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Chapter

Cardiovascular and Biochemical Responses in Exercise Recuperation in Diabetic Rats

Luiz Augusto da Silva, Jéssica Wouk and Vinicius Muller Reis Weber

Abstract

The objective of this study was to assess the cardiovascular and biochemical responses during aerobic exercise recuperation in diabetic rats. There were utilized 12 animals, of 60 days, divided in two groups: control and diabetic. On the test day, the animals performed a 60 minutes' session of predominantly aerobic exercise, using an overload of 6% of their body's weight. After and before the exercise, the animals had their systolic blood pressure (SBP) and heart rate (HR), lactate, glycerol and glucose measured. The animals were trained during 30 days by swimming tank, with an extra weight equivalent to 4% extra weight a 40-min session. A decrease in glucose value occurred in the diabetic animals after exercising, as well as an increase of lactate in the same group. 1', 3', 5' and 7' after the exercise, a significant reduction of HR in the diabetic group was noticed when compared with the control group, such behavior was also observed with double product (DP) together with SBP values 1', 3' and 5' after the exercise. The diabetic animals' recovery has been possibly affected by a reduction of blood flow and a reduction of energetic substrates contribution, as well as lactate clearance.

Keywords: exercise, glycemia, recuperation

1. Introduction

Diabetes mellitus (DM) is a complication that triggers problems to public health all around the world [1]. It most frequently type, diabetes mellitus type 2 (T2DM), face to hyperglycemia impact, may evolve to cardiovascular, neuromuscular and degenerative complications [2], being able to rise considerably the morbidity and mortality [3].

During DM complications' evolution, cardiac dysfunctions or diabetic cardiomyopathies occur, independent of the presence of vascular diseases, arteriosclerosis or heart attack [4, 5]. The development of diabetic condition alters the hemodynamic balance and, as a consequence, triggers a reduction of physical capacities of the organism [6, 7].

With regard to the muscular system, a good functioning of it causes the action of insulin which connects itself to its receptor leading to the phosphorylation of its tyrosine receptor to the substrate of the insulin's receptor (IRS-1 and 2). IRS-1 and 2 mediate the effects over glucose metabolism, through the activation of

phosphatidylinositol (PI)-3 kinase, PKA/AKt and the increase of glucose transporter type 4 (GLUT4), from intracellular compartments into plasma membrane. However, the non-functioning of the insulin's receptor with its respective hormone cause its resistance over the cell, in that way, glucose metabolism does not occur [8, 9], what entails blood's hyperglycemia and fatigue of the skeletal muscle involved.

It is well accepted that physical exercise may be related to the enhancement of insulin sensibility, GLUT4 expression and to the glycogen synthase enzyme activity in muscular cells of patients with DMT2, and that this stimulus may remain for up to 48 h [10, 11]. The physical exercise causes important changes in glucose homeostasis, actuating in specific proteins such as adenosine monophosphate-activated protein kinase (AMPK) that assists in the stimulus of liberation of glucose transporter 4 (GLUT4) of its cellular vesicles, in order to actuate in the glucose's input in the cell [12]. In this way, the exercise might rapidly decrease the glucose level in hyperglycemia condition.

There is the necessity of comprehending the way in which physical exercise may act in the physiological behavior of the organism, and the cardiovascular and biochemical responses bring along directions to understand how the organism reacts to physical exercise, in detriment of training variables as volume and intensity. In this way, the objective of this study was to evaluate the cardiovascular and biochemical responses during the recovering of aerobic exercise in diabetic rats.

2. Material and methods

2.1 Animals

Twelve male Wistar rats at 60 days of age were used in the study. The animals were kept in cages with controlled temperature (23 ± 2°C) and humidity (55 ± 10% humidity), and a light/dark cycle of 12 h. This study was approved by the Ethics Committee of research studies using animals (015/2015 Protocol).

2.2 Diabetes induction and experimental design

The animals were divided into two groups: [1] control (weights of 393 ± 44 g), [2] diabetic (weights of 308 ± 40 g). Alloxan (ALX) (Sigma, St. Louis, USA) dissolved in sodium chloride solution (0.9%) was administered intraperitoneally (ip) (120 mg/kg), after 12 h of fasting. Rats with fasting BG values between 150 and 250 mg/dL were considered diabetic. With 90 days old, the animals were submitted to an oral glucose tolerance test (OGTT) to verify their glycemic curve. Thus, a maximal exercise test (MET) was performed to evaluate the biochemical (glucose, lactate and glycerol) and cardiovascular (HR and SBP) responses before and after the exercise.

