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ARTICLE ORIGINAL

The Effects of Resistance and Endurance Training on Levels of Nesfatin-1, HSP70, Insulin Resistance and Body Composition in Women with Type 2 Diabetes Mellitus

Effets de l'exercice en résistance et en endurance sur la Nesfatine 1, l'HSP70, un index de résistance à l'insuline et la composition corporelle de femmes diabétiques de Type 2

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KEYWORDS
Nesfatin-1;
Insulin Resistance;
Resistance Training;
Endurance Training;
Type 2 Diabetes Mellitus.

Summary
Objectives. — Nesfatin-1 and HSP70 are involved in the regulating mechanisms of insulin and glucose metabolism. The aim of this study was to evaluate the effects of 10 weeks of resistance and endurance exercise training on the serum levels of nesfatin-1, HSP70 and insulin resistance (IR) in women with type 2 diabetes.
Materials and Methods. — 26 women with type 2 diabetes were selected using purposive sampling and were randomly divided into three groups. 10 subjects participated in the resistance training group (3 sessions per week, exercising with 30—80% of one repetition maximum (1RM)), 8 subjects participated in the endurance training group (3 sessions per week, exercising with 40—80% of maximum heart rate (HR max), for 20—45 minutes), and 8 subjects were placed in the control group who did not engage in any physical exercise during the study period. Blood samples were collected after a 12 hour [overnight]

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fast in order to evaluate nesfatin-1, HSP70, insulin and glucose levels in the pre- and post-tests. The obtained data were analyzed using the Kolmogorov-Smirnov (K-S) test, paired-samples t-test, one-way ANOVA and LSD post-hoc test in SPSS software, version 21 at the significance level of α <0.05.
Results. — There was a significant increase in nesfatin-1 levels and a significant decrease in HSP70 levels of the resistance training group, ($P < 0.05$), whereas no significant changes were observed in nesfatin-1 and HSP70 levels of the endurance training group ($P > 0.05$). Glucose levels, insulin resistance (HOMA1-IR) and body composition indices (except for WHR) significantly decreased in both training groups ($P < 0.05$). However, there were no significant changes in insulin levels of the training groups ($P > 0.05$). Moreover, comparing the pre- and post-test levels of glucose changes, a significant difference was observed in the resistance and endurance training groups but not in the control group ($P < 0.05$).
Conclusion. — Resistance and endurance training are recommended as complementary therapy for women with type 2 diabetes mellitus.

MOTS CLÉS
Nesfatine 1 ;
Résistanceà l'insuline ;
Exercice avec résistance ;
exercice d'endurance ;
Diabète 2.

Résumé
Objectifs. — la nesfatine 1 et l'HSP70 sont impliquées dans l'action de l'insuline et dans la régulation du métabolisme glucidique. L'objectif de cette recherche est d'analyser les effets de 10 semaines d'exercice en résistance et endurance sur les concentrations sériques de nesfatine 1 et d'HSP70 et de la résistance du corps de femmes diabétiques de type 2.
Méthodes. — Les investigateurs ont randomisé 26 patientes diabétiques qui ont été divisées en 3 groupes. 10 femmes réalisaient l'exercice en résistance (3 fois par semaines 60 minutes à une intensité de 30—80 % d'une repetition maximale) [1RM]. 8femmes réalisaient un exercice en endurance (3fois 20—40 minutes par semaine à une intensité de 40—80 % de la fréquence cardiaque maximale). Les 8 personnes du groupe contrôle n'avaient pas d'activité physique. Les échantillons de sang étaient prélevés après 12 heures de jeûne pour le dosage la Nesfatine 1, de HSP 70, de l'insuline et du glucose avant et après le protocole. Les données ont été analyses avec le test de Kolmogrov-Smirnov (K-S), le test *t* de Student pour valeurs appariées, l'analyse de variance à une voie, et le test de Différence Significative Minimale (LSD) de Fisher, avec la version de SPSS 21.
Résultats. — L'exercice en résistance augmentait la Nesfatine 1 et diminuait l'HSP70, alors que ces paramètres n'étaient pas significativement modifies par l'exercice en endurance. Résistance et endurance diminuaient toutes deux la glycémie, l'insulino-résistance, et les parameters d'adiposité (sauf le rapport taille sur hanche). Par contre ces entrainements ne diminuaient significativement pas l'insulinémie.
Conclusion. — Les exercices en résistance et en endurance ont des effets bénéfiques distincts chez les patientes atteintes de diabète de type 2.

