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The Significance of Determining the Level of Visfatin in Blood Serum in Pregnant Women with Obesity

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Abstract

Obesity is currently considered as a polyethological, chronic, recurrent disease. With abdominal obesity, the synthesis of adipose tissue hormones – adipokines – increases significantly. Among the adipokines secreted by adipose tissue and affecting the development of insulin resistance and metabolic disorders, visfatin can be noted.

The purpose of the study was to determine the level of visfatin in the blood serum of pregnant women with obesity and to study its effect on metabolic parameters.

Materials and methods. The main group consisted of 213 women with abdominal obesity diagnosed before pregnancy. The control group included 80 women who had a normal body mass index before pregnancy. The average age of women in the main group was 29.0±0.44 years, in the control group – 25.7±0.47 years. Anthropometric studies conducted once in the 1st trimester included measurements of height, body weight, waist circumference (FROM) and hips (ABOUT). Calculated the ratio FROM/ABOUT and body mass index (BMI). Anthropometry was performed according to a standard procedure with an accuracy of 0.1 cm for height and circumference and 0.1 kg for weight. Obesity was diagnosed based on the calculation of the BMI index according to the Quetelet formula: BMI = body weight (kg) / height (m^2). The criteria for inclusion of patients in the main group were BMI values above 25 kg/m^2. The control group included women with a BMI from 18.5 to 25 kg/m^2. Obesity was regarded as abdominal with a waist circumference of more than 80 cm and an OT/OB ratio of ≥0.85.

The patients' blood was taken in the morning strictly on an empty stomach from the ulnar vein. The state of fat metabolism was assessed according to lipidogram data. In accordance with the goal, 52 pregnant women of the main group and 80 women of the control group at 8–12 weeks of gestation were determined the concentration of total cholesterol (OH), triglycerides (TG), low-density lipoproteins (LDL) and high-density lipoproteins (HDL).

To assess the degree of insulin resistance, a small homeostasis model (HOMA) was used to determine the HOMA-IR index, which was calculated using the formula: HOMA-IR = [insulin, μed/ml × glucose, mmol/l] / 22.5. A HOMA-IR value greater than 2.77 is considered as the presence of insulin resistance. Another criterion for insulin resistance is the calculation of the CARO coefficient according to the formula: CARO = [glucose, mmol/ l / insulin, MME/ ml]. CARO values below 0.33 indicate insulin resistance. The level of visfatin (ng/ml) in blood serum was studied by enzyme immunoassay.

The results of the study showed the presence of a relationship between serum visfatin and BMI. The negative correlation between the level of visfatin and anthropometric indicators indicates a decrease in its level with an increase in adipose tissue mass. In obese pregnant women, an inverse correlation was established between the level of visfatin and insulin. Analysis of the results showed that in abdominal obesity in pregnant women there is a close relationship between impaired lipid metabolism, insulin resistance and the level of visfatin in the blood serum.
Keywords: pregnant women, obesity, adipokines, visfatin

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Значение определения уровня висфатина в сыворотке крови у беременных с ожирением

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Резюме

Ожирение в настоящее время рассматривают как полиэтиологическое, хроническое, рецидивирующее заболевание. При абдоминальном ожирении значительно повышается синтез гормонов жировой ткани – адипокинов. Среди адипокинов, секретируемых жировой тканью и оказывающих воздействие на развитие инсулинорезистентности и метаболических нарушений, можно отметить висфатин.

Цель. Определение уровня висфатина в сыворотке крови беременных женщин с ожирением и изучение его влияния на показатели метаболизма.

Материалы и методы. Основную группу составили 213 женщин с абдоминальным ожирением, диагностированным до беременности. В контрольную группу вошли 80 женщин, имевших до беременности нормальный индекс массы тела. Средний возраст женщин основной группы составил 29,0±0,44 года, контрольной группы – 25,7±0,47 года. Антропометрические исследования, проводимые однократно в 1-м триместре, включали измерение роста, массы тела, окружности талии (ОТ) и бедер (ОБ). Вычисляли отношение ОТ/ОБ и индекс массы тела (ИМТ). Антропометрию проводили согласно стандартной методике с точностью до 0,1 см для роста и окружностей и 0,1 кг – для массы. Ожирение диагностировали на основании расчета показателя ИМТ по формуле Кетле: ИМТ = масса тела (кг) / рост ($м^2$). Критериями включения пациенток в основную группу были значения ИМТ выше 25 $кг/м^2$. В контрольную группу вошли женщины с ИМТ от 18,5 до 25 $кг/м^2$. Ожирение расценивалось как абдоминальное при окружности талии более 80 см и отношении ОТ/ОБ ≥0,85.

