



Impact of Aerobic Exercise on Serum Vaspin Level in Female Patients With Type 2 Diabetes Mellitus

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Abstract

Objectives: As a metabolic syndrome, type 2 diabetes mellitus (T2DM) has had a worldwide increase associated with the incidence of obesity. Vaspin acts as a new biomarker for obesity and interactive exercise. Our study aimed to survey the effect of aerobic exercise on vaspin level in the female patients with T2DM.

Materials and Methods: Forty female patients (age = 33.00 ± 8.08 years) as diagnosed with T2DM based on the International Diabetes Federation (IDF) were selected. The participants were randomly divided into exercise (E) and control groups (C). At the beginning and at the end of the study, all the variables were measured. Group E participated in 8-week training sessions, 3 days/week for 60 minutes, with an intensity of 60%-70% of maximum heart rate. The C group continued its usual life.

Results: Thirty-one subjects completed the study period ((E [n = 18] and C [n = 13]). Statistical analysis showed that group E had a significant increase in vaspin level ($F = 8.888$, $P = 0.001$) and a significant decrease in BW (body mass weight), BMI (body mass index), WC (waist circumference), FP (fat percentage), FM (fat mass), FFM (fat free mass), TC (total cholesterol), FBS (fast blood sugar) and insulin level, whereas there was no significant change in HC (hip circumference), WHR (waist to hip ratio), TG (triglyceride), HOMA-IR, and quantitative insulin sensitivity check index (QUICKI) in the E group compared with the C group ($P < 0.05$).

Conclusions: Our data suggested that vaspin behavior is reversed by increasing the duration and progressive stage of T2DM and its level increases following exercise and weight loss.

Keywords: Aerobic exercise, T2DM, Vaspin

Introduction

As a metabolic syndrome, type 2 diabetes mellitus (T2DM) has had a worldwide increase associated with the incidence of obesity, and has been strongly influenced by lifestyle habits like high calorie nutrition and lack of physical activity (1). The prevalence of T2DM in the general population in the world is 415 million people from which more than 35.4 million are in the MENA (Middle East and North Africa) and it is estimated that this number will rise to 72.1 million by 2040 (2). In Iran, there were over 4.6 million cases of diabetes in 2015, and its national prevalence will be 8.43% by 2040 (2).

Vaspin (visceral adipose tissue-derived serine protease inhibitor) is expressed in fat tissue (3). Vaspin concentration reflects body fat mass and fitness (4,5) and is positively correlated with an increase in fasting insulin level (6) and insulin resistance (4-6). In fact, significant higher levels of vaspin were reported in obese individuals and T2DM patients (7-9) and considering positive correlation with other biochemical parameters, vaspin may play a leading role in obesity and the pathogenesis of T2DM (10,11).

No significant difference was reported for serum vaspin concentrations between first-degree relatives (FDR) of the patients with T2DM and the healthy (12), and it decreases with progression of diabetes and body weight loss in rat models of T2DM (13). Increased vaspin levels are reported in the persons with lower physical activity in combination with a higher percentage of total body fat (5). Barzegari and Amouzad Mahdirejei noted a significant decrease in vaspin level after 8-week resistance trainings in the male patients with T2DM (14), whereas Amouzad Mahdirejei et al reported no significant change in vaspin level after 8-week resistance trainings in the male patients with T2DM (15) and Kadoglou et al reported vaspin increase after aerobic, resistance, and aerobic plus resistance trainings in the patients with T2DM (16). Safarzade et al reported that 4-week resistance trainings in non-diabetic rats significantly decreased serum vaspin levels, while in the trained diabetic group, serum vaspin levels increased significantly compared with sedentary T2DM (17).

The contradictory results of this research led us to study the effect of aerobic exercise training on vaspin level in the

Received 6 January 2017, Accepted 13 August 2017, Available online 3 September 2017

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female patients with T2DM.