2.3 Effort exercise test and training

All animals were adapted to an aquatic environment to be able to swim during the test, through one daily session of 10 min, for 7 days prior to the experiment. On testing days, the animals performed a 60-min session of predominantly aerobic exercise by carrying an extra weight equivalent to 6% of their body weight in a swimming tank with 40 cm in depth, 70 cm in diameter, and water heated to 30 ± 1°C, according to the protocol proposed by Gobatto et al. [13]

Post testing, the animals were trained during 30 days by swimming tank, with an extra weight equivalent to 4% extra weight a 40-min session, according to the

protocol modified proposed by Scariot et al. [14]. Exercise sessions and laboratory procedures were always conducted at the same time of the day (08:00 am).

2.4 Oral glucose tolerance test

Blood was collected from the tail vein in animals that fasted for 12 h to a posterior glucose analysis. These animals subsequently received one single dose of glucose (1 mg/kg of body weight) by gavage, and new blood samples were collected at times 30, 60, and 120 min. Blood glucose levels were determined in a glucometer (Accu-chek Advantage®).

2.5 Biochemical analyses

Blood glucose, lactate, and glycerol doses were performed in a glucometer (ACCU-CHEK® Active®) using approximately 25 μl of blood collected through caudal puncture, before and after the effort test.

2.6 Cardiovascular analyses

Heart rate values (HR) and systolic blood pressure (SBP) were obtained using a tail plethysmograph that transmitted data to a software that codified the results (Insight®, Ribeirão Preto, Brazil). In order to adapt animals to this device, it was attached to animals' tails three times a day for 5 days before the test. On test day, HR and SBP were obtained in triplicate for all animals, by the same evaluator, before and after treatments and prior to exercise. The Double Product index was used as an indirect indicator of the cardiac work, calculated through the formula:

$$DP = \text{Systolic pressure} \times \text{Heart rate} \quad (1)$$

2.7 Statistical analyses

All results are presented as mean ± E.P.M. Statistical analysis was performed using a Student's t-test for unpaired sample or one-way ANOVA. Values were considered statistically significant based on $P < 0.05$. The post hoc Student-Newman-Keuls test was used, when appropriate, to identify differences between groups.

3. Results

3.1 Oral glucose tolerance test

Figure 1 represents the blood glucose values during OGTT of the rats from different groups. The glycemic curve was significantly higher to the diabetic group, when comparing with the values related to the controls and diabetes post trained groups at times 0, 30, 60 and 120 min.

3.2 Biochemical responses

Figure 2 represents the blood glucose values before and after exercise. The glucose values were significantly different between control and diabetes groups, and intragroup a significant reduction occurred to the diabetic group after exercising ($P < 0.05$). Furthermore, the glucose post training, pre and post exercise was smaller than the same diabetes group pre-training ($P < 0.05$).

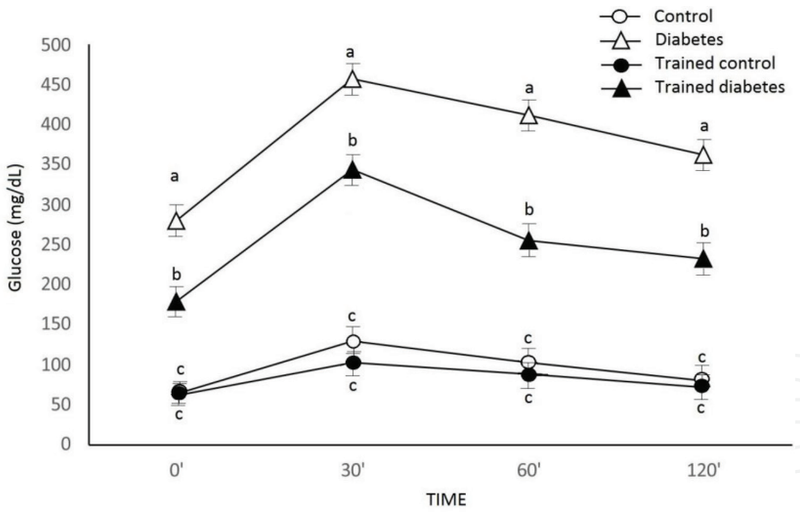

Figure 1.
Oral glucose tolerance test results of control and diabetes groups rats pre and post 30 days of training. The data represent the average ± E.P.M, n = 6, (a,b,c) difference letters = P < 0.05 (Student-Newman-Keuls after one-way ANOVA).