Забор крови пациенток производился утром строго натощак из локтевой вены. Состояние жирового обмена оценивалось по данным липидограммы. В соответствии с поставленной целью 52 беременным основной группы и 80 женщинам

контрольной группы на 8–12-й нед. гестации проводили определение концентрации общего холестерина (ОХ), триглицеридов (ТГ), липопротеинов низкой (ЛПНП) и высокой плотности (ЛПВП).
Для оценки степени резистентности к инсулину использовали малую модель гомеостаза (Homeostasis Model Assessment – HOMA) с определением показателя HOMA-IR, который рассчитывали по формуле: HOMA-IR = [инсулин, мкЕД/мл × глюкоза, ммоль/л] / 22,5. Значение HOMA-IR больше чем 2,77 рассматривается как наличие инсулинорезистентности. Еще одним критерием инсулинорезистентности служит расчет коэффициента CARO по формуле: CARO = [глюкоза, ммоль/л / инсулин, мкМЕ/мл]. Значения CARO ниже 0,33 свидетельствуют об инсулинорезистентности. Уровень висфатина (нг/мл) в сыворотке крови изучали методом иммуноферментного анализа.
Результаты. Показано наличие связи сывороточного висфатина с ИМТ. Отрицательная корреляционная взаимосвязь между уровнем висфатина и антропометрическими показателями свидетельствует об уменьшении его уровня при увеличении массы жировой ткани. У беременных с ожирением была установлена обратная корреляционная связь между уровнем висфатина и инсулина. Анализ полученных результатов показал, что при абдоминальном ожирении у беременных женщин имеется тесная связь между нарушением липидного обмена, инсулинорезистентности и уровнем висфатина в сыворотке крови.
Ключевые слова: беременные, ожирение, адипокины, висфатин

■ INTRODUCTION

Obesity is a chronic multifactorial disease that develops under the influence of metabolic and genetic factors, changes in the function of the endocrine system, and energy balance disorders. Adipose tissue plays a special role in regulating the constancy of body weight and energy homeostasis of the body [1]. Adipose tissue is an active endocrine organ that produces a large number of hormones – adipokines [2, 4, 5]. Adipose tissue hormones affect almost all systems of the human body, regulating insulin sensitivity and energy metabolism, neuroendocrine and immune processes, activate blood clotting and inflammatory reactions [2, 4]. Currently, more than 50 adipokines are known, which differ in structure and functions performed [6, 8].

Among the adipokines secreted by adipose tissue and affecting the development of insulin resistance and metabolic disorders, visfatin can be noted [7, 8]. Visfatin is a protein with a crystalline structure that has the properties of a cytokine and an enzyme involved in the biosynthesis of nicotinamide adenine dinucleotide. Visfatin is a hormone of white adipose tissue, found in chondrocytes, skeletal muscles and synovial membrane cells [9]. To date, there is no unified understanding of the physiological and pathophysiological role of visfatin, however, recent studies suggest the involvement of this adipokine in the pathogenesis of the development of obesity-related metabolic disorders. It has been proven that the level of visfatin increases in proportion to the level of obesity and correlates with the indicators of total cholesterol and low-density lipoprotein cholesterol [7, 9].

In obesity, a number of factors lead to metabolic changes, affecting the course of pregnancy. Given the widespread prevalence of maternal obesity in the modern world,

the role of adipose tissue hormones in the development of pregnancy complications in this group of women deserves special attention. Currently, it has been convincingly proven that an increase in body mass index and obesity are associated with the development of reproductive health disorders. Overweight women have an increased risk of developing preeclampsia, eclampsia, gestational diabetes mellitus, fetal macrosomia, caesarean section, intrauterine fetal death and infant mortality [3, 4]. Visfatin is expressed by fetal membranes, secreted by amniotic epithelial cells during pregnancy and has anti-apoptotic properties [8].

■ THE PURPOSE OF THE STUDY

To determine the level of visfatin in the blood serum of pregnant women with obesity and to study its effect on metabolic parameters.

■ MATERIALS AND METHODS

The study of clinical and anamnestic indicators allowed us to distinguish two groups of patients. The main group consisted of 213 women with abdominal obesity diagnosed before pregnancy. The control group included 80 women who had a normal body mass index before pregnancy. The average age of women in the main group was 29.0±0.44 years, in the control group – 25.7±0.47 years. Anthropometric studies conducted once in the 1st trimester included measurements of height, body weight, waist circumference (WC) and hips (HC). Calculated the ratio WC/HC and body mass index (BMI). Anthropometry was performed according to a standard procedure with an accuracy of 0.1 cm for height and circumference and 0.1 kg for weight. Obesity was diagnosed based on the calculation of the BMI index according to the Quetelet formula: BMI = body weight (kg) / height (m^2). The criteria for inclusion of patients in the main group were BMI values above 25 kg/m^2. The control group included women with a BMI from 18.5 to 25 kg/m^2. Obesity was regarded as abdominal with a waist circumference of more than 80 cm and an WC/HC ratio of ≥0.85.

