Original Article (short paper)

Glycemic behavior in patients with type 2 diabetes during a short period of a combined training program

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Abstract — Aim: The present study investigated the behavior of glycemia in subjects with type 2 diabetes (T2DM) during 36 sessions of a combined training program. **Methods:** This is a single arm clinical study with 20 patients with T2DM submitted to combined exercise training (strength and aerobic exercise). The sessions occurred on alternate days, 3x/week, lasting ~ 80 minutes, totaling ~ 240 minutes/week, for 12 weeks, over a total of 36 sessions. Capillary glycemia was measured before and 10 to 15 minutes after the end of each combined exercise session. **Results:** There was a significant reduction ($p<0.05$) in glycemia after application of the combined training program in 27 (75%) of the 36 sessions. Regarding the maintenance of this reduction after about 48 hours, no significant differences were identified ($p>0.05$). When investigating the cumulative effect of the 36 sessions of combined training program on capillary glycemia, no significant differences were observed ($p>0.05$). **Conclusion:** Glycemia exhibits a behavior of reduction immediately after concurrent strength and aerobic training programs in patients with T2DM. However, the immediate reduction of glycemia is not maintained until 48 hours, nor is there a cumulative effect of the 36 training sessions on baseline glycemia.

Keywords: concurrent training program; diabetes mellitus; glycemic control.

Introduction

The literature is robust regarding the practice of physical activities for the management of patients with diabetes mellitus, especially type 2 diabetes mellitus (T2DM) [1,2]. The positive effect of physical activity programs can be identified by the improvement in glycemic control according to the glycated hemoglobin (HbA1c) exam, since glycemia is evaluated over a long period, reflecting the glucose concentrations within of the last 120 days [3].

It is already well established that both types of physical exercise, i.e. aerobic and strength, bring innumerable benefits to patients with T2DM [4,5], such as increased maximal oxygen utilization (VO_2max) and cardiopulmonary fitness, as well as peripheral adaptations, represented by the increased transport and oxidation of fatty acids, improved capillary density [6] and mitochondrial capacity [7].

Additionally, combined training has shown positive results for glycemic control, as seen by HbA1c analysis [2,8]. However, it is known that hyperglycemic peaks experienced on a day to day basis and between physical training sessions have been strongly associated with the development of diabetes complications [9], regardless of the values of fasting glycemia and HbA1c [10]. In this sense, little is known about the effects of successive physical training sessions, especially of the programs that combine strength and aerobic in the same session, on the capillary glycemia of patients with T2DM. In view of the above, the present study investigated the behavior of glycemia in subjects with T2DM during 36 sessions of a combined training program.

Methods

Design

This is a single arm clinical study, an analysis of secondary data from Bassi et al.[2], which was registered in the Brazilian Registry of Clinical Trials (protocol RBR-492q8z). In addition, the study procedures were approved by the Research Ethics Committee of the University Center of Araraquara (protocol 1318/11). In this sense, individuals with a clinical diagnosis of T2DM according to the Brazilian Society of Diabetes [3] were interviewed and evaluated, considering the inclusion and exclusion criteria of the study.

Participants

Participants were recruited through advertisements in newspapers, local magazines and flyers. All those who

responded to the advertisements were prescreened by phone to confirm interest in, followed by in person with the aim of verifying the criteria of eligibility for, the study prior to clinic-based enrollment visits. All of the enrolled subjects provided written informed consent. Participants with T2DM, of both sexes, were recruited to this study. Of these, 20 subjects agreed to participate in combined physical training, consisting of strength and aerobic exercise.

Sample size was calculated based on a previous study by Mikus, Oberlin, Libla, Boyle, Thyfault[11]. Sample size was determined using Ene Software, version 3.0 (Autonomous University of Barcelona, Spain), considering a significance level of 0.05 and a power of 0.80. We considered for the calculation the difference between the mean of 0.3 mmol/L and the standard deviation of 0.4 mmol/L. Based on these criteria, at least 16 participants were necessary.