1. Introduction

Type 2 diabetes mellitus is a metabolic disorder that is defined with high levels of blood sugar, insulin resistance (IR) and a relative lack of insulin in the body [1]. IR, which is defined as the decreased response of peripheral tissues to insulin, is considered as one of the main factors in the prevalence of type 2 diabetes mellitus and its long-term side effects [2]. Adipose tissue is not considered only as a fat and energy storage tissue; as an active endocrine organ, it produces numerous proactive cytokines called ''adipokines''. Nesfatin is one of these adipokines and plays a significant role in the mechanisms of appetiteregulation, energy homeostasis and metabolism [3]. Nesfatin-1 is a neuro peptide that was discovered in 2006 by Ohet al., as an anti-appetite polypeptide with 82 amino acids derived from the post-translation process of nucleobindin-2 gene (NUBC2), in the hypothalamus of rats [3]. Nesfatin-1 regulates whole-body glucose, energy homeostasis and insulin secretion [4]. Fasting nesfatin-1 levels are significantly lower in patients with type 2 diabetes as compared to healthy people and patients with type1 diabetes [5]. Furthermore, oxidative stress plays an important role in IR and beta-cell dysfunction. These two mechanisms are related to the patho physiology of type 2 diabetes mellitus and its vascular complications [6]. In the incidence of oxidative stress, factors such as heat shock proteins (HSPs) are involved and protect the cell function and survival [7]. The most sensitive group of heat shock proteins

is heat shock protein 70 (HSP70) [8]. Type 2 diabetes mellitus elevates HSP70 [9].

Today, performing physical activity is proposed as one of the effective ways for reducing IR index and improving the physical performance of diabetic patients [10]. Various factors, including physical exercise, affect the secretion of adipokines and HSPs, each responding separately to the intensity and duration of physical exercise. However, few studies regarding the impact of exercise on nesfatin-1 and HSP70 have heretofore been conducted. Chaolu et al. [11] found that 12 weeks of endurance exercise training significantly increases nesfatin-1 levels in male obese rats. In another study, Jafari et al. [12] showed a significant increase in nesfatin-1 levels after 8 weeks of endurance and strength training in overweight and obese females. Studies by Ogawa et al. [14] indicated that 12 weeks of low-intensity resistance training significantly reduced HSP70 levels. Considering the fact that adipokines play a major role in regulating inflammation, numerous studies have revealed the antioxidant and anti-inflammatory effects of heat shock proteins [15,16], however limited and contradictory studies have been conducted on the effects of physical exercise on heat shock proteins and specifically on HSP70. And to our knowledge, no investigation have, to date, studied the effects of resistance and endurance training on levels of nesfatin-1, HSP70-1 and IR index in women with type 2 diabetes mellitus. The present study aimed to explore the effects of 10 weeks of resistance and endurance training on serum levels of nesfatin-1, HSP70 and IR index in women with type 2 diabetes mellitus.

