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Original Article

Relationship of visfatin level to pancreatic endocrine hormone level, HOMA-IR index, and HOMA β-cell index in overweight women who performed hydraulic resistance exercise

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Abstract. [Purpose] This study aimed to examine the correlation of visfatin level to pancreatic endocrine hormone level, homeostasis model assessment of insulin resistance (HOMA-IR) index, and HOMA β-cell index in hydraulic resistance exercise. Furthermore, it investigated the relationship between visfatin level and other variables affected by exercise in overweight women. [Subjects and Methods] The exercise group trained for 12 weeks, 70 minutes/day, 5 days/week. Visfatin level, pancreatic endocrine hormone level, HOMA-IR index, and HOMA β-cell index were measured before and after the intervention. Based on the blood insulin and glucose concentrations, HOMA-IR index, the indicator of insulin resistance, and HOMA β-cell index, the indicator of insulin secretion level, were assessed. [Results] Interaction effects on visfatin level, insulin level, HOMA-IR index, and HOMA β-cell index were observed. Interaction effects on glucagon and glucose levels were not observed between the intervention groups. The correlations of visfatin level to insulin, glucagon, and glucose levels, and HOMA-IR and HOMA β-cell indexes were not significant for any of the subjects. [Conclusion] Therefore, the 12-week resistance exercise affected body composition, visfatin level, insulin level, HOMA-IR index, and HOMA β-cell index. Finally, visfatin was not related to insulin, glucagon, and glucose levels, and HOMA-IR and HOMA β-cell indexes.
Key words: Visfatin, Pancreatic endocrine hormones, Hydraulic resistance exercise

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INTRODUCTION

Visfatin (also known as nicotinamide phosphoribosyltransferase and pre-B cell colony-enhancing factor) is a multifunctional protein. Visfatin has been reported to be involved in several biological processes in the type 2 diabetes mellitus system[1–4].

Visfatin is a regulator of insulin secretion. In both human and animal models, visfatin appears to be upregulated as levels of obesity increase. Visfatin is also upregulated by hypoxia, inflammation, and hypoglycemia, and downregulated by insulin[2]. As the distribution of body fat, particularly visceral abdominal fat, might be even be more relevant than the total amount of stored fat, scientists have tried, with limited success, to identify the differences between these topographically distinct depots in order to understand what makes the intra-abdominal depot so deleterious[5].

Plasma visfatin has a stronger relationship to intra-abdominal (visceral) fat than to subcutaneous fat. In addition, similar to the action of insulin, visfatin may play a role in insulin resistance[6]. However, because several other studies have shown that visfatin levels are not correlated to fat mass, these relationships must continue to be investigated[1–4, 7].

Insulin resistance indicates a failing physiological response to insulin. Even if insulin is normally secreted, it has an impaired ability to remove glucose from the bloodstream to control blood sugar concentrations and results in high blood sugar levels[8]. Chronic high blood sugar levels increase the risk of diabetes and cardiovascular diseases[6].

Sedentary individuals and individuals with lower percentages of lean body mass have higher prevalence rates of insulin resistance. Regular exercise improves these factors, which relate to insulin resistance[6], and reduces the risk of comorbid conditions such as cardiovascular disease[9]. Given the role of exercise in the improvement of insulin resistance, and the potential role of visfatin in insulin resistance, exercise could potentiate a change in visfatin as insulin resistance is improved. Many studies that report visfatin levels simply rely on the relationship of visfatin to anthropometric variables or to the diagnosis of diabetes, but fail to account for the role of physical activity on these levels.

Another feature of type II diabetic patients is the failure

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of the functionality and decreased numbers of β-cells. The damage in the β-cell function, which reduces insulin secretion and inhibits the proper control of blood sugar levels, is explained as a crucial feature of the occurrence of chronic uncontrolled type II diabetes.

Several studies have examined the relationship between visfatin expression levels and homeostasis model assessment of insulin resistance (HOMA-IR) index in response to exercise training[10, 11]. However, the potential relationship between exercise training and changes in visfatin level and HOMA-IR index related to obesity, type 2 diabetes, and cardiovascular diseases has not been analyzed. In addition, while several research studies have used the HOMA-IR index as a parameter of diabetic risk, research studies that use the HOMA β-cell index are less common[12]. Preclinical changes and mediation of these variables utilizing lifestyle behavior modifications such as exercise have potential to alleviate the progression to diagnosed obesity-related disease such as diabetes and cardiovascular disease. In order to establish this potential mediation, first, preclinical changes should be examined and assessed.