Materials and Methods

Subjects

This study was conducted from April to July 2016 under the auspices of Najafabad Branch, Islamic Azad University, and International Diabetes Prevention and Control Foundation, Mashhad, Iran (IDPCF). The participants were volunteers who had registered in IDPCF. In this study, the patients who were diagnosed with T2DM for 3 years in Diabetes Clinic of Fourth People's Hospital of Mashhad City, Iran, were included. T2DM was diagnosed according to the International Diabetes Federation (IDF) (1). Metformin tablets were used as a glucose-lowering drug. The exclusion criteria included the patients with other types of diabetes, thyroid disorders, iron deficiency anemia, blood pressure and coronary arterial diseases, chronic kidney diseases, infection, recent major surgery or illness, or those who were under treatment with steroids or lipid-lowering drugs, and those with orthopedic disorders leading to movement limitation, and pregnant.

Clinical and Biochemical Assessment

All the patients underwent physical examination and biochemical analyses of blood before and after the exercise protocol. The subjects were weighted, dressed in light clothes, using a portable scale (Seca Vogel & Halke German model: 760 1029009). The heights of the subjects were measured without shoes by a portable wall mounted ruler in the upright position (accuracy 0.1 cm). Moreover, body mass index (BMI [$\text{kg}\cdot\text{m}^{-2}$]) was calculated for the study subjects (18). The waist circumference (WC) and hip circumference (HC) were measured at the umbilicus and the gluteal fold in the standing position, respectively, and the waist-to-hip ratio (WHR) was calculated as a body index (18). The body fat percentage was calculated based on the Jackson-Pollock 4-site Skinfold equation:

$$\% \text{ Body Fat} = (0.29669 \times \text{sum of skinfolds}) - (0.00043 \times \text{square of the sum of skinfolds}) + (0.02963 \times \text{age}) + 1.4072$$

The skinfold sites (measured in mm) included abdominal, triceps, thigh, and supra-iliac (18).

The blood samples were taken from the subjects after an overnight fasting (12 hours). The samples were centrifuged and the obtained serums were kept at -80°C until the next uses. Plasma vaspin, TC (total cholesterol), TG (triglyceride), FBS (fast blood sugar), and insulin levels were measured in the morning at 08:00 AM by venipuncture after an overnight fasting. After clotting, the serum was separated and instantly explored for cholesterol, TG and FBS. Concentration was measured by colorimetric technique which is based on enzyme measurement (Auto analyzer, Alpha-Classic machine using Quantity Recognition Kit, Pars Azmoon Co, IRAN). Fasting insulin concentration was measured by enzyme-linked immunosorbent assay (Insulin ELISA kit, Demeditec Co, Germany), and vaspin concentration was

measured through enzyme-linked immunosorbent assay (Vaspin ELISA kit, Eastbiopharm, Co, China). All samples were analyzed at a private Medical Diagnostic Center, Mashhad, Iran.

The fasting index of homeostasis model assessment was used for estimation of insulin resistance ($\text{HOMA-IR} = \text{fasting insulin (mU/L)} \times \text{fasting glucose (mg/dL)} / 405$) and quantitative insulin sensitivity check index ($\text{QUICKI} = 1 / [\log (\text{fasting insulin, } \mu\text{U/mL}) + \log (\text{fasting glucose, mg/dL})]$) (19).

The patients were classified into 2 exercise and control groups, who were age and weight-matched. Subjects in the exercise group benefited from the protocol of training for 8-week, while the control group continued their routine life.

Protocol of Training

The protocol of training included aerobic activities which involved 8-week (1 hour per day, 3 days per week). The intensity of aerobic training was determined by applying 60-70 percentage of maximum heart rate using the 220-age equation. The first training session was about 30 minutes. However, every 2-week, a 5-minute gradual increase was applied to the intensity of training. Each training session started with 10-minute warm up, 30-minute exercise training, and 5-minute final cooling down. The exercise training included 15-minute juggling, three sets of one-minute walking with 1-minute rest in between, 3 sets of 1-minute rhythmic exercise accompanied by music with 60-70 percentage of maximum heart rate and 1-minute rest in between, and 3-minute rest between each exercise. During the 2-month training period, subjects in the control group did not participate in any regular training program, and the patients (at each session) did not participate in exercises in the case of hypoglycemia or glucose levels greater than 250 mg /dL. The aerobic activities were held in a municipal park in Mashhad city, and the permission for the exercise was obtained from region 11 Municipality.