The inclusion criteria were: 1) individuals with T2DM with a sedentary lifestyle for at least 6 months according to the American Heart Association criteria [12]. The exclusion criteria were: 1) a confirmed diagnosis of any heart disease, 2) uncontrolled hypertension, 3) any musculoskeletal disorders, 4) any confirmed diagnosis of respiratory disease, and 5) confirmed autonomic neuropathy.

All participants were instructed to maintain their usual medical care and received dietary advice on healthy eating by a nutritionist; however, there was no specific dietary intervention with regard to eating habits.

Strength and endurance training program

Combined exercise training consisted of individually supervised sessions under the supervision of exercise specialists. Sessions occurred on alternate days, 3x/week, lasting ~ 80 minutes, totaling ~ 240 minutes/week, for 12 weeks, over a total of 36 sessions.

The sessions included: 1) 5 min warm-up; 2) combined training protocol for 60 min; and 3) 5 min of cool-down. The determination of the loads for the 1 repetition maximal test (1RM) was applied, gradually increasing the resistance until the volunteer could perform no more than one repetition [13]. The equipment was familiarized by the individuals, for three previous sessions of the 1RM determination. The order of training was alternated with each session, meaning that the aerobic training was followed by strength training in the first session, and in the next session the strength training was followed by aerobic training; this was in order to avoid any bias.

The aerobic training was performed with heart rate corresponding to 60-70% of peak VO_2 for a period of 30 minutes per session on a stationary bicycle [14]. Strength training was performed with the intensity of 60-80% of 1RM, as recommended by the American College of Sports Medicine [12,15]. The program consisted of eight strength exercises, with the major muscle groups being worked out, as recommended by the American Diabetes Association [16]. The subjects performed four exercises for the upper limbs: biceps with free weights, seated paddling, triceps and supine; and four exercises for the lower limbs: leg press, extensor chair, calf, and flexor chair. Each exercise consisted of three sets of 10-12 repetitions. The amount of weight lifted was progressively increased at each session in order to maintain consistent repetitions, that is, with correct and complete movements during the training program. A rest period of 2-3 minutes between the sets was performed allowing maximum muscle recovery.

Capillary glycemia

Capillary glycemia was measured before and 10 to 15 minutes after the end of each combined exercise session using an Accu-Chek Active portable gauge (Roche Diagnostics GmbH, Mannheim, Germany), according to the manufacturer's instructions. If the blood glucose was >13.9 mmol/L (or 250 mg/dL) before starting the exercise, the session would be cancelled, and if it was >13.9 mmol/L more than twice in one week, the patient would be referred for a medical visit.

Statistical analysis

Initially, the normality of the data was verified by means of histograms. After normal distribution was determined, the comparisons between glycemia values throughout the 36 treatment sessions were performed using the repeated measures analysis of variance (ANOVA) post hoc Bonferroni. Data processing was performed in SPSS, version 17.0 (Chicago, IL, USA), assuming a significance level of 5%.

Results

Table 1 shows the anthropometric and sociodemographic characteristics of the sample. Regarding the comparisons between training sessions, as shown in Table 2, there was a significant reduction ($p<0.05$) in glycemia after application of the combined training program in 27 (75%) of the 36 sessions. In addition, HbA1c also showed significant reduction after the training period, as shown in Table 2. Regarding the maintenance of this reduction after about 48 hours, Table 3 presents the blood glucose comparisons before each training session; no significant differences were identified ($p>0.05$). Finally, when investigating the cumulative effect of the combined training program on capillary glycemia, Table 4 presents the comparisons after each training session, and no significant differences were observed ($p>0.05$).

Table 1. Demographical and clinical characteristics for individuals with type 2 diabetes mellitus (T2DM) at baseline.

