uma terapêutica adjuvante e eficaz no controle do DM2, pois evita o declínio funcional, complicações cardiovasculares e melhora a qualidade de vida. **OBJETIVO:** Apresentar a repercussão de um programa de reabilitação cardiovascular e metabólica sobre o controle glicêmico e capacidade funcional em uma paciente com DM2 e insuficiência cardíaca classe III. **MÉTODOS:** Trata-se de um relato de caso envolvendo uma mulher de 63 anos, irregularmente ativa, eutrófica, sarcopênica, hipertensa e com DM2 em uso de insulina (NPH e ultrarrápida) há 6 anos, com diagnóstico de insuficiência cardíaca(IC) classe funcional III. Ingressa em programa de reabilitação cardiovascular e metabólica supervisionado. Realiza avaliação de perfil lipídico, hemoglobina glicada, teste de caminhada de 6 minutos (TC6), glicemia de jejum. Durante a sessão foi monitorizada a glicemia capilar, pressão arterial sistêmica (PAS) e o traçado eletrocardiográfico. O protocolo consistia em alongamento, exercícios neuromusculares e esteira ergométrica realizados com carga de 12-14 da escala de Borg. O programa durou 16 semanas, sendo realizado 2 vezes na semana totalizando 80 min por sessão. **RESULTADOS:** Houve acréscimo de 128,57% no TC6 (350 vs 800m). Os valores da hemoglobina glicada pré e pós-programa de treinamento foram 12%-vs-7,5%; glicemia de jejum 346mg/dL-vs-105mg/dL; colesterol total 158mg/dL-vs-108mg/dL; lipoproteína de baixa densidade(LDL) 95mg/dL-vs-58mg/dL; lipoproteína de alta densidade (HDL) 31mg/dL-vs-41mg/dL; triglicerídeos 115mg/dL-vs-97mg/dL e PA 185x95mmHg vs 139x85mmHg. Ao final do programa foi retirada a utilização da insulina subcutânea. **CONCLUSÃO:** O programa demonstrou-se adequado na melhora da capacidade funcional submáxima e no controle dos níveis glicêmicos e lipídicos plasmáticos.

PALAVRAS-CHAVE: Síndrome metabólica. Reabilitação cardíaca. Glicemia. Qualidade de vida.

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Introduction

Diabetes mellitus (DM) is the most prevalent metabolic syndrome in the world, with a projection of 592 million in 2035. In Brazil, more than 60% of deaths are associated with cardiovascular diseases, which warn of the importance of preventive measures, given the great social and economic impact generated by DM, including amputations, neuropathies, organ failure and the referred cardiovascular diseases[1,2]. Cardiovascular diseases represent the major cause of death in patients with type 2 diabetes mellitus (DM2) due to the unfavorable changes in blood glucose, insulin, lipid profile of these patients, as well as the association with systemic arterial hypertension (SAH) and inflammation[2].

One of the ways to control blood glucose levels is through drug therapy Biguanides, Insulin, Sulphonylureas and Meglitinides and others), but, the form of application and frequency represent one of the main complaints among patients[3]. Physical exercise, in turn, is an adjunctive and effective therapy in the control of DM2 because, in addition to preventing functional decline, it increases the body's sensitivity to insulin, prevents renal, cardiovascular, neuromuscular complications and improves quality of life[3,4].

Despite the recognition of the importance of physical exercise, as demonstrated by the Brazilian Diabetes Society, little has been reported about its potential effect in removing drug therapies with a structured and individualized cardiometabolic rehabilitation program[4,5]. Therefore, this case report presents the repercussions of a cardiovascular and metabolic rehabilitation program on the glycemic control and functional capacity of a patient with DM2 and class III heart failure.

Case description

The present case report was evaluated by the Ethics and Research Committee of the State University of Feira de Santana under the number 033/2011 (CAAE 0036.059.000-11) according CNS 196/96, current at the time.

Patient data

CLES, 65 years old, female, white, Brazilian, housewife, irregularly active through analysis by International Physical Activity Questionnaire (IPAQ) long version, body mass index of 20kg/m^2, diagnosed with Chronic Heart Failure (CHF), dyslipidemia and Systemic Arterial Hypertension (SAH) all 20 years ago. Did not perform intervention with exercise previously, only drug treatment. Joined the Cardiovascular and Metabolic Rehabilitation (CMR) service at the clinic ACTUS CORDIOS in August 2015, diagnosed with DM2 15 years ago, with fasting blood glucose 346mg/dL and Glycated Hemoglobin (HbA1c) of 12%. Using insulin (NPH and ultra fast) 6 years ago, Losartana (50mg) e Atorvastatina (20mg). As the patient reported tiredness due to light efforts, such as shopping or climbing a flight of stairs, CHF was functionally classified as grade III, by the responsible specialist. His main complaint, besides tiredness, was the daily use of subcutaneous insulin. In the family history, factors such as dyslipidemia, SAH and DM2 were found.

