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Changes in irisin levels in patients with hyperemesis gravidarum

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Summary

Purpose: The aim of this study was to compare levels of serum irisin in hyperemesis gravidarum (HG) patients to healthy gravidas. *Materials and Methods:* Twenty pregnant women with hyperemesis gravidarum (Group 1) and 20 healthy pregnant women (Group 2) all of similar ages, body mass index, and all at similar pregnancy development comprised the study cohort. Fasting serum samples were obtained and measured for irisin levels. Comparisons between groups were done by Mann Whitney U (MWU) test and $p < 0.05$ was considered as statistically significant. *Results:* All the patients in groups 1 and 2 were primigravid and age, gestational week, and body mass index values were similar. No statistically significant difference were present among these parameters ($p > 0.05$, MWU test). The plasma irisin concentrations in group 1 were significantly higher (irisin (average ±S D): 116.9 ± 32.3 ng/ml *vs.* 87.7 ± 26.2 ng/ml) compared to the control group. *Conclusion:* This study suggests a possible role of irisin, which might be involved in the pathology of HG.

Key words: Hyperemesis gravidarum; Primigravida; Irisin.

Introduction

Hyperemesis gravidarum (HG) is defined as intractable form of nausea and vomiting severe enough to require hospital admission [1]. It affects 2.3% of pregnancies [2]. To ensure a continuous supply of nutrients to the growing fetus despite intermittent food intake, changes in carbohydrate and lipid metabolism appears in normal pregnancy. HG can cause severe maternal nutritional deprivation.

Irisin, a novel peptide, has been described by Boström *et al.* in 2012 [3]. It is a muscle-derived messenger substance (myokine) and is involved in the mediation of systemic, health-related benefits from regular physical exercise. Preliminary studies showed that irisin has the potential to induce 'browning' of white adipocytes in mice.

It is known that serum lipid profile is altered in HG [4, 5]. The levels of irisin, a myokine affecting adipocytes, in pregnant women with HG is not known. The purpose of this study was to measure the levels of irisin in patients with HG and to compare them with healthy pregnant women. By this way, the authors aimed to find the probable relationships of irisin with energy metabolism other than exercise.

Materials and Methods

The study was conducted in Fırat University Obstetric and Gynecology Clinic after taking approval from Fırat University local ethics committee (Acceptance Number: 07/05). This trial was performed in compliance with the Declaration of Helsinki. All patients participating in the study were informed and signed concent forms were taken.

All the pregnant patients participating in the study were housewives in their first pregnancies. They were all in first trimester. Gestational-age, calculated according to last menstrual period, were also confirmed by measuring fetal crown-rump length by ultrasound. Socio-demographic and obstetric properties of all patients were recorded. Forty pregnant women were totally included in the study. Twenty pregnant women with HG constituted group 1 and 20 healthy pregnant without HG constituted group 2. The diagnosis of HG was based on the following criteria: presence of ketonuria in a spot urine analysis, dehydration, and need for hospital admission [6].

Pregnant patients who had any systemic disease as diabetes mellitus, thyroid dysfunction, medical problems as gastroenteritis or urinary tract infection, any psychiatric problems, and multiple pregnancy were excluded from the study. All the patients in the study group were below 35 years old and their body mass index were lower than 30. Urine analysis of all patients' specific gravidy, which indicated the water balance, were within normal ranges at the time of blood sampling.

Eight ml of venous blood samples were taken after eight-hour fasting in the morning between 8.00-9.00 a.m. four ml of these samples were centrifuged at 4,000 rpm for five minutes and stored at -80°C until analysis for irisin. Irisin levels were measured by device using commercial enzyme-linked immunosorbent assay (ELISA) kit. Measurements were completely done according to the manufacturer's instructions. Four ml of these venous blood samples were also centrifuged at 4,000 rpm for five minutes and the serums were stored at -80°C. The obtained serums were used for measuring triglycerides (TG), cholesterol, and high density lipoprotein (HDL). The levels of VLDL and LDL were calculated by

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Table 1. — *Demographic properties of the two groups (values shown as average ± SD).*

Characteristics	Group1 (n=20)	Group2 (n=20)	p value
Maternal age (years)	26.6±3.3	26.5±4.1	>0.05[+]
Gestational Week (weeks)	9.3±1.2	9.6±1.0	>0.05[+]
BMI (kg/m^2)	22.8±2.9	22.2±1.4	>0.05[+]

[+] MWU test, BMI: body mass index.

Table 2. — *Comparison of lipid parameters and serum irisin levels of the groups (values shown as average ± SD).*

Biochemical Parameters	Group 1 (n=20)	Group 2 (n=20)	p value
Triglycerides (mg/dl)	95.5±22.1	138.7±44.4	*<0.05*[+]
Total cholesterol (mg/dl)	139.0±29.4	156.0±19.9	>0.05[+]
VLDL (mg/dl)	21.4±6.3	34.5±3.8	*<0.05*[+]
LDL (mg/dl)	70.9±16.6	79.0±12.1	>0.05[+]
HDL (mg/dl)	47.9±11.2	56.1±16.7	>0.05[+]
Irisin (ng/ml)	116.9±32.3	87.7±26.2	*<0.05*[+]

[+]: MWU test.
VLDL: very low density lipoprotein, LDL: low density lipoprotein, HDL: high density lipoprotein.

