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EFFECT OF AEROBIC EXERCISE, RESISTANCE TRAINING OR COMBINED TRAINING ON GLYCAEMIC CONTROL AND CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH TYPE 2 DIABETES

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ABSTRACT: Physical activity has been proven as a useful intervention for prevention and treatment of type 2 diabetes mellitus (T2DM). The purpose of this article was to compare the effects of aerobic exercise alone and resistance training alone as well as the combination of aerobic plus resistance training on glycaemic control, cardiovascular risk factors, and body composition in patients with T2DM. Eighty T2DM participants (37 men, 43 women), aged 33-69 years, were randomly divided in equal numbers (n=20) into one of four groups (aerobic, resistance, combined training, and control). Exercise training was performed three times per week for 52 weeks. After one year, 60 subjects (15 subjects in each group) were entered into the statistical analysis. Seventeen parameters were evaluated. Mean HbA1c showed statistically significant reductions in the three training groups. All subjects of training groups experienced improvement in postprandial glucose, blood pressure, VO_2max, and muscular percentage. Furthermore, the reduced concentration of plasma triglycerides was significant in both aerobic exercise and combined training groups. Also, a significant reduction was observed in body fat percentage in resistance and combined groups. Combination of two forms of exercise training led to an additional improvement in some of the parameters such as A1c and triglycerides compared with aerobic alone or resistance training alone. In general, the reported results in previous studies were not obtained for whole lipid profile and BMI. Both aerobic and resistance training are effective interventions for the management of T2DM complications, but combined training is associated with greater positive changes.

KEY WORDS: A1c, combined exercise training, diabetic complications, physical activity, type 2 diabetes mellitus

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a global health problem and one of the leading causes of morbidity and mortality for 90-95% of all diabetic cases [3]. According to estimations, the number of patients with T2DM worldwide is expected to rise to 300 million by 2025 [25]. Both insulin resistance and cell dysfunction are contributing factors to the disease, as are environmental and genetic factors [32]. The increase in T2DM prevalence can only partly be attributed to the increasing prevalence of obesity and a sedentary lifestyle [26,32]. T2DM is associated with dysfunction of various organs, especially the heart and peripheral blood vessels. T2DM has severe long-term complications including microvascular complications such as retinopathy and nephropathy, macrovascular complications such as coronary artery disease and stroke, with an increased risk of premature death [25,32]. Achieving and maintaining appropriate glycaemic control is vital to management of these comorbidities and this aim has traditionally been obtained using novel pharmacological solutions, dietary intervention, and physical activity [18,25].

For decades, exercise has been considered a cornerstone of diabetic management, along with diet and medication [29]. Regular physical exercise is an important factor to reduce the indices of cardiovascular and all-cause morbi-mortality [4]. Aerobic exercise refers to activities such as walking or jogging with continuous, repetitive movement of large muscle groups for at least 10 minutes at a time. Aerobic exercise may modify the insulin action of each fibre without increasing fibre size [32].

Aerobic exercise is known to manage glycaemic control and cardiovascular risk factors. It has also beneficial effects for metabolic profile in patients with T2DM [24]. Aerobic (endurance) exercise increases skeletal muscle capitalization and blood flow, muscular GLUT4 levels, hexokinase, and glycogen synthase activities [11]. The American Diabetes Association (ADA) recommends at least 150 min·week^{-1} of moderate-intensity aerobic physical activity or at least 90 min·week^{-1} of vigorous aerobic exercise distributed over at least 3 day·week^{-1} and with no more than 2 consecutive days without physical activity [26]. Resistance training has been shown to induce a hypertrophic response and a muscle-fibre type shift in exercising muscles, which causes an increase in whole-body glucose utilization [22]. Resistance training improves muscular strength and endurance, enhances flexibility and body composition, and decreases the risk of cardiovascular disease [3].

Possible underlining mechanisms for positive effects of resistance (strength) training may be the increase in the number of glucose transporter (GLUT) proteins, increasing total muscle mass, and an increased number of insulin receptors in the muscle cell [11]. In contrast to aerobic exercise, the ADA only began recommending resistance exercise in 2006. According to this guideline, in the absence of contraindications, diabetes patients should be encouraged to perform resistance exercise 3 times a week, targeting all major muscle groups, progressing to 3 sets of 8-10 repetitions at a weight that cannot be lifted more than 8-10 times [26,31]. The American College of Sport Medicine (ACSM) has recommended the use of progressive training as part of a well-rounded exercise programme for individuals with diabetes [28].