This study examined not only the relationship between adipocytokines such as visfatin and HOMA-IR index in response to exercise training in overweight college-aged women. Furthermore, the primary objective of this study was to establish the relationship between visfatin, pancreatic endocrine hormones, HOMA-IR index, and HOMA β-cell index by using a 12-week hydraulic resistance exercise program.

SUBJECTS AND METHODS

The subjects were sedentary female overweight college students aged 20–26 years who had not been previously diagnosed with abnormal glucose metabolism or other health problems, and had body fat percentages greater than 25%. The subjects were randomly assigned to an exercise group (n = 15) and a control group (n = 12). The characteristics of the subjects are shown in Table 1.

This study was approved and reviewed by the institutional review board of the Human Care and Use Committee of the Society of Sport Research Institute of Dongguk University. Written consent was obtained from all of the subjects. The subjects were scheduled to participate in the hydraulic resistance exercise training at Dongguk University fitness center in Gyeong-Ju, South Korea.

During the 12-week intervention, the subjects in the hydraulic resistance exercise group were trained 5 days per week (from Monday to Friday), 70 minutes per day. The subjects in both the control and exercise intervention groups were instructed to maintain their current dietary intake and physical activity patterns for the duration of the study, and compliance with this instruction was assessed via physical activity and food frequency questionnaires administered at the beginning and end of the study.

Visfatin concentration was measured by using an EIA reader (E-max precision, Molecular Devices, USA). Insulin concentration was measured by using modular analytics (E170, Roche, Germany). Glucagon concentrations were measured by using a γ-counter (Cobra-5010 Quantum, Packard, USA). Glucose concentrations were measured by using the automated analyzer (ADVIA 1650, USA).

Table 1. Characteristics of the subjects (mean ± SD)

Variables	Exercise group (n = 15)	Control group (n = 12)
Age (years)	21.6 ± 1.6	20.8 ± 1.7
Height (cm)	162.1 ± 6.0	162.1 ± 5.9
Weight (kg)	62.0 ± 10.0	61.9 ± 6.8
Body mass index (kg/m^2)	23.5 ± 2.7	23.5 ± 1.7
Muscle mass (kg)	40.1 ± 6.1	39.2 ± 4.3
Body fat (%)	31.3 ± 3.9	31.0 ± 3.0

A human visfatin enzyme-linked immunosorbent assay kit (Biovision, USA), insulin (Roche), double antibody glucagon (Siemens, USA), and glucose (Bayer, USA) were used to determine the concentrations of visfatin (ng/mL), insulin (IU/mL), glucagon (pg/mL), and glucose (mg/dL), respectively. By using the analyzed insulin and glucose concentration level in the blood, HOMA-IR, which is the indicator of insulin resistance, was estimated and HOMA β-cell index, the indicator for insulin secretion level, was also assessed[13].

All of the subjects in the exercise group were asked to perform the same stretching routine prior to (warm up, 10 min) and after (cool down, 10 min) each training session. They performed a 50-min main exercise program that included a 50-min resistance training using hydraulic resistance exercise equipment (Neocean, Korea). The hydraulic resistance exercises each consisted of 1-min repetitions for each machine. Exercise intensity was monitored during the training sessions by using a Polar real-time system (Polar S610, Finland). The hydraulic resistance exercise training programs are shown in Table 2.

All of the descriptive data were expressed in terms of mean ± standard deviation. Independent t tests were performed to examine differences in the baseline characteristics of the subjects between the 2 groups. Two-way repeated analysis of variance was used to evaluate significant changes in dependent variables in the exercise group before and after the exercise program and to compare these values with those for the control group before and after the study period. The Pearson correlation was calculated to examine the relationship between visfatin and other variables such as insulin, glucagon, glucose, HOMA-IR index, and HOMA β-cell index. All of the analyses were performed by using SPSS version 18.0 (SPSS, Chicago, IL, USA). The statistical significance level was set at $p < 0.05$.

RESULTS

The subjects' baseline characteristics did not significantly differ between the groups ($p > 0.05$). The changes in body composition, visfatin level, pancreatic endocrine hormone level, HOMA-IR index, and HOMA β-cell index after hydraulic resistance exercise for 12 weeks are shown in Table 3. The interaction effects (time × group) on weight ($p = 0.04$), body mass index (BMI; $p = 0.02$), and body fat

Table 2. The hydraulic resistance exercise program[14)]