2. Methods

2.1. Treatment

This quasi-experimental study included a pre-test, a post-test, two experimental and one control group. The study population included all the women with type 2 diabetes mellitus who visited the Diabetes Clinic of Zahedan City. From these, a total number of 30 volunteers were chosen to participate in the study according to the inclusion criteria and through non-probability, purposive sampling procedure. The inclusion criteria were as follows: being female, having 40 to 55 years of age, having at least a 3 year history of type 2 diabetes mellitus, (according to medical diagnosis and records), a fasting blood glucose level of 126–250 [mg/dl] and taking the same medications (metformin and glibenclamide). The exclusion criteria included: a history of cardiovascular disease, having other complications of diabetes such as diabetic foot ulcer (DFU), menopause, insulin intake, smoking and engagement in regular physical exercise at least in the past 6 months. The aforementioned individuals were evaluated using the Medical History Questionnaire and the Physical Activity Readiness Questionnaire (PAR-Q3) before starting the exercise [17]. After filling out the consent form to participate in the study, the subjects were randomly divided into three groups of resistance training ($n = 10$), endurance training ($n = 10$) and control ($n = 10$) groups. The training groups participated in a 10 week exercise training program, whereas the control group was asked to stay sedentary and continue their normal life during the study. After starting the exercise training program, 2 subjects from the endurance training and 2 from the control group left the study for different reasons, so, 10, 8, and 8 subjects remained in the resistance, endurance, and control groups, respectively. All the participants were taking blood glucose-lowering medications prior to the study (e.g., Metformin and Glibenclamide), and no changes were made to their dose and type of medications during the study period. The subjects were asked to avoid engaging in other types of physical exercise while engaging in the exercise training program and to control their diet as recommended.

2.2. Anthropometric measurements

Anthropometric indices and VO_{2max} of the subjects were measured before the beginning of the exercise training program. The participants were wearing light clothing and no shoes during the anthropometric indices measurements (including weight, height, body mass index (BMI), waist-to-hip ratio (WHR) and body fat percentage (PBF)). Standing height and weight were measured with a wall-mounted stadiometer (to the nearest 0.5 cm) and a digital scale (to the nearest 0.1). BMI was calculated by dividing the body weight (in kilograms) to the square of the height (in meters). WHR was calculated using anon-elastic measuring tape and without bearing any pressure on the body (with an accuracy of 1 cm) by measuring the waist circumference (WC) midway between the lowest ribs and the iliac crest, and having it divided by the hip circumference in the gluteus maximus [18]. Skin fold thickness was measured on the right side of the body and at three sites: the triceps (in the middle of the upper arm), the suprailiac (at anterior axillary) and the front thigh (mid-thigh) using a caliper (Yangdeok-dong model, South Korea). PBF was calculated using the three-point equation for women by Jackson et al. [19].

$$\begin{aligned} \text{PBF} &= [(4/95/Db) - 4/5] \times 100 Bodydensity(Db) \\ &= 1.099421 - (0.0009929 \times \text{S}) \\ &+ (0.0000023 \times S_2)(0.0001392 \times \text{subjectage}) \end{aligned}$$

S = total subcutaneous fat thickness in the triceps, supra iliac and front thigh.

The subjects' maximal oxygen uptake (VO_{2max}) was measured applying Rockport 1 mile walking test and using the following equation [20]:

$$\begin{aligned} VO_{2max}\,(\text{ml/kg/min}) &= 132/853 - 0.0769(\text{bodyweight}) \\ &- 0.3877(\text{age}) + 6.315(\text{type}) - 3.2649(\text{time}) \\ &- 0.1565(\text{heartrate}) \end{aligned}$$

The experimental groups, exercised for 10 weeks, three sessions per week.

2.3. Training protocol

Participants in the resistance training group were provided with safety tips of weight training and working with fitness machines before starting their workout.

Two workout sessions using minimal weights and several sub maximal repetitions were also held to order to familiarize the participants with the training protocol and the correct movements. Subsequently, strength assessment was done using one 1RM test according to the Brzycki equation [21]:

$$\text{One repetition maximum (1RM)} = \frac{\text{Resistance weight (kg)}}{[1.0278 - (\text{The number of repetitions to fatigue} \times 0.0278)]}$$

