

Gender characteristics of carbohydrate and lipid metabolism and vaspin levels in hypertensive patients with obesity

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The aim of this study is to analyze gender features of patients with arterial hypertension (AH) associated with obesity and to investigate their interaction with the indicators of carbohydrate and lipid metabolism and vaspin levels.

Materials and methods. 72 patients with AH were selected for the study. In dependence to the presence of obesity, the patients were divided into 3 groups. The 1st group with AH included 32 patients without obesity. Among them there were 19 (59.4 %) women and 13 (40.6 %) men. The 2nd group consisted of 40 patients with overweight and obesity. Among them there were 17 (42.5 %) women and 23 (57.5 %) men. The 3rd (control) group consisted of 16 healthy individuals aged from 28 to 41 years old. Among them there were 10 (62.5 %) women and 6 (37.5 %) men. All the examined patients underwent anthropometric measurements, blood pressure levels, blood levels of insulin, glucose, blood lipid levels, serum vaspin concentrations, insulin resistance (IR) index.

Results. Gender differences in vaspin levels and the degree of IR have been found only in males of both study groups. In this case, these parameters significantly correlated with anthropometric indices and insulin levels in men.

Conclusions. The study showed that the increase of the studied parameters of carbohydrate and lipid metabolism and vaspin levels was observed in men and women with hypertension associated with obesity and without it. However, gender differences were found in vaspin levels and the IR degree only in males of both study groups. The parameters of vaspin and IR significantly correlated with anthropometric indices and HOMA – IR in men. Perhaps, gender characteristics should be taken into account in the treatment tactics choice of patients with hypertension and obesity.

Key words:

obesity, hypertension, gender, insulin resistance, lipid metabolism, adipokines, vaspin.

Zaporozhye medical journal
2017; 19 (6), 711–715

DOI:
10.14739/2310-1210.2017.6.114501

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Гендерні характеристики вуглеводного та ліпідного обміну й рівнів васпіну при артеріальній гіпертензії в пацієнтів з ожирінням

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Мета роботи – аналіз гендерних особливостей пацієнтів з артеріальною гіпертензією (АГ), що пов'язані з ожирінням, і дослідження їх взаємодії з показниками вуглеводного та ліпідного обміну та рівнями васпіну.

Матеріали та методи. 72 хворих з АГ відібрали для дослідження. Залежно від наявності ожиріння пацієнти були розділені на 3 групи. До 1 групи з АГ включені 32 пацієнти без ожиріння. Серед них 19 (59,4 %) жінок і 13 (40,6 %) чоловіків. Другу групу становили 40 пацієнтів із надмірною вагою та ожирінням. Серед них 17 (42,5 %) жінок і 23 (57,5 %) чоловіків. Третя (контрольна) група – 16 здорових осіб віком від 28 до 41 року. Серед них 10 (62,5 %) жінок і 6 (37,5 %) чоловіків. Усі досліджувані пацієнти пройшли вимірювання антропометричних показників, рівнів артеріального тиску, рівнів інсуліну в крові, глюкози, ліпідів крові, сироваткової концентрації васпіну, розрахунок індексу інсулінорезистентності (ІР).

Результати. Гендерні відмінності в рівнях васпіну та ступені ІР виявлені тільки в чоловіків з обох досліджуваних груп. У цьому випадку визначені параметри вірогідно корелюють з антропометричними показниками та рівнями інсуліну в чоловіків.

Висновки. Дослідження показало, що збільшення досліджуваних показників вуглеводного й ліпідного обміну та рівнів васпіну спостерігалось як у чоловіків і жінок із гіпертензією, що асоційована з ожирінням, так і без нього. Однак гендерні відмінності виявляються в рівнях васпіну та ступенях ІР тільки в чоловіків в обох досліджуваних групах. Параметри васпіну та ІР вірогідно корелюють з антропометричними показниками та HOMA–ІР у чоловіків. Можливо, у виборі тактики лікування хворих із гіпертонією та ожирінням слід брати до уваги гендерні характеристики.

Ключові слова:

ожиріння, артеріальна гіпертензія, гендерні особливості, інсуліно-резистентність, обмін ліпідів, адіпокіни, васпін.

Запорізький медичний журнал. – 2017. – Т. 19, № 6(105). – С. 711–715

Гендерные характеристики углеводного и липидного обмена и уровней васпина при артериальной гипертензии у пациентов с ожирением

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Цель работы – анализ гендерных особенностей пациентов с артериальной гипертензией (АГ) и ожирением, исследование их взаимосвязей с показателями углеводного и липидного обменов и уровнями васпина.

Материалы и методы. 72 больных с АГ были отобраны для исследования. В зависимости от наличия ожирения пациенты разделены на 3 группы. В первую группу с АГ включены 32 пациента без ожирения. Среди них 19 (59,4 %) женщины и 13 (40,6 %) мужчины. Вторую группу составила из 40 пациентов с избыточным весом и ожирением. Среди них 17 (42,5 %) женщин и 23 (57,5 %) мужчины. Третью (контрольную) группу составили 16 здоровых лиц в возрасте от 28 до 41 года. Среди них 10 (62,5 %) женщин и 6 (37,5 %) мужчин. Все исследуемые пациенты прошли измерения антропометрических показателей, уровней артериального давления, уровней инсулина, глюкозы, липидов крови, сывороточной концентрации васпина, расчет индекса инсулинорезистентности (ІР).