Upon physical examination, the suspicion of sarcopenia was identified, determined by the circumference of the calf (assessed value of 28cm; reference value of 33cm)[6]. Systemic arterial pressure (SAP) was measured with a littmann Classic III stethoscope and a Welch Allyn sphygmomanometer, model Durashock Ds44-br, obtaining the value 185x95mmHg and the patient used the medication on the days of the intervention, and continuously. Muscle strength assessed by the scale Medical Research Council (MRC) was grade 4 and in the 6-Minute Walk Test (6MWT) a value of 300m was obtained, below that predicted for age (502,5m) by the equation of Iwama et al.[7].

Prescription strategy

To assess the intensity of the physical exercise program, the Borg subjective perception scale was used (with measures ranging from 6 to 20 points)[8]. Before each session, the volunteer received instructions on the operation of the instrument and the objective of reporting the sensation of cardiorespiratory fatigue. The values of SAP, heart rate (HR) and capillary glycemia were measured respectively using the Littmann Classic III 5620 stethoscope and Welch Allyn Aneroid Sphygmomanometer, Durashock Ds44-br model, portable G-tech pulse oximeter Oled finger monitor and the One Touch Ultra Plus Flex blood glucose at the beginning, during and at the end of each session.

The program applied to the study consisted of resistance and cyclical exercises, performed twice a

week, lasting about 80 minutes in each session, during the period of four months. In the first month, only adaptive neuromuscular training was performed with two sets of 15 repetitions, with 2-minute intervals, two exercises for upper limbs (upper limbs): Direct curl for biceps and shoulder lift and two for lower limbs (lower limbs): Static walking with anklet and calf exercise, (with intensity between 9 to 11 on the Borg scale) and treadmill for 10 minutes at light intensity (Borg from 9 to 11).

From the second month, the sessions were held in order to increase muscle mass, therefore focusing on neuromuscular exercises with two sets of 8 repetitions with an interval of two minutes between sets for 4 multiarticular exercises divided into: bench press with alter and row for upper limbs and squat and static gait with ankle brace for lower limbs, performed on alternate days. Intensity determined for a Borg of 12 to 14.

From the second month on, the cyclic exercise on the treadmill was modified, being for 5 minutes at light intensity (Borg from 9 to 11) plus 10 minutes at moderate intensity (Borg from 12 to 14), ending with 3 minutes of cooling down in intensity regressive. At the end of each session, relaxation techniques with massage therapy were performed. The program had a weekly frequency of 2 days. The neuromuscular exercise loads and the treadmill speed were progressively adjusted in the other months of intervention, following the program prescribed according to the Borg scale.

Inspiratory muscle training (IMT) started to be performed from the third month, 30 repetitions, five times a week, at the clinic, under load at 30% of the maximum inhalation pressure assessed.

Results

After 16 weeks of CMR, there was a reduction of 70% in fasting glycemia and 37.5% in HbA1c, showing control of glycemic levels including postprandial. Concomitantly, we observed 128% improvement in functional capacity assessed using the 6MWT, as shown in Table 1.

Table 1. Variables Comparison before and after 16 weeks of intervention through a cardiovascular and metabolic rehabilitation program for DM2

Variables	Pre-CMR	Post-CMR	% of Improvement	Normality value
HbA1c (%)	12	7,5	37,5	5,6#
Fasting blood glucose (mg/dL)	346	105	70	<100#
Total cholesterol (mg/dL)	158	108	32	<200*
LDL (mg/dL)	95	58	61	<130*
HDL (mg/dL)	31	41	32	>60*
Triglycerides (mg/dL)	115	97	16	≤150*
SAP (mmHg)	185	139	25	<140*
DBP (mmHg)	95	85	5	<90*
6MWT (metros)	350	800	128	502,5$

HbA1c - Glycated hemoglobin; HDL - High density lipoprotein; LDL - Low density lipoprotein; DBP – Diastolic Blood Pressure; SBP - Systolic Blood Pressure; CMR - Cardiovascular and Metabolic Rehabilitation; 6MWT - 6-minute walk test. # According to the American Diabetes Association Guideline [9]; * According to the update of the Brazilian Dyslipidemia and Atherosclerosis Directive -2017[10] $ According to the equation of Iwama *et al.*, [7]

The CMR program also enabled the reduction of drugs administered to control dyslipidemia and SAH, as well as the use of subcutaneous insulin was withdrawn under the guidance of the endocrinologist, as shown in Table 2.

Table 2. Drugs used before and after the cardiovascular and metabolic rehabilitation program for DM2

Drugs	Pre-RCVM	Post-RCVM
Atorvastatin	1x per day (80mg)	1x per day (10mg)
Isosorbide Monohydrate	2x per day	1x per day
Lantus Insulin (slow action - 24 hours)	1x per day	Removed
Apidra Insulin (ultrafast)	3x per day	Removed

CMR - Cardiovascular and Metabolic Rehabilitation.