The resistance training program included exercising with 8 fitness machines (including bench press, leg flexion, leg extension, shoulder press, leg press, standing cable curl with rope, rope press down, and seated row) and free weights. Thus, a total of 9 different movements were performed in 3 sets of 10 repetitions. There was 1—2 min rest time between each two sets and a 3 min rest time between each two machines. The training program began at an intensity of 30—50% of 1RM and with a gradual increase of intensity to 70—80% of one 1RM in the final sessions. Each 60 minute workout session included warm-up (10 minutes of jogging, stretching and kinetic exercises), resistance training with fitness machines (40 minutes) and cool down (10 minutes of flexibility and stretching exercises). In the endurance training group, the subjects exercised with a cycle ergometer (Monarch 893). Each workout session included warm-up (10 minutes of stretching and light exercises), training program (workout with a cycle ergometer) and cool down (10 minutes of flexibility and stretching exercises). The training program was initially performed at an intensity of 40—50% of maximum heart rate (HR max) for 20—25 minutes, which gradually reached 70—80% of HR max and 40—45 minutes. To determine exercise intensity, HR max was calculated using the following equation:

$$\text{HRmax} = 220 - \text{age(years)}.$$

Training intensity was controlled using Polar heart rate monitor (Finland) at specified intervals. The control group did not participate in any exercise training programs during the study. The control group did not participate in any exercise training programs during the investigation period.

2.4. Biochemical measurements

To measure the biochemical variables, 10 ml of blood was collected from all the subjects in their luteal phase of the menstrual cycle, following12 hours of fasting. Blood sampling was done 48 hours before the first and 48 hours after final workout session, from anticubital venous of the participants, by the laboratory technician. Blood samples were stored at −20 °C after serum centrifugation and separation processes for biochemical analyses. Fasting blood glucose levels were measured using Pars test kit (manufacturer Japan-Germany) and by Auto analyzer system (Hitachi 704). Fasting serum insulin levels were measured using human insulin ELISA kit (Q-1-DiaPlus, China-America). The homeostasis assessment model (HOMA1-IR = fasting insulin (μU/mL) × fasting glucose (mmol/L)/22.5) was used as a surrogate measure of whole-body insulin resistance [23]. In addition, the HOMA2-IRwas calculated as a stronger surrogate for insulin resistance using the HOMA2-IR calculator v2.2.3 [24].

Serum nesfatin-1 and HSP70 levels were measured applying sandwich ELISA using East biopharm human kit (China-America) with the sensitivity of 0.15 ng/ml and within-group and between—group coefficient variances of CV < 12% and CV < 10%, respectively.

2.5. Statistics

Kolmogorov-Smirnov (K-S) test was used to verify the normality of data distribution. Paired samples t-test and one-way ANOVA with LSD post-hoc test were utilized to investigate the intra- and inter-group differences, respectively. The significance level was set at $P < 0.05$ and data analyses were performed using SPSS software version 21.

3. Results

The normality of data distribution was confirmed by Kolmogorov-Smirnov test. ANOVA showed no significant differences in basal demographic measurements between the three groups ($P < 0.05$) (Table 1). Paired-sample t-test showed a significant decrease in weight, fat free mass, BMI, body fat percent, glucose levels, and HOMA1-IR of the two training groups and a significant decrease in the HSP70 of the resistance group ($P < 0.05$).$VO_{2max}$and nesfatin-1 levels increased significantly in endurance and resistance groups ($P < 0.05$). No significant inter- or intra-group differences were observed for HOMA2-IR. All the changes in the control group were insignificant ($P > 0.05$). According to one-way ANOVA, there were significant differences between the training groups and the control group in weight, BMI, body fat percent and glucose levels ($P < 0.05$), while no significant differences were observed in WHR, VO_{2max}, nesfatin-1, HSP70 and insulin changes between the training groups as compared to the control group ($P > 0.05$) (Table 2). The LSD test showed significant differences between the training groups and the control group in weight, BMI, body fat percent and glucose levels, while differences in other factors were not significant between resistance and endurance training groups (Table 3).