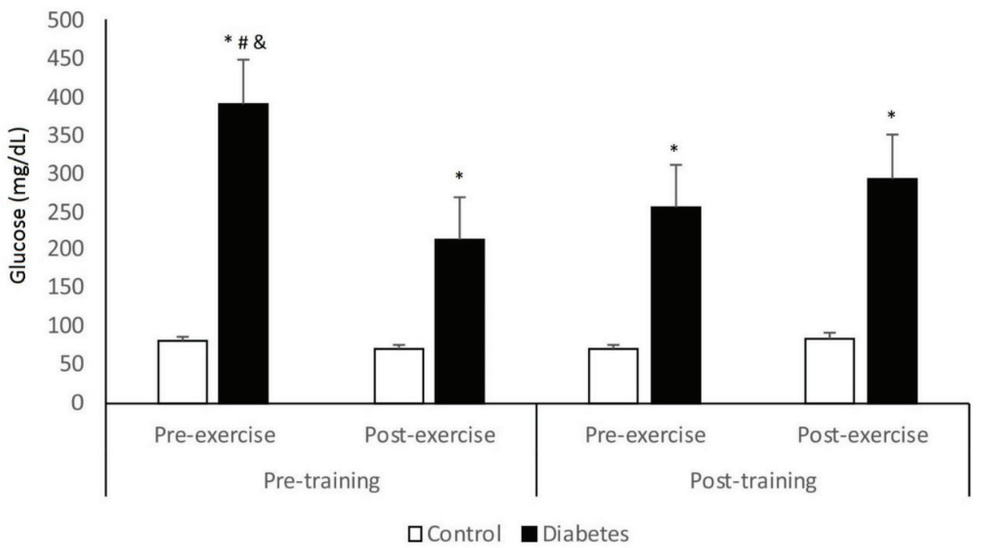

Figure 2.
*Plasma concentration of glucose levels before and after the exercise protocol and 30 days of training. The data represent the average ± E.P.M, n = 6, * = P < 0.05 when compared with the control group, # = P < 0.05 when compared with the same group, & = P < 0.05 when compared with the same group post-training (Student-Newman-Keuls after one-way ANOVA).*

Figure 3 represents the glycerol and lactate values before and after exercise. No difference was observed in glycerol values between groups. Concerning the lactate values, a significant difference occurred between groups, both for pre and post-training and diabetes pre-training groups.

3.3 Cardiovascular responses

Figure 4 represents the HR, SBP and double product in rats of different groups. No statistical difference was noticed concerning the hemodynamic measures during resting. 1, 3, 5 and 7 min after the exercise, a significant reduction of HR in the diabetic group was noticed when compared with the control group, such behavior was also observed with DP together with SBP values 1, 3 and 5 min after the exercise. After 30 days of training, the diabetes and control groups maintained their HR similar between the time of 1, 4, 5 and 7 min, being that they were different