Ключевые слова:

ожирение, артериальная гипертензия, гендерные особенности, инсулинорезистентность, обмен липидов, адипокины, васпин.

Запорожский медицинский журнал. – 2017. – Т. 19, № 6(105). – С. 711–715

Результаты. Различия в уровнях васпина и степени ИР были обнаружены только у мужчин в обеих исследуемых группах. В этом случае данные параметры достоверно коррелируют с антропометрическими показателями и уровнями инсулина у мужчин.

Выводы. Исследование показало, что увеличение исследуемых показателей углеводного и липидного обменов и уровней васпина наблюдалось как у мужчин и женщин с гипертензией, ассоциированной с ожирением, так и без него. Однако различия проявляются в уровнях васпина и степенях ИР только у мужчин в обеих исследуемых группах. Параметры васпина и ИР достоверно коррелируют с антропометрическими показателями и HOMA-ИР у мужчин. Возможно, в выборе тактики лечения больных с гипертензией и ожирением следует принимать во внимание гендерные характеристики.

Introduction

The growth of cardiovascular diseases, arterial hypertension (AH) in particular, and its complications is accompanied by changes of lipid and carbohydrate metabolism parameters in almost all patients. AH and metabolic changes are characterized by high prevalence and chronic course, constant increase of patient population and high disability [1].

One of the primary pathogenetic mechanisms of AH and associated metabolic syndrome (MS) is the development of insulin resistance (IR) and hyperinsulinemia, which occur in case of insulin hormonal effect insufficiency [2]. Alimentary obesity (OB) as a distinct metabolic disease is also associated with hyperinsulinemia and insulin resistance (IR). In the presence of OB the main role in IR development and progression and its various manifestations is played by fat tissue that synthesizes adipokines with various local, peripheral and central effects. Over the past few year an idea has emerged there that adipose tissue is not only energy depot but also an active organ, participating in life support of an organism [3].

Visceral adipose tissue synthesizes and secretes a huge amount of hormonally active substances that determines the development of eating disorders, IR and impaired glucose metabolism with the development of diabetes, AH and LV hypertrophy, dyslipidemia, microalbuminuria, hypercoagulation syndrome [4].

Vaspin, visceral adipose tissue-derived serpin, belongs to the family of serine proteases inhibitors and has been identified recently. It has been found that vaspin consists of 395 amino acids and shares 40 % identity with alpha₁-antitrypsin. It was experimentally confirmed that in case of its expression insufficiency in adipose tissue, worsening of metabolic parameters was observed in models of obesity in rats, and administration of vaspin to animals has improved glucose tolerance, insulin sensitivity and stimulated the expression of genes related to IR [5]. The authors [5] demonstrated that the administration of vaspin to animals resulted in a persistent effect of reducing blood glucose level.

Purpose

The aim of this study is to analyze gender features of patients with AH associated with OB and to investigate their interaction with the indicators of carbohydrate and lipid metabolism and vaspin levels.

Materials and methods

The latest recommendations of the Ministry of Healthcare of Ukraine for AH treatment have formed the basis for selecting the study groups [6]. Patients with symptomatic AH, type 1 diabetes and other endocrinological disorders and

clinical evidence of coronary artery disease were excluded from this study.

Blood pressure (BP) was assessed according to the average BP, obtained from the three measurements in 2-minute intervals in the sitting position. The body mass index (BMI) was determined according to the formula: BMI = weight (kg)/height (m²). Normal values of BMI up to 27 kg/m². The fasting insulin concentration in serum was determined by ELISA using a set manufactured by "DRG" (USA). Measured by ELISA, insulin level on an empty stomach higher than 12.5 mu/ml was considered to be hyperinsulinemia indicator. To determine the IR index HOMA – IR was used (normal value up to 2.7). Lipid metabolism indices (levels of total cholesterol (TC), triglycerides (TG) and cholesterol of high density lipoproteins (HDL cholesterol)) and fasting glucose concentration in serum were determined by accepted laboratory diagnostic methods. Estimation of vaspin concentration in serum was performed by ELISA using a set manufactured by "Ray Biotech, Inc." (Belgium).

72 patients with AH were selected for the study. Depending on the presence of obesity the patients were divided into 3 groups. The first group with AH included 32 patients without obesity (BMI < 25 kg/m²). The average age of the patients was (39.0 ± 8.5) years. Among them there were 19 (59.4 %) women and 13 (40.6 %) men.

The second group consisted of 40 patients with overweight and obesity (BMI ≥ 25.0 kg/m²). The average age was (44.2 ± 10.2) years. Among them there were 17 (42.5 %) women and 23 (57.5 %) men. Among the 40 patients selected for the study (45.5 %), 22 (55 %) patients had the 1 degree of obesity, 10 (25 %) patients had the 2 degree of obesity, and the third degree of obesity was diagnosed in 8 (20 %) patients.