Variables	Mean (standard deviation)
Gender (F/M)	8/12
Age (years)	49.40 (5.54)
Weight (kg)	82.18 (18.88)
Height (cm)	1.68 (0.11)
BMI (kg/m2)	28.96 (5.13)
HbA1c Pre Training Period (%)	8.33 (1.69)
HbA1c Post Training Period (%)	7.30 (1.20)
Duration of T2DM (years)	5.70 (5.50)
Cholesterol (mg/dL)	195.00 (47.89)

Data are reported as means (SD). BMI: body mass index, HbA1c: Glycated haemoglobin.

Table 2 . Comparison of blood glucose values (mg/dL) before and after each session of strength and aerobic training program.

Session	Mean (SD)	MD (95% CI)	p value	Session	Mean (SD)	DM (95% CI)	p value
Pre 1st	197.04 (60.35)	44.64 (3.98, 85.29)	0.014*	Pre 19th	167.48 (54.68)	29.12 (-11.90, 70.14)	1.000
Post 1st	152.40 (55.86)			Post 19th	138.36 (37.96)		
Pre 2nd	181.48 (77.71)	34.96 (-5.10, 75.02)	0.277	Pre 20th	182.36 (55.79)	39.64 (3.42, 75.85)	0.014*
Post 2nd	146.52 (61.84)			Post 20th	142.72 (45.16)		
Pre 3rd	189.64 (59.25)	43.20 (8.00, 78.39)	0.003*	Pre 21st	176.64 (46.74)	44.56 (9.38, 79.73)	0.002*
Post 3rd	146.44 (47.67)			Post 21st	132.08 (34.17)		
Pre 4th	181.28 (69.76)	43.72 (6.55, 80.88)	0.005*	Pre 22nd	179.88 (52.87)	44.48 (6.19, 82.76)	0.006*
Post 4th	137.56 (52.58)			Post 22nd	135.40 (38.65)		
Pre 5th	181.36 (56.98)	47.36 (7.48, 87.23)	0.004*	Pre 23rd	191.04 (59.62)	54.00 (9.70, 98.29)	0.003*
Post 5th	134.00 (39.04)			Post 23rd	137.04 (32.54)		
Pre 6th	170.08 (54.43)	40.04 (12.26, 75.81)	<0.001*	Pre 24th	190.28 (67.36)	39.00 (0.41, 77.58)	0.043*
Post 6th	126.04 (45.25)			Post 24th	151.28 (57.64)		
Pre 7th	182.00 (78.47)	48.12 (-0.50, 96.74)	0.057	Pre 25th	175.48 (56.65)	39.40 (6.55, 72.24)	0.004*
Post 7th	133.88 (53.44)			Post 25th	136.08 (43.97)		
Pre 8th	179.16 (58.13)	44.16 (-2.58, 90.90)	0.105	Pre 26th	182.96 (58.49)	47.52 (7.05, 87.98)	0.005*
Post 8th	135.00 (41.92)			Post 26th	135.44 (44.05)		
Pre 9th	174.12 (55.38)	35.68 (-16.35, 87.92)	1.000	Pre 27th	196.76 (65.00)	52.76 (6.93, 98.58)	0.007*
Post 9th	138.44 (42.33)			Post 27th	144.00 (42.49)		
Pre 10th	179.32 (74.02)	45.40 (5.49, 86.20)	0.011*	Pre 28th	185.08 (50.61)	47.24 (0.26, 94.21)	0.046*
Post 10th	133.92 (45.80)			Post 28th	137.84 (37.18)		
Pre 11th	176.52 (51.43)	40.96 (0.30, 81.61)	0.045*	Pre 29th	187.52 (53.02)	48.52 (8.09, 88.94)	0.004*
Post 11th	135.56 (46.04)			Post 29th	139.00 (39.49)		
Pre 12th	185.24 (55.31)	45.48 (10.55, 80.41)	0.001*	Pre 30th	177.12 (52.44)	42.68 (2.65, 82.71)	0.021*
Post 12th	139.76 (42.08)			Post 30th	134.44 (36.44)		
Pre 13th	187.92 (51.61)	50.00 (12.62, 87.38)	0.001*	Pre 31st	166.20 (49.29)	31.16 (-9.91, 72.23)	1.000
Post 13th	137.92 (41.85)			Post 31st	135.04 (34.13)		
Pre 14th	176.96 (47.17)	44.44 (5.72, 83.15)	0.007*	Pre 32nd	190.48 (69.60)	51.52 (4.57, 98.46)	0.014*
Post 14th	132.52 (33.45)			Post 32nd	138.96 (46.20)		