As is supported by the literature, the reduction of sedentary behaviours has general and specific health benefits in T2DM. Detection and evaluation of appropriate modes of training programmes (regarding the intensity, duration and frequency of exercise) in conjunction with other nutritional and medicinal choices have been studied by a number of investigators. Therefore, the present study aimed to evaluate the role of exercise in the regulation of glycaemic, metabolic, body composition and cardiovascular parameters in T2DM. In addition, we compare the effectiveness of different modes of exercise (aerobic and resistance training as well as combined exercise programme versus a sedentary control group) in blood glucose control, minimization of cardiovascular risk factors and management of long-term complications associated with T2DM.

MATERIALS AND METHODS

Subjects. In this interventional trial, 152 patients with T2DM at the mean age of 33-69 years were recruited through endocrine and metabolic clinics of Tabriz University of Medical Sciences. The study was approved by Ethics Committee of the university and all patients gave their written informed consent.

Inclusion criteria were as follows: established T2DM for more than one year duration, treatment only with oral hypoglycaemic agents (not taking insulin), an inactive previous lifestyle, A1c level < 11%. Exclusion criteria were BMI 43, age over 70 years, severe retinopathy, nephropathy and neuropathy, history of serious cerebrovascular or cardiovascular diseases, and severe musculoskeletal problems restricting physical activity.

After a medical screening with the given criteria, a 2-week run-in phase was performed three sessions per week with a progressive time of 15-40 minutes including warm-up movements, doing aerobic exercise at a moderate intensity (50% of maximum heart rate), familiarizing the participants with the resistance training machines, and doing 1 set of each exercise on different weight machines that were repeated 8-10 times. These combined readiness activities were followed by cool-down movements. Among the subjects who showed better adherence and acceptance to perform a one-year exercise training protocol, 80 patients were randomly assigned in equal numbers (n=20) into one of the four groups: Aerobic exercise, Resistance training, Combined exercise training, Control group

The exercise programme was determined in accordance with the ACSM guidelines [5] and was conducted during Oct 2008 to Sep 2009.

Parameters

All the subjects in 4 groups were recommended to continue their previous medications and diets. Furthermore, subjects of the control group were instructed to maintain their present lifestyle until the end of the project. Baseline biochemical tests including HbA1c, fasting blood glucose (FBG), 2-hour postprandial glucose (2 hr pp) ($mg \cdot dl^{-1}$), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c) and triglycerides ($mg \cdot dl^{-1}$) were performed both before and after the intervention.

Biochemical tests of blood glucose, total cholesterol, HDL-c, and triglyceride were carried out in a photometric End Point method using Pars Azmoon® enzyme kits (made in Iran), through auto-analyser devices (Hitachi®, model 704, 902 made in Japan). We used the Friedwald equation for calculation of LDL-C levels. HbA1c levels were measured by the auto-analyser devices (Hitachi®, model 704, 902, made in Japan).

These tests were also repeated by their physicians at 3-monthly visits. All of the subjects repeatedly monitored their blood sugar tests using a glucometer. Their heart rate and blood pressure were measured not only both before and after the project, but also during the sessions. The body height and body mass of the subjects were measured using a digital device at two time points, both before and after the study. For the estimation of maximal oxygen uptake ($\dot{V}O_2max$ $ml \cdot kg^{-1} \cdot min^{-1}$) the Rockport 1600 m Walking Test was applied both before and after the intervention. A body composition monitor (model BF500, OMRON®, 2007) was used to determine the basal metabolic rate (BMR%), body fat percentage (%BF), body mass index (BMI, $kg \cdot m^{-2}$) and muscular percentage (%).

Exercise training protocol

The exercise sessions were regularly held two or three times a week with the close supervision of the project staff and trainers. Moreover, the probability of hypoglycaemic episodes during the sessions was monitored and blood pressure fluctuations were assessed regularly. The subjects were asked to have sweet eatable or drinkable things and not to use their lunches or medications just before the beginning of training. However, they could supply the water required by their bodies in the middle of the sessions.

All types of exercise training were done according to the ACSM guidelines. All sessions included 10-15 minutes of stretching and flexibility movements to warm up as well as 10-15 minutes of relaxation activities to cool down.

Aerobic exercise programme

Participants of this group performed their activities using treadmill, elliptical or bicycle ergometers three times per week (on non consecutive days). Time of exercise was increased from 20 minutes per session (at 60% of maximum heart rate) to 60 minutes (at 75% of maximum heart rate) per session. Heart rate was regularly determined by the monitor's treadmill or cycle ergometers. Required heart rate was calculated by the Karvonen formula [19].