4. Discussion

The present data showed significant increases in nesfatin-1 levels in the resistance training group, while no significant changes were shown in the endurance training group. Also, the participants' nesfatin-1 response to endurance and resistance trainings did not change significantly as compared to the control group. The increased serum nesfatin-1 levels in the resistance training group was in line with Jafari et al. [12] who showed the same result after 8 weeks of resistance training in obese and overweight women, and contradicted with Nazarali et al. [25] who reported no significant changes after 8 weeks of resistance training in overweight women.

Observation of no changes in nesfatin-1 levels in the endurance training group was similar to the results of

Table 1 Basal demographic variables of participants.

Variables	Control	Endurance	Resistance
Age (year)	50.3 ± 7.97	51.4 ± 7.85	47.1 ± 6.27
Height (cm)	157.8 ± 5.81	158.1 ± 6.15	154.8 ± 5.09
BMI (kg/m^2)	28.78 ± 2.45	28.50 ± 2.38	28.45 ± 3.32
WHR	0.92 ± 0.04	0.93 ± 0.06	0.90 ± 0.07
Percent body fat (%)	38.88 ± 2.40	39.44 ± 3.34	38.76 ± 3.81
VO_{2max} (ml/kg/min)	25.84 ± 7.06	23.70 ± 7.89	25.53 ± 7.26
Fasting glucose (mg/dl)	159.50 ± 29.94	173.75 ± 40.88	182.70 ± 48.70
Insulin (μu/ml)	9.98 ± 4.22	11.83 ± 4.02	10.62 ± 5.75
HOMA1-IR	3.96 ± 2.02	4.83 ± 1.51	4.92 ± 3.54
HOMA2-IR	1.47 ± 0.62	1.74 ± 0.55	1.62 ± 0.92
Nesfatin-1 (ng/ml)	9.71 ± 5.79	10.48 ± 9.40	8.64 ± 2.81
HSP70 (ng/ml)	14.22 ± 5.14	17.49 ± 2.04	16.18 ± 3.38

Data are shown as mean ± standard deviation.

Table 2 The pre—post test of biochemical and anthropometric markers of participants in the training and control groups.