Pre 15th	179.40 (44.68)	41.64 (7.61, 75.66)	0.003*	Pre 33th	184.04 (61.87)	44.92 (1.94, 87.89)	0.027*
Post 15th	137.76 (27.55)			Post 33th	139.12 (40.19)		
Pre 16th	172.80 (52.33)	35.32 (-9.70, 80.34)	0.906	Pre 34th	200.28 (71.56)	45.96 (6.14, 85.77)	0.007*
Post 16th	137.48 (41.62)			Post 34th	154.32 (48.66)		
Pre 17th	169.76 (43.76)	46.88 (-0.34, 96.10)	0.055	Pre 35th	188.52 (60.81)	47.80 (6.96, 88.63)	0.005*
Post 17th	121.88 (25.04)			Post 35th	140.72 (46.57)		
Pre 18th	182.32 (44.25)	47.44 (16.02, 78.85)	<0.001*	Pre 36th	191.44 (64.89)	44.24 (-1.45, 89.93)	0.076
Post 18th	134.88 (30.82)			Post 36th	147.20 (55.67)		

SD: Standard deviation; MD: Mean difference; CI: Confidence interval of difference; *Significant difference ($p < 0.05$, Repeated measures ANOVA post hoc Bonferroni).

Table 3. Comparison of blood glucose values (mg/dL) before each session of strength and aerobic training program.

Sessions	MD (95% CI)	p value
1st versus 2nd	15.56 (-41.19, 72.31)	1.000
2nd versus 3rd	-8.16 (-69.71, 53.39)	1.000
3rd versus 4th	8.36 (-37.08, 53.80)	1.000
4th versus 5th	-0.08 (-62.18, 62.02)	1.000
5th versus 6th	11.28 (-34.98, 57.54)	1.000
6th versus 7th	-11.92 (-69.81, 45.97)	1.000
7th versus 8th	2.84 (-45.70, 51.38)	1.000
8th versus 9th	5.04 (-50.92, 61.00)	1.000
9th versus 10th	-5.20 (-60.35, 49.95)	1.000
10th versus 11th	2.80 (61.33, 66.93)	1.000
11th versus 12th	-8.72 (-53.92, 36.48)	1.000
12th versus 13th	-2.68 (-54.96, 49.60)	1.000
13th versus 14th	10.96 (-44.40, 66.32)	1.000
14th versus 15th	-2.44 (-46.23, 41.35)	1.000
15th versus 16th	6.60 (-43.81, 57.01)	1.000
16th versus 17th	3.04 (-46.11, 52.19)	1.000
17th versus 18th	-12.56 (-55.00, 29.88)	1.000
18th versus 19th	14.84 (-24.45, 54.13)	1.000
19th versus 20th	-14.88 (-73.46, 43.70)	1.000
20th versus 21st	5.72 (-48.17, 59.61)	1.000
21st versus 22nd	-3.24 (-39.47, 32.99)	1.000
22nd versus 23rd	-11.16 (-61.98, 39.66)	1.000
23rd versus 24th	0.76 (-66.69, 68.21)	1.000
24th versus 25th	14.80 (-33.92, 63.52)	1.000
25th versus 26th	-7.48 (-49.21, 34.25)	1.000
26th versus 27th	-13.80 (-65.11, 37.51)	1.000
27th versus 28th	11.68 (-48.13, 71.49)	1.000
28th versus 29th	-2.44 (-42.78, 37.90)	1.000
29th versus 30th	10.40 (-34.59, 55.39)	1.000
30th versus 31st	10.92 (-29.68, 51.52)	1.000
31st versus 32nd	-24.28 (-85.39, 36.83)	1.000