Classification	Type of exercise	%HRmax (rating of perceived exertion)			Note
		Adaptation	Improvement	Maintenance	
		Weeks 1 and 2	Weeks 3–11	Week 12	
Warm-up	Stretching (5 or 6 kinds)	40% (11)	40% (11)	40% (11)	8–10 min
Hydraulic resistance training	Pectoral fly/rear deltoid Leg press Shoulder press Squat Upright row Biceps/triceps Abdominal/low back Inner/outer thigh Rotary torso Glute/hamstrings Chest press Leg curl	40–60% (11–14)	50–80% (13–16)	65–75% (14–15)	45–50 min Speed: max Time: 1 min/each 12 min/1 set Rest time 20 sec/between each machine 5 min/between set
Cool down	Stretching (5 or 6 kinds)	40–50% (11–13)	40–50% (11–13)	40–50% (11–13)	8–10 min

Table 3. The change in body composition, visfatin, pancreatic endocrine hormones, HOMA-IR, HOMA cell after hydraulic resistance exercise for 12 weeks

	Exercise	Pre-exercise	Post-exercise	
Weight (kg)	Exercise	62.0 ± 10.0	61.4 ± 10.4	*
	Control	61.9 ± 6.8	62.5 ± 6.9	
BMI (kg/m^2)	Exercise	23.5 ± 2.7	23.2 ± 2.8	*
	Control	23.5 ± 1.7	23.9 ± 1.5	
Muscle mass (kg)	Exercise	40.1 ± 6.1	40.6 ± 6.0	
	Control	39.2 ± 4.3	38.9 ± 4.3	
Body fat (%)	Exercise	31.3 ± 3.9	29.6 ± 4.7	***
	Control	31.0 ± 3.0	32.0 ± 3.2	
Visfatin (ng/mL)	Exercise	2.3 ± 1.5	1.9 ± 0.9	*
	Control	1.8 ± 0.7	2.6 ± 1.5	
Insulin (IU/mL)	Exercise	9.1 ± 3.3	4.9 ± 2.8	***
	Control	6.1 ± 2.5	7.8 ± 1.7	
Glucagon (pg/mL)	Exercise	85.3 ± 6.7	55.4 ± 13.2	
	Control	87.9 ± 5.7	69.5 ± 11.3	
Glucose (mg/dL)	Exercise	85.3 ± 7.7	84.9 ± 6.2	
	Control	87.9 ± 5.7	91.3 ± 5.8	
HOMA-IR	Exercise	1.9 ± 0.8	1.1 ± 0.6	***
	Control	1.3 ± 0.6	1.8 ± 0.4	
HOMA β-cell	Exercise	153.0 ± 48.5	82.4 ± 43.8	***
	Control	89.8 ± 33.3	103.1 ± 28.8	

($p < 0.001$) were observed in body composition. However, the interaction effect (time × group) on muscle mass ($p = 0.086$) was not observed in body composition. The interaction effects (time × group) on visfatin ($p = 0.04$), insulin ($p < 0.001$), HOMA-IR ($p < 0.001$), and HOMA β-cell index ($p < 0.001$) were observed. However, the interaction effects (time × group) on glucagon and glucose were not observed between the exercise and control groups ($p > 0.05$). The correlations of visfatin to insulin level, glucagon level, glucose level, HOMA-IR index, and HOMA β-cell index are shown in Table 4. In the "all subjects" dataset, visfatin was not significantly correlated with any of the subjects ($p > 0.05$).

DISCUSSION

Obesity is the main factor of diabetic and cardiovascular diseases and their complications. In South Korea, changes in diet and physical activity that occur in women aged 20–30 years marks this as a crucial stage for intervention, but often they do not have prevalent signs or symptoms of

Table 4. Correlation of visfatin level with pancreatic endocrine hormone level, HOMA-IR index, and HOMA β-cell index

Category	Visfatin in hydraulic resistance (n = 15)		Visfatin in control (n = 12)	
	Pre	Post	Pre	Post
	r	r	r	r
Insulin	0.24	−0.06	0.27	0.26
Glucagon	−0.01	−0.23	−0.38	0.41
Glucose	−0.01	0.01	−0.38	−0.40
HOMA IR	0.19	−0.07	0.19	0.15
HOMA β-cell	0.25	−0.08	0.47	0.30

disease and still appear to be physically fit. Thus, the interest in investigating the impact of exercise has been low. However, the impact of exercise on preclinical measures demands further elucidation within this age group.

This study focused on the effectiveness of 12 weeks of hydraulic resistance exercise training on potential changes in body composition, visfatin level, insulin level, glucagon level, glucose level, HOMA-IR index, HOMA β-cell index, and the relationship between these variables. A significant decrease in visfatin level was observed, and visfatin level was not significantly correlated with the aforementioned variables in any of the subjects.