Variables	Groups	Pre test	Post test	Changes	P paired *t* test	*P* Anova
Weight (kg)	Control	68.98 ± 7.26	69.79 ± 9.37	0.81 ± 2.84	0.445	0.007*
	Endurance	71.44 ± 8.80	69.44 ± 8.41	−2.00 ± 1.65	0.011*	
	Resistance	71.05 ± 10.28	68.83 ± 9.77	−2.22 ± 1.26	0.000*	
BMI (kg/m^2)	Control	28.78 ± 2.45	29.09 ± 3.01	0.30 ± 1.12	0.470	0.008*
	Endurance	28.50 ± 2.38	27.70 ± 2.20	−0.80 ± 0.67	0.011*	
	Resistance	28.45 ± 3.32	27.56 ± 3.15	−0.89 ± 0.48	0.000*	
WHR	Control	0.92 ± 0.04	0.92 ± 0.05	0.00 ± 0.02	0.685	0.121
	Endurance	0.93 ± 0.06	0.90 ± 0.05	−0.03 ± 0.04	0.035	
	Resistance	0.90 ± 0.07	0.88 ± 0.08	−0.03 ± 0.044	0.106	
Percent body fat (%)	Control	38.88 ± 2.40	39.68 ± 3.32	0.80 ± 1.76	0.242	0.000*
	Endurance	39.44 ± 3.34	36.08 ± 3.04	−3.35 ± 2.07	0.003*	
	Resistance	38.76 ± 3.81	35.85 ± 3.32	−2.90 ± 2.02	0.001*	
VO_{2max} (mL/kg/min)	Control	25.84 ± 7.06	25.13 ± 8.57	−0.71 ± 3.76	0.612	0.085
	Endurance	23.70 ± 7.89	28.07 ± 4.82	4.37 ± 4.98	0.042*	
	Resistance	25.53 ± 7.26	28.65 ± 8.46	3.12 ± 4.71	0.066	
Fasting glucose (mg/dL)	Control	159.50 ± 29.94	175.25 ± 40.82	15.75 ± 18.93	0.051	0.000*
	Endurance	173.75 ± 40.88	138.63 ± 35.33	−35.13 ± 27.59	0.009*	
	Resistance	182.70 ± 48.70	138.80 ± 43.96	−43.90 ± 4.74	0.000*	
Insulin (μu/mL)	Control	9.98 ± 4.22	9.79 ± 3.66	−0.19 ± 4.50	0.910	0.490
	Endurance	11.83 ± 4.02	9.95 ± 4.17	−1.88 ± 4.56	0.283	
	Resistance	10.62 ± 5.75	7.87 ± 3.39	−2.75 ± 4.40	0.080	
HOMA1-IR	Control	3.96 ± 2.02	4.25 ± 2.01	0.28 ± 2.10	0.714	0.111
	Endurance	4.83 ± 1.51	3.30 ± 1.33	−1.54 ± 1.78	0.045*	
	Resistance	4.92 ± 3.54	2.87 ± 1.78	−2.05 ± 1.76	0.044*	
HOMA2-IR	Control	1.47 ± 0.62	1.47 ± 0.56	0.007 ± 0.66	0.975	0.315
	Endurance	1.74 ± 0.55	1.40 ± 0.56	−0.34 ± 0.64	0.178	
	Resistance	1.62 ± 0.92	1.13 ± 0.52	−0.48 ± 0.70	0.058	
HSP70 (ng/mL)	Control	14.22 ± 5.14	14.83 ± 2.64	0.60 ± 4.33	0.712	0.060
	Endurance	17.49 ± 2.04	16.72 ± 4.64	−0.77 ± 4.98	0.675	
	Resistance	16.18 ± 3.38	12.30 ± 2.39	−3.88 ± 2.74	0.002*	
Nesfatin (ng/mL)	Control	9.71 ± 5.79	8.64 ± 2.81	−1.08 ± 4.94	0.557	0.118
	Endurance	10.48 ± 9.40	14.10 ± 13.12	3.63 ± 6.94	0.183	
	Resistance	9.21 ± 4.90	14.39 ± 9.96	5.18 ± 5.06	0.034*	

The *P* value accounts for paired T and Anova tests.
* $P < 0.05$.

Table 3 The LSD post hoc test for Anova.

Variable	Group	Mean diff	Standard error	*P* value
Weight (kg)				
Control	Endurance	2.81250	0.98811	0.009*
	Resistance	3.03250	0.93740	0.004*
Endurance	Resistance	0.22000	0.93740	0.817
BMI (kg/m²)				
Control	Endurance	1.10375	0.39071	0.010*
	Resistance	1.19275	0.37066	0.004*
Endurance	Resistance	0.08900	0.37066	0.812
Percent body fat (%)				
Control	Endurance	4.14750	0.98090	0.000*
	Resistance	3.70125	0.93056	0.001*
Endurance	Resistance	−0.44625	0.93056	0.636
Glucose (mg/dl)				
Control	Endurance	50.87500	11.86668	0.000*
	Resistance	59.65000	11.25773	0.000*
Endurance	Resistance	8.77500	11.25773	0.444

* $P < 0.05$.

Ghanbari-Niaki [13] but differed from Chaolu et al. [11] and Jafari et al. [12] who confirmed that endurance training increased plasma nesfatin-1 levels. These disagreements could be due to differences in some factors such as gender and age of the participants, and diversity in type, duration and exercise intensity. It should be noted that low number of participants in each study group of the present investigation could be assumed as a limitation which may responsible for observing no inter-group differences.

Another citable limitation of the present study may be the participants' similar diet within all the groups, as Ramanjaneya et al. [26] reported that the reduction in nesfatin-1 content may be affected by diet. In addition, fasting might also be effective onnesfatin-1 levels and may decrease nesfatin-1 serum levels up to 18 percent [27].