Discussion

This case report demonstrated that an CMR program was able to improve glycemic control leading to a reduction in the amount of drugs, an increase in functional capacity and an improvement in the lipid profile and a reduction in SAP in a patient with DM and CI class III.

The beginning of the use of the device for inspiratory muscle training occurred late due to the delay in the delivery of the equipment, even so, the results were satisfactory and raise gaps about how extensive the benefits of physical exercise can be when done in a personalized way for each patient. Still in this sense, the application of IMT is a great ally in rehabilitation for acting directly on the meta-reflex[11], therefore, we believe that the insertion of this strategy at the beginning of the program could have provided even better results in conditioning the patient. Clinical studies of cause and effect have pointed out that physical exercise is an important therapeutic resource for glycemic control in diabetics[12,13]. According to the study by Chibalin et al.[12] exercise increases the expression and action of insulin receptors (IRS-1 e IRS-2) present in the plasma membrane of striated muscle cells (skeletal and cardiac). Insulin is the hormone responsible for initiating the signaling of the intracellular translocation of glucose-carrying proteins (GLUTs) into the sarcolemma. GLUT-4, present in striated muscle cells, is responsible for the process of facilitated diffusion of blood glucose into muscle cells and its production is also induced by exercise[12,14]. Therefore, the increase in the expression and activity of insulin receptors, present in the sarcolemma, and the increase in the intracellular expression of GLUT-4, both promoted in a chronic way by physical exercise, contribute strongly to improve the glycemic metabolism in patients with diabetes mellitus[15].

In the study of Andrade et al.[4] it was found that a 12-week cyclic aerobic training program promoted significant effects in reducing postprandial glycemic levels and glycated hemoglobin in patients with DM2. However, these effects were visible in the long term, from the 8th and 12th week, showing that the benefits from physical exercises are substantially acquired after 2 or 3 months, reinforcing the importance of regular training programs for prevention and treatment of DM2.

However, the effect of physical exercise goes beyond the balance of insulin action, since GLUT-4 translocation also occurs through the release of calcium from the sarcoplasmic reticulum during muscle contraction, a mechanism that is not dependent on insulin and that lasts for up to two hours post-exercise. There is also evidence in studies of Lima[16] e Junior et al.[17] that physical exercise stimulates the production of autocrine and paracrine substances, such as kallikrein, adenosine and nitric oxide, which also promote signaling for GLUT-4 translocation. Thus, the effect of exercise is not restricted only to patients who have normal insulin production (like most patients with DM2), but also to those with decreased or absent production, as in type I diabetes mellitus[17].

Deepening this discussion about the non-insulin dependent mechanisms, we remember that at rest, part of GLUT-4 remains stored in vesicles and its translocation through exercise has a more prolonged effect by increasing the rate of exocytosis and attenuating the endocytosis of this protein. Signaling can occur via phosphorylation of protein kinase activated by adenosine monophosphate (AMPK), which is stimulated by liver kinase B1 (LKB1), expressed with the change in the cell balance between adenosine monophosphate (AMP) and adenosine triphosphate (ATP), increase and decrease respectively during the year. From the activation of AMPK some axes can determine the transport of GLUT-4 to the periphery, such as the decrease in the activity of proteins that prevent the vesicular release of GLUT-4 (mediated by the GLUT-4 stimulating factor), activation of the AS160 protein which signals the Rab-GTP protein to initiate transport. Another function of AMPK is linked to the increase in GLUT-4 gene expression, with a consequent increase in the amount of available carrier proteins[18].

It is important to note that an CMR program contributes not only to the biological mechanisms promoted by physical exercise, but also to the pleiotropic factors, such as decreased anxiety and emotional stress and better dietary control, which consequently influence the results of the CMR[19]. Finally, the sum of these mechanisms (biological and pleiotropic), can reduce or even abolish the use of drugs by many of the patients, as was observed in this report, which directly implies the cost-benefit ratio of CMR and the improvement of quality of life observed in patients included in these programs.

Conclusion

The results described in this case report showed that a cardiovascular and metabolic rehabilitation program was able to modify glycemic levels, dispensing with the use of subcutaneous insulin and promoting improved functional capacity in a patient with heart failure and type 2 diabetes mellitus.

Author contributions

Cerqueira DGLES, Oliveira IM, Petto J conceived and designed the study. Cerqueira DGLES, Oliveira IM, Jesus TC, Petto J. analyzed and interpreted the data. Cerqueira DGLES, Sacramento MS, Santos VR, Jesus TC, Petto J wrote the manuscript. Sacramento MS, Petto J critically reviewed the manuscript for important intellectual content.

Competing interests

Dr. Petto, Dr. Cerqueira and Dr. Sacramento inform having received fees from ACTUS CORDIOS, not related to this report. No financial, legal or political conflicts involving third parties (government, companies and private foundations, among others.) have been declared for any aspect of the submitted work (including, but not limited to, grants and funding, participation in advisory council, study

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