Resistance training programme

This programme was performed on different weight machines. Correct training techniques were instructed and supervised by professional trainers. The protocol was started on 2 days of the week during the first month and was increased to 3 non-consecutive days per week. Training was started during weeks 1 and 2 with intensity 60% one-repetition maximum (1RM) and was progressed to intensity 75-80% 1RM. The number of sets was 1-2 during the first month. This programme included 10 different exercises for upper and lower body. Participants performed 3 sets of 8-10 repetitions (with a 90- 120 s rest between sets) of the following exercises: bench press, seated row, shoulder press, chest press, lateral pulldown, abdominal crunches, leg press, leg extension, triceps pushdown and seated bicep curls.

Combined exercise training programme

The subjects of this group did the aerobic exercise plus resistance training programmes 3 times a week. After a warm-up stage, they worked for 20-30 minutes on a treadmill or bicycle plus 2 sets of each of 8 exercises with 8-10 repetitions on weight machines.

Adverse events

Three whole types of exercise training programmes were performed under the supervision of trainers and no serious adverse effect was reported in these groups. The dropped-out cases were eliminated for the following reasons: 3 cases of added insulin therapy, 7 dropped out because of insufficient numbers of the sessions, 2 dropped out due to repeated severe hypoglycaemia in the first month of this protocol, 1 case of death due to a non-diabetic cause (car accident), and 2 cases of change of address.

Finally, the subjects who attended more than 80% of total sessions in 52 weeks were included in the statistical analysis. They had been recommended to continue their physical activity also at home on days when they could not participate in sessions. In the end, after the last determination of required parameters and laboratory tests, 60 of 65 patients (in an equal number of 15 subjects) were entered into the analysis. Five cases were eliminated due to invalidity of their tests due to performing the tests in laboratories other than the proposed ones. The mean age of 60 participants (28 men, 32 women) was 50.5 ± 8.45 years (33 to 69 years).

Statistical analysis

Statistical analyses were performed using SPSS software (version 16.0). We used Tukey post hoc test for obtaining a significant ANOVA to compare the changes between the groups. All results are shown as means SD, and a p value less than 0.05 was considered as a statistically significant value.

RESULTS

The average age of subjects was 50.5±8.45 years (range 33-69 years). Table 1 shows the BMI and age characteristics of participants in the four groups.

Table 2 presents the comparative values of metabolic, body composition, and cardiovascular risk factors of four groups before and after intervention. A1c (%) showed significant changes in three groups, whereas a significant change was not observed in the control group. BMI showed a significant reduction only in the combination group. Systolic and diastolic blood pressure and also $\dot{V}O_2$max showed significant changes in the three training groups. The comparison of differences in parameters is shown in Table 3. According to this table, fasting and 2 hr pp blood glucose, triglycerides (TGs), body fat percentage and muscular percentage showed significant changes. However, TC, HDL-c, LDL-c, BMI, visceral fat, blood pressure (systolic or diastolic) (mmHg), basal metabolic rate (BMR) ($kcal \cdot h^{-1}$) and $\dot{V}O_2$max showed no significant differences.

Results of the Tukey post hoc test for within-group comparison of significant variables in the four groups are reported in Table 4. These results suggest that FBG ($mg \cdot dl^{-1}$) and 2 hr pp ($mg \cdot dl^{-1}$) in the aerobic training and combination groups were significantly different as compared with the control group (respectively 34% and 0.001). The same association is shown for A1c (>0.001 in two groups). Furthermore, the resistance training group shows a significant difference relative to the combination and control groups, whereas the same relation is shown in a difference of the combined training group as compared with the resistance training group. Also,

TABLE 1. COMPARISON OF AGE AND BMI OF SUBJECTS

Variable / Group	Aerobic exercise	Resistance	Combined Training	Control group	P value
Age (year)	48.2 ± 9.2	51.5 ± 6.3	50.9 ± 9.8	51.5 ± 8.5	0.677
BMI ($kg \cdot m^{-2}$)	29.4 ± 5.7	30.3 ± 4.0	28.8 ± 5.4	32.0 ± 4.9	0.34

there is a significant difference between aerobic and combination training groups in changes of TGs (0.02 and 0.001). On the other hand, changes of BF% show a significant difference between aerobic and combination groups (0.004), whereas muscular percentage shows the same difference between combination and control groups.