Other findings of the present study indicate the significant increase in HSP70 levels in the resistance, but not the endurance training group. Significant decrease in HSP70 levels of the resistance training group was in line with the report of Ogawa et al. [14] who showed significant reduction in HSP70 after 12 weeks of low intensity resistance training in old women, and differed from the study by Paulsen et al. [28] who observed an increase in HSP70 levels after 11 weeks of acute strength training in young men.

We observed no change in HSP70 levels which diverged from the results of Matos et al. [15] who reported decreased HSP70 levels and improved insulin resistance after one session of endurance training on ergo meter with 60% of VO_{2max}.

To mention the limitations accounts for no change in HSP70 in endurance group and between group comparisons may be the participant's diet in training and control groups, which might affect HSP70 levels, as researches have shown that HSPs are produced by mechanical stresses, diet, protein distraction or free radicals [29]. The endurance training intensity may be the other important factor regarding the HSP70 levels in the endurance training group. The mentioned study results confirmed that in people with high basal HSP70 values (due to inflammation caused by diseases), low intensity endurance training cannot be effective in improving HSP70 levels. The studies showed multiple factors can regulate the HSP70 levels. In a study by Earl et al. [30] numbers of training sessions, training intensity, age and participants' characteristics are shown to be effective factors on HSP70 changes. In addition, limited number of participants can also be responsible for the insignificant changes in nesfatin-1 and HSP70 values in the endurance training group and in inter-group comparisons.

According to the results, nesfatin-1 increase in the resistance training group was accompanied by HSP70 decrease, while neither of the mentioned variables changed in endurance training group. Possibly, nesfatin-1 and HSP70 values have some interactions. Another possibility is that some other cytokines affect nesfatin-1 and HSP70 levels. Some documents proved that mechanisms that decrease levels of cytokines and pro inflammatory factors such as IL-6, consequently lead to HSP70 reduction [31]. Nesfatin-1 release is also affected by inflammatory cytokines and insulin [26]. Unfortunately as we did not measure changes of other cytokines in this study we were unable to investigate their relationship to nesfatin-1 and HSP70 changes. More BMI reduction in resistance training group as compared to the endurance training group could be another reason for the significant increase in nesfatin-1 and HSP70 in the former group compared to the latter.

In the present study, the fasting glucose level and insulin resistance (HOMA1-IR) markers decreased significantly in both training groups, with a slight decrease in insulin levels in both training groups. In addition, HOMA2-IR index, which is a stronger surrogate for calculating insulin resistance in diabetic patients whose fasting plasma glucose in higher than7 mmol, did not change significantly in either of the groups. Decreased HOMA should not be concluded just from a decrease in blood glucose levels and without taking into account insulinemia changes. Since no significant decreases were observed in insulin levels of the training groups, no significant changes in HOMA2-IR were observed

either. In this index the marker of insulin resistance is insulin concentration, which is a reliable index as far as the pancreas can compensate and maintain blood glucose. A change in fasting glucose concentrations rather indicates a decrease in hepatic glucose output (which can be explained by an improvement in insulin sensitivity). It is noteworthy that a decrease in blood glucose may induce a decrease in HOMA which does not mean that insulin sensitivity has improved.

Also, the participant's glucose response to resistance and endurance training significantly differed from the control group; however changes in the insulin and insulin resistance response to resistance and endurance training were not significant as compared to the control group.

The other finding of the present study included the significant decrease in insulin resistance in the endurance and resistance training groups which is in line with the investigation done by Shehab et al. [32] who showed a significant decrease in insulin resistance in type 2 diabetic patients after 12 months of resistance and endurance training, and contradicted with Jorge et al. [18] who reported no significant changes in insulin resistance after 12 weeks of resistance and endurance training. In the current paper, more insulin resistance decrease in the resistance training group was seen as compared to the endurance training group. The reason may be the effect of resistance training on muscle mass. The present documents indicated the benefits of resistance trainings on type 2 diabetes through affecting the insulin action. As the skeletal muscle tissue is more sensitive to insulin, increasing muscle mass by doing resistance training results in glycemic control and insulin resistance decrease [33]. It is also recommended that adults undertake muscle-strengthening such as weight training two or more days a week. However, although studies have shown that muscle-strengthening activity improves glycemic control in people who already have diabetes; it is unclear whether this form of exercise prevents diabetes. The observed contradictions may be related to differences in blood sampling time, exercise protocols, and participant's dissimilarities.