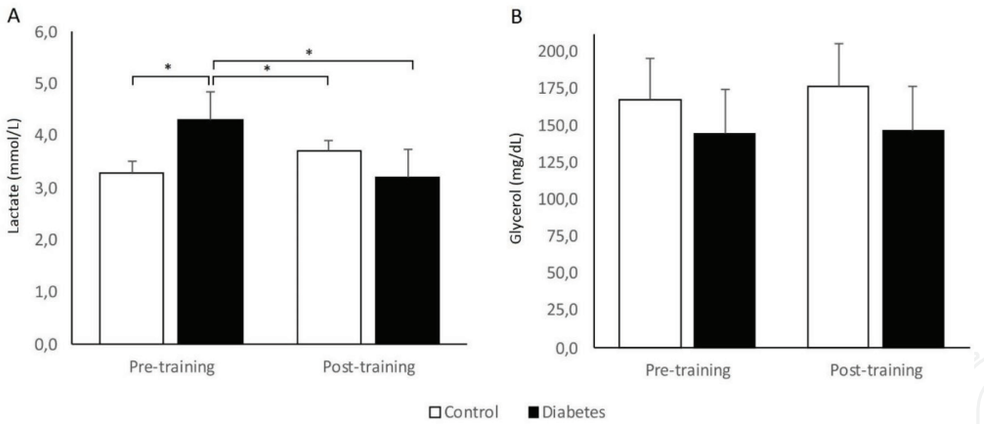

Figure 3.
*Plasma concentration of (A) lactate and (B) glycerol levels after the exercise protocol pre and post 30 days of training. The data represent the average ± E.P.M, n = 6, * = P < 0.05 when compared with the control group, # = P < 0.05 when compared with the same group (Student-Newman-Keuls after one-way ANOVA).*

from their respective groups before the training. Significant reduction of SBP and DP values was observed for the control group after training compared to the same group ($P < 0.05$). The diabetic groups did not show significant differences.

4. Discussion

This study demonstrates that the HR analysis post-exercise presents intensity and performance information as well as the physical condition of the organism. The relation between the recuperation time and HR must be characterized, investigated and explained in order to obtain a better understanding of the whole picture, in other words, the clinical condition or hemodynamic/metabolic balance to the exercise with the intensity in question.

The HR revealed a better recuperation in the diabetic animals, what may be related to the quantity of muscle present in these animals. According to Polito and Farinatti [15], this happens because in dynamic exercises, a greater volumetric load occurs in the left ventricle and the cardiac and hemodynamic responses are proportional to the intensity and to the muscular mass involved in this activity. In this case, this event would trigger a reduction of muscular mass in these animals due to the metabolic deregulation and consequent atrophy displayed in this clinical condition related to the diseases [16].

The lactate increased after exercise in diabetic animals compared to the healthy ones, what would have related to the muscular metabolic capacity, because with a smaller consumption of glucose due to its reduced input in the muscle, the utilization of existent substrates or reutilization of resulting metabolites that derive lactate is necessary [17], in this situation, a better recuperation and a greater lactate removal from bloodstreams occurs, that demonstrates a better capacity of the animal to face physical stress.

The heart of a patient with a diabetic condition has lower metabolic capacity because the main glucose capturer in cardiac muscle is also GLUT-4 [17], tending to have a lower response to recuperation after exercising due to the minor consumption of glucose. Some conditions associated with this response, such as the metabolic acidosis, general fatigue and reduction of neuronal function are due to hyperglycemia [18], causing a reduction of prompt reply to exercise in the body's systems.

Although this phase of exercise may be starting to be investigated, the results still diverge about the necessary time to a total restoration to the rest levels after exercise, and the autonomic nervous system (ANS) might be involved in this event