DISCUSSION

It is well known that regular aerobic exercise and resistance training produce positive effects in patients with T2DM, resulting in improved glycaemic control and the reduction of diabetic complications such as cardiovascular problems [11]. The present study was designed to

TABLE 2. COMPARISON OF BEFORE (PRE) AND AFTER (POST) INTERVENTION VALUES OF MEASURED VARIABLES (MEANS ± SD)

Parameter	Aerobic exercise	P value	Resistance training	P value	Combined training	P value	Control group	P value
HbA1c (%)								
Pre	8.5 ± 1.1	<0.001	7.9 ± 1.1	<0.001	8.7 ± 1.1	<0.001	7.1 ± 0.6	NS
Post	7.2 ± 0.8		7.3 ± 1.1		6.9 ± 0.9		8.2 ± 1.0	
FBS ($mg \cdot dl^{-1}$)								
Pre	157.9 ± 39.3	*=0.07*	144.9 ± 27.0	<0.05	163.7 ± 47.5	<0.001	146.1 ± 40.9	NS
Post	130.6 ± 31.2		122.7 ± 23.4		117.2 ± 37.5		157.0 ± 37. 3	
2hr pp ($mg \cdot dl^{-1}$)								
Pre	243.1 ± 57.7	<0.01	205.3 ± 65.5	<0.05	243.3 ± 87.2	<0.001	216.4 ± 54.8	NS
Post	198.4 ± 50.2		172.8 ± 38.9		181.4 ± 59.1		228.2 ± 62.3	
Triglycerides ($mg \cdot dl^{-1}$)								
Pre	182.0 ± 76.7	<0.01	185.1 ± 53.7	NS	243.4 ± 145.9	NS	171.3 ± 78.5	NS
Post	123.1 ± 28.7		156.5 ± 78.9		143.9 ± 85.7		220.9± 97.9	
TC ($mg \cdot dl^{-1}$)								
Pre	178.0 ± 45.3	NS	166.8 ± 38.8	NS	170.7 ± 28.7	NS	167.5 ± 44.4	NS
Post	168.8 ± 29.3		176.1 ± 49.3		157.2 ± 27.5		180.1 ± 44.5	
LDL-C ($mg \cdot dl^{-1}$)								
Pre	101.6 ± 40.8	NS	89.5 ± 40.1	NS	111.1 ± 49.3	*=0.07*	88.1 ± 41.1	NS
Post	95.3 ± 30.0		100.6 ± 45.2		92.7 ± 23.2		93.3 ± 32.7	
HDL-C ($mg \cdot dl^{-1}$)								
Pre	47.7 ± 8.9	NS	40.6± 9.6	<0.01	39.0 ± 4.9	NS	44.2 ± 8.7	NS
Post	47.7 ± 10.5		45.2 ± 8.7		38.5 ± 5.9		43.1 ± 8	
Weight (kg)								
Pre	68.6 ± 12.6	NS	84.1 ± 9.0	NS	82.6 ± 16.6	NS	75.2 ± 12.7	NS
Post	69.3 ± 12.4		82.9 ± 9.4		81.1 ± 14.4		75.2 ± 12.8	
BMI ($kg \cdot m^{-2}$)								
Pre	29.4 ± 5.7	NS	30.3 ± 4.0	NS	28.8± 5.4	<0.05	32.0 ± 4.9	NS
Post	28.5 ± 4.7		29.7 ± 3.9		27.8 ± 4.9		31.3 ± 5.2	
BF (%)								
Pre	40.0 ± 5.9	NS	32.7 ± 9.6	<0.001	29.4 ± 9.8	<0.001	42.1 ± 11.3	NS
Post	39.0 ± 5.7		30.5 ± 10.5		26.1 ± 9.9		40.8 ± 11.3	
Visceral fat (%)								
Pre	8.4 ± 2.4	NS	12.8 ± 3.8	*=0.05*	11.8 ± 5.2	<0.001	11.2 ± 2.8	NS
Post	8.3 ± 2.3		12.1 ± 3.4		10.7 ± 4.7		10.7 ± 2.7	
Muscular percentage (%)								
Pre	25.6 ± 1.8	<0.05	30.8 ± 4.9	<0.001	31.8 ± 4.9	<0.001	24.7 ± 4.3	NS
Post	26.4 ± 1.8		31.9 ± 5.4		33.7 ± 4.9		25.5 ± 4.4	
SBP (mmHg)								
Pre	131.5 ± 18.3	<0.01	129.7 ± 15.5	<0.05	135.8 ± 13.3	<0.05	122.3 ± 16.9	NS
Post	118.5 ± 20.1		118.4 ± 12.2		123.0 ± 12.5		121.3 ± 14.4	
DBP (mmHg)								
Pre	79.9 ± 9.0	<0.05	82.6 ± 9.5	<0.01	83.6 ± 9.5	<0.05	74.9 ± 14.4	NS
Post	71.9 ± 8.5		75.8 ± 8.5		78.3 ± 8.8		76.0 ± 7.2	
HR (bpm)								
Pre	86.8 ± 16.8	NS	85.3 ± 12.8	*=0.10*	89.2 ± 18.9	NS	80.3 ± 13.8	NS
Post	82.0 ± 9.6		81.5 ± 13.2		76.1 ± 9.50		79.6 ± 12.9	
BMR ($kcal \cdot h^{-1}$)								
Pre	1372.3 ± 149	NS	1711.9 ± 168	NS	1721.3 ± 255	NS	1478.7 ± 200	NS
Post	1381.3 ± 154		1701.4 ± 157		1691.9 ± 223		1455.9 ± 216	
$\dot{V}O_2max$ ($ml \cdot kg^{-1} \cdot min^{-1}$)								
Pre	26.7 ± 7.6	<0.01	32.2 ± 10.8	<0.01	32.0 ± 7.4	<0.05	25.1± 8.5	NS
Post	30.3 ± 9.5		35.9 ± 10.7		34.8 ± 6.9		27.9 ± 6.7	