The patients' blood was taken in the morning strictly on an empty stomach from the ulnar vein. The state of fat metabolism was assessed according to lipidogram data. In accordance with the goal, 52 pregnant women of the main group and 80 women of the control group at 8–12 weeks of gestation were determined the concentration of total cholesterol (OH), triglycerides (TG), low-density lipoproteins (LDL) and high-density lipoproteins (HDL). High- and low-density lipoproteins were determined by the homogeneous method, total cholesterol and triglycerides were determined by the enzymatic colorimetric method. The atherogenicity coefficient was calculated by the formula: AC = (OH – HDL) / HDL. The ratio of HDL was also determined/LDL and calculated the concentration of very low-density lipoproteins (LDL) according to the formula: VLDL = TG / 2.18. To study carbohydrate metabolism, the concentration of venous blood glucose and fasting immunoreactive insulin was measured. To assess the degree of insulin resistance, a small homeostasis model (HOMA) was used to determine the HOMA-IR index, which was calculated using the formula: HOMA-IR = [insulin, μed/ml × glucose, mmol/l] / 22.5. A HOMA-IR value greater than 2.77 is considered as the presence of insulin resistance. Another criterion for insulin resistance is the calculation of the CARO coefficient according to the formula: CARO = [glucose, mmol/l / insulin, MME/ml]. CARO values below 0.33 indicate insulin resistance. The level of visfatin (ng/ml) in blood serum was studied by enzyme immunoassay.

Statistical data analysis was carried out using the MedCalc statistical software package for biomedical research. The evaluation of the obtained results was carried out by methods of statistical description and verification of statistical hypotheses. To compare normally distributed quantities, the Student's t-test was used, in the case of a difference in the distribution from the normal, the nonparametric Mann-Whitney criterion (U-criterion) was used. The data for the parametric distribution are presented in the form of the average value of the measured value and the standard error (M±m) and in the form of the median Me (25%; 75%) for features with a distribution other than normal. The evaluation of the strength and relationship between phenomena or signs was carried out using the Pearson pair correlation coefficient (r). The critical value of the level of statistical significance (p) when testing null hypotheses was assumed to be 0.05.

■ RESULTS AND DISCUSSION

During the clinical and anthropometric examination in the comparison groups, statistically significant differences in the studied parameters were revealed between pregnant women with obesity (the main group) and the control group, $p<0.05$ (Table 1).

The average BMI in pregnant women of the main group was 39.5±0.57 kg/m^2, which was 1.6 times higher than this indicator in women of the control group (24.1±0.34 kg/m^2, $p<0.05$). The average weight in pregnant women of the main group was 103.0±1.38 kg ($p<0.05$). When comparing anthropometric indicators in pregnant women of the main group, higher values of WC, HC and WC/HC index were also revealed, which corresponds to the abdominal type of distribution of adipose tissue. In pregnant women with abdominal obesity, WC corresponded to 90.0±0.73 cm, HC – 99.1±0.72 cm, the ratio of WC/HC – 0.90±0.004, which significantly exceeded the average values in women of the control group ($p<0.05$). At the same time, the indicators of women of the control group with normal body weight were significantly lower in comparison with the patients of the main group according to somatometric parameters. In women of the control group, the average body weight was 62.1±0.87 kg, WC – 73.4±0.48 cm, HC – 88.1±0.65 cm, the ratio WC/HC – 0.83±0.004.

Table 1
Characteristics of anthropometric parameters in women of the examined groups (M±m) (min-max)

Anthropometric parameter	Main group (n=213)	Control group (n=80)
Age, years	29.8±0.54* (19–44)	25.7±0.47 (17–39)
Height, cm	161.6±0.56 (146–176)	160.6±0.59 (148–171)
Weight, kg	103.0±1.38* (72–145)	62.1±0.87 (46–82)
BMI, kg/m^2	39.5±0.57* (26.3–55.3)	24.1±0.34 (17.8–32.5)
WC, cm	90.0±0.73* (70–101)	73.4±0.48 (67–84)
HC, cm	99.1±0.72* (82–114)	88.1±0.65 (76–103)
WC/HC	0.90±0.004* (0.79–0.99)	0.83±0.004 (0.76–0.90)

Note: * $p<0.05$ compared to the control group.