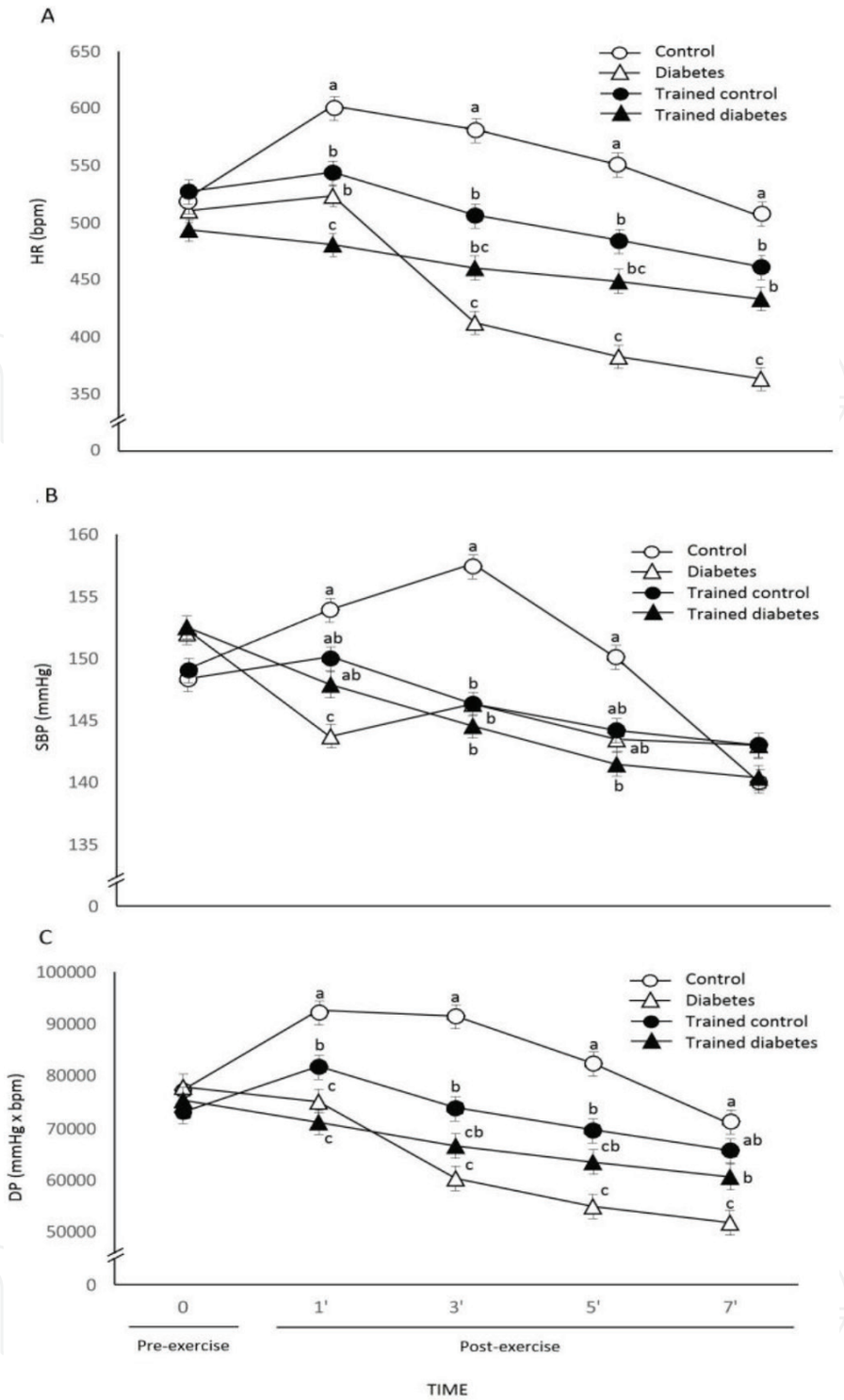

Figure 4.
Heart rate (A), systolic blood pressure (B), and double product (C) pre and post exercise in control and diabetes group rats pre and post 30 days of training. The data represent the average ± E.P.M, n = 6, (a,b,c) difference letters = P < 0.05 (Student-Newman-Keuls after one-way ANOVA).

[19–21]. The time spent to the HR to return to resting levels depends on the interaction between the autonomic functions, the level of physical conditioning and the exercise intensity as well [22]. Evaluation post-effort show a hypotension after exercise in a gradual way, as it can be observed in the healthy animals [23]; however, the ANS reduced the resting values of the diabetic animals, demonstrating a failure in the hemodynamic involvement to a muscular recuperation and a desirable lactate removal, what could be hindered with the reduction of the bloodstream [24] due to the diabetic condition, demonstrating that after exercise complication are visible.

What must be observed is the recuperation of the diabetic animals that was harmed by a possible reduction of bloodstream, a reduction in the contribution of energetic substrates, as well as a lactate removal, that demonstrate the effects of the diseases upon the organism. This information demonstrates how homeostasis is unregulated due to a clinical condition that triggers complications in many tissues of the body. Yet, if the progression of the disease is slow, the complication of diabetes would also be reduced and the beginning of its limitations in tissues could be prevented or eliminated.

In this way, exercise is an important tool to glucose control for the animals because it may enhance systems that are essential to metabolic balance, such as the skeletal muscle, which has an important function in the movement, increasing the physical capability of the organism to resist to situations that aim to adapt the tissues to a better function.

5. Conclusion

This chapter showed which diabetic animals' recovery has been possibly affected by a reduction of blood flow and a reduction of energetic substrates contribution as well as lactate clearance. This information demonstrates how homeostasis is dysregulated due to a clinical condition that triggers complications in several body tissues.

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Declaration of interest

There are no issues to disclose. There is no potential conflict of interest with the mentioned trademarks.

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