Statistical Analysis

Data were analyzed using SPSS statistical software version 15.0. Descriptive analysis, reported as means \pm SD, was applied for demographic and clinical characteristics. Before the statistical analysis, Shapiro-Wilk test was used to determine the normality of distributions ($P > 0.05$). Moreover, Levene test was used to show the homogeneity of variances of 2 groups before the protocol application ($P > 0.05$). Differences between the groups were assessed using analysis of covariate (ANCOVA) to compare post-tests by considering covariation in pretest ($P < 0.05$).

Results

In this study, 31 female patients with T2DM (mean age = 44.48 ± 4.17 years, $\text{BMI} = 29.30 \pm 3.70 \text{ kg}\cdot\text{m}^{-2}$) were enrolled. Demographic characteristics and biochemical test results for the patients and controls are summarized

in Table 1. Age and BW distribution were similar in both groups (exercise and control groups). Shapiro-Wilk test was used to show the distribution for normality in the pretest of variables ($P > 0.05$). The pretest of BMI, TG, FBS, insulin and HOMA-IR was lower than 0.05, so Log_{10} of these variables was used in the statistical analysis (ANCOVA). Levene test was utilized to show the homogeneity of variances between the patient and control groups before the protocol application ($P > 0.05$). Levene test of variables included BW ($F = 0.000, P = 0.993$), BMI ($F = 0.801, P = 0.378$), WC ($F = 1.687, P = 0.204$), HC ($F = 0.463, P = 0.502$), WHR ($F = 0.005, P = 0.944$), FP ($F = 2.236, P = 0.146$), FM ($F = 1.072, P = 0.309$), FFM ($F = 3.283, P = 0.080$), TC ($F = 0.283, P = 0.599$), TG ($F = 0.759, P = 0.391$), FBS ($F = 1.698, P = 0.203$), insulin ($F = 0.128, P = 0.724$), HOMA-IR ($F = 0.058, P = 0.811$), QUICKI ($F = 0.212, P = 0.649$) and vaspin ($F = 0.516, P = 0.480$) ($P > 0.05$). ANCOVA test was used to compare post-tests of exercise and control groups with the pretests ($P < 0.05$). Table 1 shows the demographic and biochemical data of both groups, and Table 2 shows the ANCOVA in the study subjects.

Eight-week aerobic training caused significant changes in BW, BMI, WC, FP, FM, FFM, TC, insulin, FBS, and vaspin, whereas there was no significant change in WHR, TG, HOMA-IR in the exercise group compared with the control group ($P < 0.05$).

Discussion

Our results indicated a significant increase in serum vaspin concentration in the obese females with T2DM followed by a significant weight loss and that this happened along

with improvements in anthropometric parameters such as BMI, WC, FP and FM. The magnitude of increment in vaspin level was $16.18 \pm 0.11\%$ in the exercise group, whereas the magnitude of decrement in vaspin level was $0.651 \pm 16.87\%$ in the control group. The magnitude of reduction in BW, BMI, and WC was 0.78%, 0.77%, and 1.36%, respectively. The magnitude of increment in FFM was 2.45%, whereas there was no significant change in WHR and FP in the exercise group.

Despite decreased fat mass, as the source of vaspin secretion, following exercise training, vaspin level increased in T2DM patients (4). The results of Kadoglou et al, Youn et al and Safarzade et al were in line with our results. They reported significant increase in vaspin levels after exercise training in the patients with T2DM (4,16,17), whereas Amouzad Mahdirezaji et al (20) and Barzegari & Amouzad Mahdirezaji (14) reported a significant decrease in vaspin level after 8-week resistance trainings in the male patients with T2DM. Furthermore, Amouzad Mahdirezaji et al reported no significant change in vaspin level after exercise in the patients with T2DM (15). Disease duration and intensity and pharmacotherapy as confounding variables which affect the results are factors which cause differences in vaspin level following changes in adipose tissues in the healthy and in the patients with T2DM. Vaspin as an adipocytokine is expressed in human adipose tissues and the expression is higher in the obese people compared to non-obese subjects (3). Moreover, vaspin concentration is significantly correlated with body composition (4,21), BMI, WHR, and WC (10), sex, insulin sensitivity and glucose metabolism (4,22,23). Weight loss occurs in result of regular exercise and caloric restriction