Note: HbA1c - glycosylated hemoglobin, FBG - fasting blood glucose, 2hr pp - 2-hour postprandial glucose, TC - total cholesterol, HDL-c - high-density lipoprotein cholesterol, LDL-c - low-density lipoprotein cholesterol, BMI - body mass index, BF - body fat, SBP - systolic blood pressure, DBP - diasystolic blood pressure, HR - heart rate, $\dot{V}O_2max$ - maximal oxygen uptake, BMR - basal metabolic rate assess and compare the effects of various types of exercise training on glycaemic control or the reduction of diabetic complications such as cardiovascular risk factors as well as the improvement of body composition. As a therapeutic intervention of diabetes, exercise has previously been evaluated in numerous studies regarding its type, duration, intensity, and frequency. Also, one or more factors were considered in previous studies.

HbA1c

HbA1c is an important indicator of glycaemic control. Good glucose control at or below 7% can reduce the long-term complications by up to 76% [28]. The changes of A1c values in our groups confirm the previous positive findings. In our study, A1c values decreased by 1.33%, 0.55%, and 1.74% in the aerobic, resistance, and combined exercise training groups respectively, whereas it had a 0.2% elevation in the control group. A meta-analysis of twelve aerobic training studies and two resistance training studies (1982-2000) by Boule et al. [9] suggests that exercise reduces A1c values by approximately 0.66%, an adequate reduction to improve glycaemic control. These findings are similar to our conclusions [9]. Kelly and Kelly reported a statistical significance in A1c reduction (0.8%) [20]. The reported reduction by Goldhaber-Fiebert et al. [16] was more than the other studies (-1.8 ± 2.3% vs -0.4 ± 2.3% in control group). This change is similar to the change in our combined training group (-1.74 ± 0.97%), which is a very favourable range for the prevention of CVD in T2DM.

In our study, it seems that the reductions of A1c in the combined group are the sum of the reductions of both the aerobic and resistance groups, and confirm the reports about the synergistic effect of combined training on glycaemic control [15]. The change of A1c in the resistance group was less than half of the aerobic group. This observation is similar to the trial of Sigal et al. [30], and the review of Zanuso et al. [35] reported that compared with aerobic or resistance training alone the combined exercise training resulted in an additional change in A1c values. Similar to the trial of Sigal et al. [30], our aerobic ex-

TABLE 3. COMPARISON OF CHANGES IN MEASURED VARIABLES DURING 12 MONTHS IN FOUR GROUPS OF PATIENTS (MEANS ± SD)

Parameter	Aerobic exercise group	Resistance training	Combined training	Control group	P value
HbA1c (%)	-1.33 ± 1.08	-0.55 ± 0.47	-174 ± 0.97	+0.20 ± 0.66	<0.001
FBS ($mg \cdot dl^{-1}$)	-27.27 ± 55.77	-22.20 ± 23.12	-46.40 ± 31.75	+10.0 ± 29.69	0.001
2hr pp ($mg \cdot dl^{-1}$)	-44.71 ± 60.2	-32.47 ± 46.11	-61.87 ± 58.51	+11.80 ± 51.68	0.004
Triglycerides ($mg \cdot dl^{-1}$)	-58.87 ± 65.12	-28.53 ± 83.92	-99.50 ± 121.03	+49.67 ± 115.9	0.001
TC ($mg \cdot dl^{-1}$)	-9.20 ± 44.7	+9.27 ± 43.2	-13.5 ± 41.3	+12.7 ± 54.8	0.320
LDL-C ($mg \cdot dl^{-1}$)	-6.27 ± 35.72	+11.05 ± 41.17	-18.47 ± 35.88	+5.28 ± 44.09	0.189
HDL-C ($mg \cdot dl^{-1}$)	+0.07 ± 8.42	+4.67 ± 5.19	-0.53 ± 6.44	-1.07 ± 8.60	0.134
Weight (kg)	+0.69 ± 2.49	-1.2 ± 3.43	-1.56 ± 4.87	+0.09 ± 2.46	0.247
BMI ($kg \cdot m^{-2}$)	-0.87 ± 2.99	-0.56 ± 1.09	-1.01 ± 1.77	-0.73 ± 2.23	0.945
BF (%)	-0.97 ± 2.40	-2.18 ± 1.67	-3.35 ± 1.73	-1.23 ± 3.32	0.035
Visceral fat (%)	-0.13 ± 0.92	-0.73 ± 1.33	-1.07 ± 1.39	-0.53 ± 1.88	0.348
Muscular percentage (%)	+0.79 ± 1.41	+1.13 ± 0.86	+1.84 ± 1.06	+0.72 ± 1.32	0.048
SBP (mmHg)	-13.0 ± 13.47	-11.3 ± 15.39	-12.86 ± 16.27	-0.93 ± 11.56	0.073
DBP (mmHg)	-7.93 ± 12.96	-6.8 ± 7.59	6.36 ± 8.69	+1.07 ± 11.66	0.09
HR (bpm)	-4.8 ± 18.05	-3.73 ± 8.28	5.79 ± 17.7	-0.67 ± 12.47	0.798
BMR ($kcal \cdot h^{-1}$)	+9.0 ± 27.77	-10.53 ± 48.01	-29.47 ± 61.70	-22.87 ± 69.34	0.233
$\dot{V}O_2max$ ($ml \cdot kg^{-1} \cdot min^{-1}$)	+3.63 ± 3.84	+3.77 ± 4.19	+2.76 ± 4.68	+3.24 ± 4.78	0.912