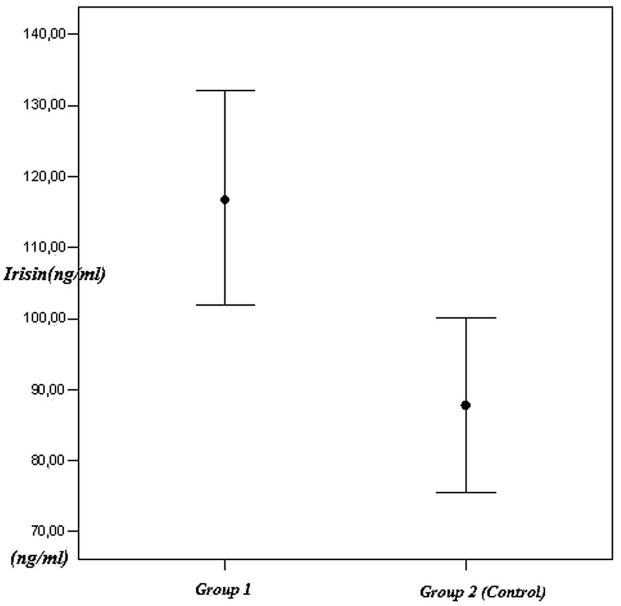

Figure 1. — The average figure of irisin levels in groups 1 and 2.

Friedewald formula. (VLDL: triglyceride/5, LDL: total cholesterol-(HDL+triglyceride/5)].

Statistical analysis

For statistical analysis, data were transferred to Statistical programme for Social Sciences Version 21.0. Comparisons between groups were done by Mann Whitney U (MWU) test and $p < 0.05$ was considered statistically significant.

Results

All the patients in groups 1 and 2 were primigravid and age, gestational week, and body mass index values were similar. No statistically significant difference were present among these parameters ($p > 0.05$, MWU test). Demographic properties of pregnants are shown in Table 1.

When lipid parameters in groups 1 and 2 were compared, it was found that levels of TG and very low density lipoproteins (VLDL) were low in statistically significant amount in group 1 (TG (average ± SD): 95.5 ± 22.1 mg/dl *vs.* 138.7 ± 44.4 mg/dl; $p < 0.05$, VLDL: 21.4 ± 6.3 mg/dl *vs.* 34.5 ± 3.8 mg/dl; $p < 0.05$, MWU test). Levels of total cholesterol, LDL, and HDL were also lower in group 1 but the differences were not statistically significant ($p > 0.05$, MWU test).

When the groups were compared according to irisin levels, it is found that irisin levels were high in a statistically significant amount in group 1 patients (116.9 ± 32.3 ng/ml *vs.* 87.7 ± 26.2 ng/ml; $p < 0.05$, MWU test). The lipid parameters and serum irisin levels are shown in table 2. The distribution of levels of irisin and their median values are shown in Figure 1.

Discussion

Irisin is a recently discovered myokine. Myokines are substances that are secreted from skeletal muscle cells in response to contraction and act in autocrine, paracrine, and endocrine pattern [7]. The positive effects of exercise on body composition, metabolic health, cardiovascular system, and mental health [8-11] were known for a long time but the mechanism was a mystery until Boström *et al.* discovered irisin [3]. Irisin is a 112 amino acids polypeptide which emerges after the cleavage of "fibronectin type III domain-containing protein 5" (FNDC5). FNDC5 is a glycoprotein which is released from the muscle in response to exercise [12, 13]. Adhesion of irisin to cell surface receptors increases the expression of "uncoupling protein 1" (UCP1) and "cell death-inducing DFFA-like effector a" (cidea) mRNA which causes browning of adipose tissue and thereby inducing thermogenesis [14].

Adipocytes are essentially two types as white adipose tissue (WAT) or brown adipose tissue (BAT). Their physical and metabolic characteristics are different. Adipocytes of WAT are primarily composed of TGs and fatty acids have few mitochondria and a relatively low metabolic rate, whereas adipocytes of BAT have many mitochondria and a relatively high metabolic rate [15]; hence WAT serve as the primary site for lipid storage, whereas adipocytes from BAT are highly specialized cells designed to produce heat. By browning of WAT, irisin increases total energy expenditure

and by this way it prolongs life-expectancy, causes weight loss, and diminishes diet induced insulin resistance in certain animal models [3]. Discovery of all these effects of irisin was fascinating because it is thought that it may be useful in treatment of obesity, diabetes, and metabolic syndrome. Much work is still needed before it can be used as a drug.

The present authors thought that in many other pathologic conditions characterized by imbalance in energy demand and expenditure, levels of irisin must be evaluated and they studied pregnant women with HG. They observed that irisin levels were high in statistically significant amount in pregnant patients with HG when compared to control group without HG. Blood lipid parameters were also low in pregnant patients with HG as shown in other studies [16].

To the present authors' knowledge, this is the first report that evaluates serum irisin levels in pregnant patients with HG. Although this data is limited, the results of this study showed the presence of increased levels of irisin in women with HG. Change in food intake in HG may cause a new distribution in energy utilization. High levels of irisin may be a compensatory mechanism to meet energy need of the starving pregnant patients with HG. By studying this peptide in different clinical situations, we can understand its other probable physiological effects.

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