Table 1. Demographic, and Biochemical Data of the Female Patients With T2DM in Exercise and Control Groups

Variables	Exercise Group (n=18)		Control Group (n=13)	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Age (y)	45.44 ± 4.54		43.15 ± 3.31	
Weight (kg)	70.611 ± 8.671	70.111 ± 9.054	72.923 ± 7.296	73.230 ± 7.304
BMI (kg.m ²)	29.039 ± 4.083	28.829 ± 4.197	29.961 ± 2.933	30.082 ± 2.893
WC (cm)	89.277 ± 9.748	88.055 ± 9.619	91.538 ± 9.430	92.615 ± 9.242
HC (cm)	104.611 ± 9.810	104.833 ± 9.544	104.615 ± 8.636	106.384 ± 7.974
WHR (numerical value)	0.853 ± 0.052	0.841 ± 0.067	0.874 ± 0.050	0.870 ± 0.052
FP (%)	36.940 ± 4.072	34.932 ± 3.958	34.363 ± 1.418	34.908 ± 1.409
FM (kg)	26.282 ± 5.618	24.711 ± 5.624	25.108 ± 3.160	25.595 ± 3.033
FFM (kg)	44.328 ± 4.194	45.399 ± 4.432	47.815 ± 4.350	47.635 ± 4.539
TC (mg/dL)	183.000 ± 42.320	149.222 ± 36.030	161.615 ± 40.976	162.769 ± 42.363
TG (mg/dL)	153.944 ± 67.649	100.833 ± 31.311	117.538 ± 49.545	110.307 ± 37.493
FBS (mg/dL)	167.944 ± 5.032	98.722 ± 25.854	130.307 ± 52.321	151.846 ± 55.944
Insulin (mU/L)	11.542 ± 6.230	14.397 ± 3.848	13.103 ± 5.664	11.581 ± 4.783
HOMA-IR	4.682 ± 2.583	3.535 ± 1.451	4.120 ± 2.372	4.124 ± 1.852
QUICKI	0.312 ± 0.021	0.321 ± 0.017	0.316 ± 0.019	0.314 ± 0.018
Vaspin (ng/dL)	3.542 ± 0.522	4.125 ± 0.773	3.826 ± 0.894	3.694 ± 0.616

Abbreviations: BMI, body mass index; WC, waist circumference; HC, hip circumference; W/H, waist to hip ratio; FP, fat percentage; FM, fat mass; FFM, fat free mass; TC, total cholesterol; TG, triglycerides; FBS, fasting blood sugar; HOMA-IR, homeostatic model assessment of insulin resistance; QUICKI, quantitative insulin sensitivity check index.

E, exercise group (n = 18); C, control group (n = 13).

Values are shown as mean ± SD.

Table 2. Analysis of Covariance (ANCOVA) in Study Subjects

Variables	F	P	Partial Eta-Squared	Observed Power
Weight (kg)	14.720	0.001*	0.345	0.959
BMI (kg.m ⁻²)	12.810	0.001*	0.314	0.932
WC (cm)	21.389	0.001*	0.433	0.994
HC (cm)	1.138	0.295	0.039	0.178
WHR (numerical value)	0.373	0.546	0.013	0.091
FP (%)	13.694	0.001*	0.328	0.946
FM (kg)	30.130	0.001*	0.158	1.000
FFM (kg)	6.840	0.014*	0.196	0.714
TC (mg/dL)	5.099	0.032*	0.154	0.587
TG (mg/dL)	1.988	0.170	0.066	0.275
FBS (mg/dL)	13.323	0.001*	0.322	0.941
Insulin (mU/L)	17.773	0.001*	0.388	0.982
HOMA-IR	1.305	0.263	0.045	0.197
QUICKI	1.566	0.221	0.053	0.227
Vaspin (ng/dL)	8.888	0.007*	0.297	0.811

Abbreviations: BMI, body mass index; WC, waist circumference; HC, hip circumference; WH, waist to hip ratio; FP, fat percentage; FM, fat mass; FFM, fat free mass; TC, total cholesterol; TG, triglycerides; FBS, fasting blood sugar; HOMA-IR, homeostatic model assessment of insulin resistance; QUICKI, quantitative insulin sensitivity check index. Partial eta-squared (estimates effect size to demonstrate the changes of variable); Observed power (to indicate an adequate number of subjects); $P < 0.05$.