Note: for definition of abreviations see Legend under Table 2.

TABLE 4. RESULTS OF TUKEY *POST HOC* TEST FOR SIGNIFICANT ANOVA

Group		Fasting blood sugar	Blood sugar(2hr. pp)	HbA1c	Triglycerides	Body Fat (%)	Muscular percentage
Aerobic Training Group	Resistance Training Group	NS	NS	NS	NS	NS	NS
	Combination Training Group	NS	NS	NS	NS	p<0.05	NS
	Control Group	p<0.05	p<0.05	p<0.001	p<0.05	NS	NS
Resistance Training Group	Combination Training Group	NS	NS	p<0.001	NS	NS	NS
	Control Group	*=0.08*	NS	p<0.05	NS	NS	NS
Combination Training Group	Control Group	p<0.001	p<0.01	p<0.001	p<0.001	NS	NS

ercise group had a greater change in A1c values (above 0.8%). This faster improvement of A1c may provide a greater benefit at least to patients with worse glycaemic control. Regardless of the duration and intensity of programmes, our findings are not consistent with a recent study that showed the superiority of resistance training compared to aerobic exercise [27]. However, there are contradicting reports such as the study of Honkola et al. [15] that no significant reduction was observed in A1c after progressive resistance training. It seems that the reduction of A1c values in our patients may be attributed to the long duration of our study. Another finding in previous studies is that participants with higher baseline A1c values showed greater improvement than those subjects with lower levels [6,31]. This issue has not been considered in the present study.

Blood glucose tests

There were significant decreases in FBG levels in the three intervention groups, although the reduction observed in the aerobic exercise group was not statistically significant (P=0.07). This finding is in line with the reported changes in the study of Shenoy et al. that indicate a greater effect of resistance training on improved FBG than aerobic exercise [28]. Our finding confirm the results of Alam et al. [2], Goldhaber-Fiebert et al. [16], and Maiorana et al. [21] that showed a reduction of FBG and is similar to the findings of Balducci et al. [7], who reported decreases of FBG values as a result of performing different types of exercise programmes. Postprandial hyperglycaemia is notably linked with increased oxidative stress and inflammation, decreased endothelial function, increased risk of cancer, and particularly with progression of retinopathy [13]. In the present study, the decreases of 2 hr pp in the three training groups were significant, with a greater improvement observed in the combined training group. In the study of Baldi it was reported that 6 weeks of resistance training was associated with no change of 2 hr pp glucose [15].

Lipid profile

The most common lipid abnormalities in T2DM are increased plasma triglycerides and low levels of HDL-c. Dyslipidaemia and insulin resistance are associated with increased fat and visceral adiposity [2]. There is consistent evidence demonstrating that high intensity and strenuous exercise has more significant positive effects on lipid profile, reducing mortality rates up to two-fold over a decade [4]. Exercise training can increase insulin sensitivity, improve abnormal lipid profile, and consequently improve visceral adiposity [2,6]. The investigations of lipid profile in all diabetic patients are associated with contradictory results [3]. The changes observed in TC and LDL-c in four groups were not statistically significant. The HDL-c showed a statistically significant increase in the resistance training group, whereas triglyceride levels showed statistically significant changes in the aerobic and combination groups.