32nd versus 33rd	6.44 (-29.33, 42.21)	1.000
33rd versus 34th	-16.24 (-62.54, 30.06)	1.000
34th versus 35th	11.76 (-43.01, 66.53)	1.000
35th versus 36th	-2.92 (-58.54, 52.70)	1.000

MD: Mean difference; CI: Confidence interval of difference. No significant difference ($p > 0.05$, Repeated measures ANOVA post hoc Bonferroni).

Table 4. Comparison of blood glucose values (mg/dL) after each session of strength and aerobic training program.

Sessions	**MD (95% CI)**	**p value**
1st versus 2nd	5.88 (-34.23, 45.99)	1.000
2nd versus 3rd	0.08 (-42.89, 43.05)	1.000
3rd versus 4th	8.88 (-35.46, 53.22)	1.000
4th versus 5th	3.56 (-39.65, 46.77)	1.000
5th versus 6th	7.96 (-23.60, 3952)	1.000
6th versus 7th	-7.84 (-47.28, 31.60)	1.000
7th versus 8th	-1.12 (-35.25, 33.01)	1.000
8th versus 9th	-3.44 (-39.92, 33.04)	1.000
9th versus 10th	4.52 (-26.92, 35.96)	1.000
10th versus 11th	-1.64 (-48.68, 45.40)	1.000
11th versus 12th	-4.20 (-33.39, 24.99)	1.000
12th versus 13th	1.84 (-33.35, 37.03)	1.000
13th versus 14th	5.40 (-36.97, 47.77)	1.000
14th versus 15th	-5.24 (-42.25, 31.77)	1.000
15th versus 16th	0.28 (-39.97, 40.53)	1.000
16th versus 17th	15.60 (-21.60, 52.80)	1.000
17th versus 18th	-13.00 (-45.10, 19.10)	1.000
18th versus 19th	-3.48 (-32.77, 25.81)	1.000
19th versus 20th	-4.36 (-50.28, 41.56)	1.000
20th versus 21st	10.64 (-30.23, 51.51)	1.000
21st versus 22nd	-3.32 (-22.11, 15.47)	1.000
22nd versus 23rd	-1.64 (-35.92, 32.64)	1.000
23rd versus 24th	-14.24 (-66.43, 37.95)	1.000
24th versus 25th	15.20 (-17.93, 48.33)	1.000
25th versus 26th	0.64 (-30.98, 32.26)	1.000
26th versus 27th	-8.56 (-35.90, 18.78)	1.000
27th versus 28th	6.16 (-29.36, 41.68)	1.000
28th versus 29th	-1.16 (-24.56, 22.24)	1.000
29th versus 30th	4.56 (-21.19, 30.31)	1.000
30th versus 31st	-0.60 (-30.41, 29.21)	1.000
31st versus 32nd	-3.92 (-40.10, 32.26)	1.000
32nd versus 33rd	-0.16 (-23.75, 23.43)	1.000
33rd versus 34th	-15.20 (-48.13, 17.73)	1.000
34th versus 35th	13.60 (-20.27, 47.47)	1.000
35th versus 36th	-6.48 (-36.66, 23.70)	1.000

MD: Mean difference; CI: Confidence interval of difference. No significant difference ($p > 0.05$, Repeated measures ANOVA post hoc Bonferroni).

Discussion

We observed in the present study that capillary glycemia presents an immediate reduction after performing the combined training. However, there is no maintenance of this reduction over time, that is, in a period of time equal to or greater than 48 hours.