* Significant.

in obese subjects, causing significant decrease in vaspin concentration (21). In pre-diabetes, in obese subjects(24), and in the early stage of T2DM, vaspin level increases as a compensatory mechanism (higher body weight and decreased insulin sensitivity), and gradually decreases with a prolonged duration (22,25,26) in T2DM-induced diseases like cardiovascular disorders and in aggravation of vascular sclerosis (27-29). Low vaspin serum levels can be used as a protector against risk factors for the progression of T2DM (22), and other studies reported no difference in vaspin levels between the subjects with and without glucose abnormalities(4,23). Choi et al reported positive correlations between plasma vaspin concentrations and body composition in male subjects, while no such association was found in the females. Higher vaspin levels were associated with the metabolic syndrome in the males, while the association of vaspin concentrations with the presence of coronary artery intensity and characteristics of coronary artery platelets in T2DM females was verified (30).

Our results indicated a significant decrease in TC, and FBS levels, and a significant increase in insulin level, while no significant alteration was found in TG, HOMA-IR and QUICKI levels in the training group compared with the control group. The magnitude of reduction in TC and FBS was 17.19%, and 35.43%, respectively, and the magnitude of increment in insulin was 43.74% in the exercise group. Misra et al reported 3-month exercises leading to significant changes in TC, TG, and insulin sensitivity in T2DM patients (31). The elevated

concentration of vaspin in the serum was associated with obesity and impaired insulin sensitivity and a mediator of obesity and T2DM (32). This concentration increase could improve glucose tolerance and insulin sensitivity, while reducing food intake (33). Pharmacotherapy for improving insulin sensitivity such as metformin treatment could be an effective modality which caused vaspin decrease (34). HOMA-IR is a surrogate marker for insulin resistance in the patients with T2DM and was influenced by anthropometric measures (21,35) and had inverse correlations with vaspin concentrations in T2DM patients (4,22) with different durations of the disease (23), whereas Chang et al noted no relation between serum vaspin concentrations and HOMA-IR in obese subjects (21). It seems there are several factors involved in the contradictory results of researches. Subjects' age, obesity and lack of physical activity are some of the risk factors involved in the development of T2DM (1), so characteristics such as the baseline of body composition, age, sex, disease duration, intensity and progression, pharmacotherapy, and also the difference in the exercise protocol method (type, duration, intensity) are factors that affect the results. In fact the difference in patient's capacity to do exercise and the difference in method of exercise are essential factors in determining main energy source, as in low-intensity exercises, lipid oxidation decreases and shifts toward greater carbohydrate oxidation (2) which affects body composition and could indirectly affect lipid profile and vaspin level.

Conclusions

In conclusion, as our data suggested vaspin is a new biomarker for obesity and interactive exercise. Vaspin level decreases after exercise and weight loss, and increases in pre-diabetes and in early stage of diabetes, whereas by increasing duration of T2DM and progressive stage, vaspin behavior reverses.

Conflict of Interests

None.

Ethical Issues

Approval for study protocol was obtained from Local Ethics Committee affiliated to Islamic Azad University, Najafabad Branch, Iran (IR.IAU.NAJAFABAD.REC.1396.44). Written informed consent was obtained from all the participants.

Financial Support

None.

Acknowledgments

We would like to thank the support of Najafabad Branch, Islamic Azad University, Najafabad, Iran, and International Diabetes Prevention and Control Foundation, Mashhad, Iran. Further, the assistance of Nima Khosravi, and Dr.

Farhad Rajabpour Sanati -General practitioner of Mashhad University of Medical Sciences- are acknowledged.

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