These results are inconsistent with the findings of Sigal et al. [30] and Castenada et al. [10], who reported no significant changes in lipid profile. Also, a meta-analysis by Thomas et al. did not find significant exercise-induced changes in plasma lipid levels [30]. In addition, the changes in measurements after a three-week walking programme reported in the study of Goldhaber-Fiebert and co-workers [16] were small and not significant. Some research suggests that favourable TG and TC reductions in type 2 diabetic patients are best achieved through weight loss, even though training-induced changes of lipids are independent of body weight. Intensity, duration and frequency of training and nutrition may influence these changes [3]. On the other hand, our findings are in contrast with the meta-analysis conducted by Kelly and Kelly [23] indicating a significant reduction by about 5% for LDL-c levels with no statistically significant improvement for TC, HDL-c, triglycerides or TC/HDL-c ratios. Our results do not confirm the findings of Balducci et al. [7], who demonstrated a significant improvement in TC, LDL-c, triglycerides as well as HDL-c values. A study in India by Arora et al. [6] showed the effectiveness of both aerobic and resistance training with the superiority of resistance exercise on the improvement of TC and triglycerides, which is not in line with our findings.

Blood pressure and heart rate

Both systolic and diastolic blood pressure decreased in the three training groups, but did not show significant changes in the control group. This conclusion is not in line with the results of Sigal et al. [30] and Goldhaber-Friebert et al. [16], but confirms the results of Maiorana et al. [21] and Bulducci et al. [7] after combined training. Our findings are consistent with the results of Arora et al. [6], which showed the significant reduction of systolic blood pressure in two types of exercise groups, whereas their groups showed no significant changes in diastolic blood pressure and heart rate (bpm). Surprisingly, the heart rate of our participants in the four groups did not show any alterations. In general, there is a controversy about these factors in the literature. Heart rate is primarily mediated by the direct activity of the autonomic nervous system with predominance of vagal activity (parasympathetic) at rest that is progressively inhibited from the onset of exercise. Studies suggest that aerobic training causes a lower resting heart rate due to higher parasympathetic activity [4]. T2DM is associated with abnormalities in central and peripheral parameters of cardiovascular structure or function. The beneficial effects of exercise are well documented with regard to changes in endothelial function (e.g. flow-mediated dilation), carotid artery intima-media thickness and arterial distensibility, improvements in exercise capacity, left ventricular ejection fractions, and left ventricular stroke volume [4,22]. Many trials have shown the reduction of systolic and diastolic blood pressure by exercise [22]. According to Hagberg et al. [17], optimal control is usually achieved by pharmacological therapy.

Body composition

Abdominal obesity is a major risk factor for cardiovascular disease and the development of T2DM [3]. Exercise improves and maintains cardiorespiratory fitness, muscular strength, endurance, and body composition. There are studies that have shown improvements in body composition. This may be due to the different methods used to assess body composition (e.g. BMI, weight (kg), or fat mass), different training regimes (aerobic or resistance), and inclusion or lack of a dietary component to accompany the intervention [22]. Combined nutrition therapy and regular exercise are more effective for the improvement of metabolic control than when applied alone [3]. Liposuction alone fails to improve T2DM, which emphasizes the mediation of benefits of weight loss through metabolic effects of exercise. Since weight loss through metabolic effects of exercise has greater potential for energy expenditure, aerobic exercise has greater potential than resistance training to yield results [22]. In the present study, the expected alteration in body composition was not observed in the training groups. It seems that a much greater volume of exercise is needed to achieve a major weight loss than is required to result in improved glycaemic control or other risk factors [3]. To our knowledge, the exercise volume in our study was not adequate to produce a greater weight loss. In many previous studies, weight loss showed no changes [1]. A reduction of this parameter was reported by Maiorana et al. [21], Cuff et al. [12], and Marcus et al. [22], who mentioned that aerobic plus resistance programmes exhibited a greater increase in muscular density than each group alone. In the study of Goldhaber-Friebert et al. [16], weight loss was significant in the intervention group, although their programme included exercise plus nutrition classes, which may have an additional positive effect. Our results indicate a significant decrease of BF% in both the resistance and combined training groups ($P<0.001$). Furthermore, muscular percentage showed more significant increases in both the resistance and combined groups ($P<0.001$). Similar effectiveness of resistance training has been reported compared to non-exercising subjects by Custaneda et al. [10] and Dunstan et al. [14], indicating a tendency to increased lean body mass. This phenomenon could be explained by the hypothesis suggesting that resistance training recruits twitch skeletal muscle fibres, which leads to greater hypertrophy. Increased lean body mass provides an additional glycogen storage capacity or other mechanisms that result in improved insulin sensitivity and an elevated resting metabolic rate (RMR) in diabetic patients [14,32]. Visceral fat represents a significant source of free fatty acids (FFAs), which may be oxidized in preference to glucose, resulting in hyperglycaemia.