The global literature has presented favorable results in the context of the improvement of long-term glycemic control evaluated by means of HbA1c in subjects with T2DM [2,12] and practitioners of combined physical exercise programs [2,8,17]. However, in the present study, we observed that the efficacy of the hypoglycemic effects evaluated through capillary glycemia during a physical training program, even when combined, are limited to a short period of time, that is, a maximum of 48 hours.

Corroborating our study, another investigation aimed to evaluate the glycemic behavior of individuals with T2DM after a single exercise session with mild to moderate intensity and identified that both the capillary glycemia levels and the amplitude of their fluctuation were lower after the session of exercise. Thus, this study was conclusive in showing the beneficial effects of physical exercise within 24 hours after the session 5.

Systematic review and meta-analysis with the objective of identifying the effect of strength training on glycemic control of individuals with T2DM suggests that such exercise modality can be recommended even in the early stages of the disease, especially for those with poor glycemic control evaluated by HbA1c [12]. However, even in the case of a systematic review, there were no reports of glycemic control in the intra-training period (over successive training sessions).

The present study expected to find a glycemic control window longer than 48 hours, since the combination of aerobic exercises, which are known to improve fasting glycemia [18,19], and strength exercises, which are better at glycemic control over time evaluated by HbA1c [2,8]. In this scenario, an interesting recent study conducted with children with type 1 diabetes mellitus aimed to evaluate the association of cardiorespiratory fitness with glycemic variability, and observed that the two are negatively correlated. Thus, lower glycemic variability indicates the better physical fitness of the individual [20].

In the present study, we observed that capillary glycemia decreases after each combined training session, but is not maintained for more than 48 hours. This fact can be explained by exercise stimulates blood glucose disposal, in addition, induces a transient increase in whole-body insulin sensitivity for 48 h [18]. Holloszy (2005) shows that the acute glucose lowering effect of exercise results from high muscle glucose uptake determined by increased insulin sensitivity induced by muscle contraction [21], in addition, King; Baldus, Sharp et al. (1995)[22] already showed this effect it lasted up to 72 h after a single exercise bout [22]. Afterwards, Figueira et al. (2013)[23] using continuous glucose monitoring, does not confirm the long glucose reduction after the combined exercise sessions (strength and aerobic exercises), corroborating our study[23]. It is known that physical exercise determines the increase in insulin sensitivity, which is achieved by the increase of the GLUT4 protein, which is determined by the AMPK activity in the increased skeletal muscle [21,24]. It has already been demonstrated in literature, for a long time these changes occur very rapidly after the exercise onset and can last 16 h after the intervention [24]. It is noteworthy that a high carbohydrate diet is associated with the development of glycogen super compensation, preventing an increase in the insulin response [25], while the carbohydrate free diet maintains an increase in GLUT4 and insulin response for days after exercise [26]. In the present study, patients were instructed to maintain their usual carbohydrate intake, which could justify the reduced duration of the exercise-induced hypoglycemic effect. However, it is emphasized that HbA1c at the end of the same training program was significantly reduced according to a previous study carried out by our group 2, suggesting that the beneficial effects of exercise on long-term glycaemic control, showed by HbA1c, can be ascribed to the cumulative effects of the succeeding bouts of exercise. Due to the implications of glycemic variation in patients with T2DM, it is still necessary to search for more specific physical exercises and/or different loads or forms of performance that aim to reduce glycemic variations and maintain glycemic capillaries at values close to normal for a longer period of time.

There are some limitations to the current study, including the non-use of continuous glucose monitoring. It is known that the continuous monitoring equipment of blood glucose would be the most indicated, but it is worth noting the high cost of the equipment. However, capillary glycemia was measured before and after each training session.

Conclusion

Glycemia exhibits a behavior of reduction immediately after concurrent strength and aerobic training programs in patients with T2DM. However, the immediate reduction of glycemia is not maintained until 48 hours, nor is there a cumulative effect of the 36 training sessions on baseline glycemia.

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