Traditionally, as aerobic exercise is associated with greater energy expenditure than resistance exercise, it is considered to be more effective in reducing body weight and fat mass[15]. However, many studies have reported that resistance exercise is more effective in increasing fat-free mass (FM)[13]. Malina[16] reported that the correlation between BMI and FM in young college students was high. Although the obese subjects in this study had high BMI, they also had higher FM than that reported for adults. In our study, hydraulic resistance exercise significantly decreased the weight, BMI, and body fat but did not increase the muscle mass.

Some plurality exists in the literature regarding the relationship of visfatin level, adiposity, and the effects of exercise on visfatin level. Furthermore, Lee et al. reported that 12 weeks of aerobic exercise training with an energy expenditure of 300–400 kcal/d decreased plasma visfatin levels in obese adolescents[11]. Meanwhile, Berndt et al. reported that they did not observe any significant relationship between visfatin levels and visceral adipose tissue as assessed by using computed tomography[16]. Furthermore, Ghanbari-Niaki et al. reported that plasma visfatin levels increased after short bouts of high-intensity exercise[17].

One potential explanation for the variance in study results is the relationship between visfatin and insulin levels. Visfatin and insulin levels operated with mechanistic similarity. However, opinions vary even on this point[18]. In particular, the relevance studies of visfatin level and HOMA-IR index reported many differing results[4, 18, 19]. Moreover, the relationship between exercise training and exhibited increases or decreases in plasma visfatin levels remains controversial. Some efforts have been made to demonstrate the relationship between exercise-induced changes in visfatin and changes in glucose and lipid metabolisms. However, research has not yet explained the mechanism thereby exercise is related to visfatin[20].

The results of this study show that hydraulic resistance exercise training decreased plasma visfatin levels in overweight college students. The precise underlying mechanisms cannot be elucidated in this study. This study, however, did agree with previous research demonstrating that 12 weeks of combined exercise reduced both visfatin and insulin secretion levels in obese female college students[21].

Based on the results shown in Table 3, a significant decrease was observed for insulin, HOMA-IR index, and HOMA β-cell index. However, no significant improvement was observed in the levels of glucagon and glucose after the hydraulic resistance exercise. Several studies also showed decreased insulin concentration[22, 23]. Without changes in blood glucose levels, reduced insulin concentrations would indicate that the speed and effectiveness of glucose clearance have improved and that insulin sensitivity increased through exercise training as expected[24]. Furthermore, regular exercise training including combined exercise might improve the ability of insulin to stimulate translocation of glucose transporter 4 (GLUT 4) to the muscle membrane after exercise[25]. In addition, the result of HOMA-IR index-related research revealed improvement in the reduction in the HOMA-IR index through exercise[26].

However, there is still the issue of which between insulin resistance and HOMA β-cell precedes the occurrence of diabetes. In the case where insulin resistance is argued to be the primary cause, decline in the function of β-cell is the later response to the gradual increase in insulin secretion due to the insulin resistance. However, those who argue that the malfunction of β-cell as the primary cause of diabetes state that the reduction in the insulin secretion is the reason that normal blood sugar levels would increase[27]. In addition, the HOMA-IR index seems to reflect insulin resistance, but there is still room for discussion regarding the correlation between HOMA β-cell index and the β-cell function of the pancreas.

Results show that β-cell malfunction is a powerful indicator, predictive of diabetes when the β-cell function is evaluated in terms of considering insulin resistance. This outcome is consistent with that of the study of Haffnet et al, in which they stated that the β-cell malfunction is the primary cause of diabetes. Through regular exercise, less insulin can carry the same amount of glucose to muscles and the liver. Therefore,

β-cells in the pancreas do not have to excessively secrete insulin, resulting in decreased HOMA-IR and HOMA β-cell indexes[28].

It was therefore believed that the effect of exercise would be beneficial to overweight women. This led to the present research that demonstrated the positive effect of hydraulic resistance exercise on overweight university students in their twenties with respect to visfatin, insulin, HOMA-IR, and HOMA β-cell measures.

The focus on young overweight women in their twenties was an advantage of this study, in contrast to previous studies that focused on middle-aged or older adults. Twelve weeks of supervised hydraulic resistance exercise did indeed affect weight, BMI, body fat, visfatin level, insulin level, HOMA-IR index, and HOMA β-cell index. However, it did not affect the muscle mass, glucagon level, and glucose level of our sample of overweight women. Thus, we conclude that hydraulic resistance exercise was useful for controlling obesity. However, visfatin did not demonstrate a relationship with insulin, glucagon, and glucose levels, and HOMA-IR and HOMA β-cell indexes.

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