It is probable that there is a relationship between insulin, glucose, nesfatin-1 and HSP-70. In addition, plasma nesfatin-1 levels are related to lifestyle-dependent diseases such as obesity and diabetes [11]. Moreover, human studies have shown that the HSP70 levels in mononuclear cells of diabetic patients are significantly higher than healthy people [34]. The hyperglycemia was determined to be one of the reasons of chronic increases of HSP70 levels in type 2 diabetic patients [35]. Thus, it is probable thatdecreasednesfatin-1 and increasedHSP70 may interfere with glucose metabolism and insulin resistance increase in diabetic patients. In the present research, nesfatin-1 increase and HSP70 decrease in the resistance training group, is probably due to increases in the number of GLUT-4s which in turn decreases glucose levels and insulin resistance.

In the present study, all the anthropometric factors decreased significantly in the endurance and resistance training groups after 10 weeks of exercise, except for WHR which did not change significantly in the resistance training group. The observed decrease in weight, BMI and body fat percent in the resistance training group was in line with the report of Feniccia et al. [36] who showed significant decreases in these variables following 6 weeks of resistance training. These findings were in contrast to those of Jorge et al. [18] who reported no significant changes in the mentioned variables following12 weeks of resistance training in diabetic people.

It is also known that exercise training increases sensitivity of insulin-mediated glucose uptake in muscles through local mechanisms which might improve due to resistance training. These mechanisms which end in a decreased reliance on insulin may reduce insulin secretion and put more emphasis on the anabolic effects on fat mass, which may act as a body weight regulator. It has been said that, resistance training can improve insulin sensitivity, which can be partially, but not entirely, attributed to changes in body composition. Thus, it is possible that insulin sensitivity improvements, also contribute to body composition enhancement [37]. Other potential mechanisms relating resistance training to weight and body fat may include changes in the adipokines' levels due to training. Both adiponectin and leptin are associated with changes in body composition, as well as metabolism. Although not tested in this study, limited evidence suggests that resistance training may have an effect on these biomarkers. On the other hand, some other studies have reported neural effects of resistance training on body composition and insulin resistance. However, these controversies may be explained according to the differences in intensity, frequency, and duration of the training protocols performed in different studies. Therefore, daily, low-intensity exercises are recommended during the early stages of resistance training, which should then continue to be performed three days per week [38]. However, there is no consensus on the minimum intensity, frequency, and duration needed to improve insulin resistance.

The present data about the insignificant decrease in the WHR of the resistance training group was in line with the results of Jorge et al. [18], but contradicted with those of Fenicchia et al. [36]. These divergences may be attributed to differences in age and other characteristics of the participants and also to the diversities in the applied exercise training protocols (duration, type, intensity). Tsuchiya et al. [39] also, showed the negative relationship between BMI and nesfatin-1 levels.

In general, the present data showed there was a significant difference in the participants' glucose response to resistance and endurance training as compared to the control group, while no significant differences were seen in nesfatin-1, HSP70, insulin and insulin resistance (HOMA1-IR and HOMA2-IR) response to resistance and endurance training as compared to the control group. As a result, diabetic patients may take advantage of exercise training, along with nutritional diet and medical interventions in order to improve their health status.

5. Conclusion

In general, resistance training may have a vital role in bringing about some positive changes which could be helpful to patients with type 2 diabetes such as increasing nesfatin-1 and decreasing HSP70 and insulin resistance. Indeed, we can assume resistance training as a positive, complementary intervention in diabetes management besides diet and pharmacological treatments.

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Disclosure of interest

The authors declare that they have no competing interest.

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