We evaluated the level of visfatin in the blood serum of healthy pregnant women, which is necessary to create an idea of its normal values. The average serum level of visfatin in healthy pregnant women was 25.7 (23.6; 26.6) ng/ml. The level of visfatin in the blood serum was evaluated in 52 obese pregnant women. When quantifying the level of visfatin, data were obtained indicating a slight decrease in it in the group of obese pregnant women compared with the group of pregnant women with normal body weight – 24.1 (22.7; 25.2) ng/ml ($p<0.01$).

When analyzing the results of the study in pregnant women with abdominal obesity, a negative correlation was revealed between the level of visfatin and anthropometric indicators: BMI ($r=–0.346$), WC ($r=–0.520$), HC ($r=–0.570$), WC/HC ($r=–0.171$) ($p<0.05$). The revealed links indicate a decrease in the level of visfatin with an increase in BMI, WC and HC.

Table 2 shows the indicators of lipid metabolism in pregnant women of the main and control observation groups.

Analysis of the results of the study showed that pregnant women of the main and control groups statistically significantly differed in terms of blood lipid spectrum (OH, TG, LDL, VLDL). Significantly higher levels of OH, TG, LDL and VLDL in the blood serum were found in obese pregnant women, which is the result of their increased production.

When conducting a correlation analysis of the level of visfatin with the studied parameters of the lipid profile of blood serum, a negative relationship was obtained with the level of LDL ($r=–0.295$), HDL ($r=–0.241$) and TG ($r=–0.219$) ($p<0.05$). There was also a positive and negative correlation between BMI and OH ($r=0.251$), BMI and TG ($r=0.401$), BMI and VLDL ($r=0.365$), BMI and HDL ($r=–0.318$) ($p<0.05$).

The levels of immunoreactive blood insulin and the HOMA-IR index in obese pregnant women significantly exceeded the indicators of the control group. The fasting serum insulin level in pregnant women with abdominal obesity was 16.1 (13.7; 17.8) mcME/ml. At the same time, the fasting insulin level in obese pregnant women was higher than in patients with a normal BMI – 8.4 (7.5; 10.3) μme/ml, $p<0.001$. The fasting serum glucose level in obese patients was 5.89 (5.82; 5.95) mmol/l and was also higher compared to the control – 4.62 (4.49; 4.76) mmol/l, $p<0.001$. The insulin resistance index (HOMA-IR) in women with abdominal obesity was 4.21(3.54; 4.70) units. At the same time, the values of this index were significantly higher in patients of the main group than in women of the control group – 1.72 (1.49; 2.17) units, $p<0.001$. The CARO coefficient in women with abdominal obesity was slightly higher than the quantitative criterion of insulin resistance

Table 2
Indicators of lipid metabolism in women of the examined groups, Me (25%; 75%)

Monitoring groups	Indicators						
	OH, mmol/l	LDL, mmol/l	HDL, mmol/l	TG, mmol/L	LDL, mmol/l	KA, Convent. units	HDL/ LDL units
Main group (n=52)	5.03* (4.70; 5.43)	2.66* (2.57; 2.77)	1.78 (1.68; 1.91)	1.77 (1.53; 1.87)**	0.81** (0.70; 0.86)	1.82 (1.79; 1.84)	0.66 (0.65; 0.68)
Control group (n=80)	4.63 (4.34; 4.98)	2.57 (2.39; 2.72)	1.72 (1.58; 1.95)	0.97 (0.90; 1.11)	0.44 (0.41; 0.50)	1.69 (1.54; 1.75)	0.67 (0.66; 071)

Note: the differences are significant in relation to the control group: * $p<0.05$, ** $p<0.001$.

and was at the level of 0.36 (0.32; 0.38) units. At the same time, the values of the indicator were significantly lower in the patients of the main group than in the women of the control group – 0.55 (0.53; 0.59) units, $p<0.001$.

There was also a significant feedback between the levels of visfatin and insulin ($r=-0.132$, $p<0.05$).

Thus, the results of our study showed the presence of a relationship between serum visfatin and BMI. A decrease in the concentration of visfatin in the blood serum is observed in pregnant women with obesity. The negative correlation between the level of visfatin and anthropometric indicators indicates a decrease in its level with an increase in adipose tissue mass. The results of our study also showed that an inverse correlation was found between the level of visfatin and insulin in obese pregnant women.

According to our data, in patients with abdominal obesity, a negative correlation was established between the level of visfatin and the levels of LDL, HDL and TG. It was also found that there was a positive and negative correlation between lipidogram and BMI. Analysis of the data of this study showed that in abdominal obesity in pregnant women there is a close relationship between impaired lipid metabolism, insulin resistance and the level of visfatin in the blood serum.

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