Loss of visceral fat may be an important benefit of exercise that leads to a significant improvement in metabolic indices [3]. Among our study groups, the combination training group showed a statistically significant improvement in BMI ($P=0.044$). This improvement is similar to the findings of Balducci et al. [7] and Marcus et al. [22] that demonstrated the superiority of combined training versus control or aerobic groups respectively. In the study of Ahmadizad et al. [1] these indices showed no significant reduction in response to 12 weeks of both aerobic and resistance training. However, in both groups BF% was significantly reduced. Body mass and BMI were not significantly altered throughout a 16-week study of combined exercise in women with T2DM [33]. In addition, in a systemic review of different types of exercise, Bolue et al. [8] found no significantly greater change in BMI. It is notable that the reduction of BMI in our combined group was less significant than the other improved factors and is negligible.

BMR and $\dot{V}O_2max$

Our subjects in the resistance and combined training groups showed a non-significant reduction in BMR, as did the control group. However, the elevation of BMR in the aerobic exercise group was not statistically significant. This parameter has not been evaluated widely in diabetes studies. Our findings are in contrast with the results of Williamson and Kirwan [34], who reported that an acute bout of resistance exercise causes a sustained increase in BMR after exercise in a healthy old population. There is a hypothesis that an increase in muscle mass due to resistance exercise results in elevated BMR. The non-significant rise in BMR of our participants in the aerobic group did not confirm this persistent finding.

There is some evidence that in patients with T2DM, $\dot{V}O_2$max values are less than the values in healthy subjects and specific pathogenic mechanisms such as hyperglycaemia, low capacity density, and alteration in oxygen delivery may contribute to this phenomenon [3]. In our study, $\dot{V}O_2$max was significantly increased in all of the training groups, which is in line with the results of two studies with a combined training design [15]. The changes reported by Ahmadizad et al. [1] were more significant than our results for endurance and resistance training groups. Boule et al. [8] reported an improvement of up to 10% in $\dot{V}O_2$max by aerobic exercise with a modest intensity. In the study of Alam et al. [2] there was a significant increase in $\dot{V}O_2$max value in a six-month supervised exercise programme. Cauzu et al. [11] observed additional improvements in $\dot{V}O_2$ peak after endurance training, whereas no such changes were seen in strength training in people with T2DM. According to these reports, the improvement of $\dot{V}O_2$max, muscle fibre capillary density, and expression of glucose transporters (GLUT4) are induced after aerobic exercise. However, some researchers reported no change in $\dot{V}O_2$max in a short-term comparison study of resistance training with non-exercise control subjects [22].

Limitations

Our study had limitations such as a small sample size to make a clear comparison between groups. This problem resulted from the prolonged duration of the study design that was associated with difficult adherence to this long-term programme. We did not exactly match the attendance time of subjects in the combination study group with the other groups. Despite that, after one year we observed a tendency toward reduction or elimination of medications. We did not include information about the drug categories used by subjects or a comparison of their alterations before and after the programme. In addition, we did not consider the psychological effect of attendance in the exercise activity. Besides the positive consequences of physical activity, the interaction with the training staff or the other participants in training groups could affect the outcomes of the exercise groups in comparison with the control group.

CONCLUSIONS

Our findings support the undeniable benefits of physical activity in T2DM patients. In general, aerobic exercise and resistance training alone induce positive effects in the prevention or management of glycaemic control and cardiovascular risk factors. Moreover, these effects may be additive in the combination of two types of training. The role of each type of aerobic or resistance training alone on the reduction of A1c levels was noteworthy. Also, the importance was considerable regarding $\dot{V}O_2$max elevation. However, the greater rise in HDL-c value in the resistance training group plus non-negligible decline of triglyceride values of aerobic and combined exercise groups indicate the role of physical activity on lipid composition in these patients. The expected outcomes were not obtained for lipid profile, BMI, and BMR. It also seems that weight loss and BMI reduction need a larger volume of exercise. Furthermore, heart rate and blood pressure are eventually more dependent on medicinal therapy than physical activity. Therefore, both aerobic and resistance exercise training should be considered as useful interventions in the management of T2DM to take advantage of different exercise types for glycaemic control, without clear superiority of either of them. The absolute improvement of variables such as A1c, blood glucose tests, triglycerides, BF%, muscular percentage, and visceral fat seems to be the sum of the altered values in both the aerobic and resistance groups alone (irrespective of being significant or not). These additive responses in the combined training group suggest that this type of exercise may be preferable for recommendation to diabetic patients. This type of exercise training should be emphasized by physicians for its long-term benefits.

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