The third (control) group consisted of 16 healthy individuals aged from 28 to 41 years. The average age was (34.5 ± 6.5) years. Among them there were 10 (62.5 %) women and 6 (37.5 %) men.

The results are presented as mean values ± standard deviation from the mean value (M ± SD). Statistical data processing was performed using Statistica, version 8.0. To assess differences between groups in the distribution close to normal, Student's test was used. Data were considered reliable by the level of statistical significance of P < 0.05.

Results and discussion

Analysis of the anthropometric parameters showed that BMI differs significantly in the group of patients with AH associated with obesity (group 2) from the control group (group 3) (P = 0.001) and from the patients of the first and second groups (P < 0.05) (Table 1). Even a slight but significant change in BMI, which occurs within normal range, evidences of metabolic processes violation and AH development.

A significant increase of the waist circumference (W)

Table 1. Anthropometric indicators in the examined patients

Indicator. Statistical indicator (P), units	Sex	Groups of patients			Statistical indicator (P)		
		1 (n = 32) AH	2 (n = 40) AH+OB	3 (n = 16) control	P ₁₋₂	P ₁₋₃	P ₂₋₃
BMI, kg/m ²	female	24.4 ± 0.4	32.6 ± 3.4	23.2 ± 1.2	0.05	0.001	0.001
	male	24.7 ± 0.3	33.3 ± 4.4	23.6 ± 1.8	0.05	0.06	0.001
	total	24.5 ± 0.35	32.9 ± 3.	23.4 ± 1.5	0.05	0.082	0.001
P _{m-f}		0.030	0.553	0.527			
W, cm	female	69.4 ± 4.7	104.1 ± 9.6	67.08 ± 4.81	0.001	0.986	0.001
	male	88.4 ± 2.4	106.4 ± 8.7	84.00 ± 10.14	0.001	0.058	0.001
	total	78.9 ± 4.1	105.2 ± 8.9	73.85 ± 11.12	0.001	0.166	0.001
P _{m-f}		0.001	0.141	0.001			
SBP, mm Hg	female	144.1 ± 6.4	161.1 ± 7.4	127.3 ± 2.9	0.05	0.05	0.001
	male	147.1 ± 5.2	164.0 ± 2.2	130.9 ± 3.0	0.001	0.05	0.001
	total	146 ± 5.8	162.6 ± 4.8	129.1 ± 3.2	0.05	0.001	0.001
P _{m-f}		0.078	0.088	0.472			
DBP, mm Hg	female	85.5 ± 4.6	95.6 ± 4.4	79.4 ± 2.0	0.110	0.146	0.001
	male	87.1 ± 7.1	96.4 ± 3.0	81.0 ± 2.5	0.174	0.416	0.001
	total	86.3 ± 5.8	96.0 ± 3.7	80.2 ± 2.1	0.110	0.306	0.05
P _{m-f}		0.106	0.096	0.317			

Table 2. Biochemical data of patients depending on OB and AH according to the gender

Indicator, units	Groups (number)				Statistical indicator P			
	AH 1 group (n = 29)		AH + OB 2 group (n = 33)		P _{1m-1f}	P _{2m-2f}	P _{1m-2f}	P _{1m-2f}
	F	M	F	M				
Fasting glucose, mmol/l	5.5 ± 0.4	5.8 ± 0.41	6.4 ± 0.31	6.0 ± 0.4	0.242	0.081	0.108	0.05
Fasting insulin, mcMU/ml	14.2 ± 1.6	17.6 ± 3.5	20.2 ± 3.5	23.4 ± 3.4	0.05	0.184	0.175	0.05
HOMA-IR	3.47 ± 0.4	4.54 ± 0.62	5.75 ± 1.81	6.24 ± 2.8	0.267	0.05	0.05	0.05
TC, mmol/l	4.90 ± 0.5	5.2 ± 0.4	5.82 ± 0.35	5.74 ± 0.5	0.116	0.144	0.121	0.190
TG, mmol/l	1.37 ± 0.2	1.5 ± 0.2	1.79 ± 0.15	1.84 ± 0.3	0.142	0.173	0.206	0.118
HDL, mmol/l	1.39 ± 0.61	1.36 ± 0.3	1.15 ± 0.6	1.09 ± 0.42	0.222	0.304	0.156	0.117
LDL, mmol/l	2.94 ± 0.7	3.03 ± 0.6	3.5 ± 0.6	3.65 ± 0.5	0.340	0.174	0.088	0.406
Vaspin concentration, pg/ml	200.8 ± 20.5	302.4 ± 30.8	440.0 ± 26.2	386.0 ± 23.6	0.05	0.05	0.05	0.05

(P = 0.001) was revealed in men compared with women in the first and third groups. A comparison of BP did not demonstrate gender differences in any of studied groups but statistically significant increase of both systolic blood pressure (SBP) and diastolic blood pressure (DBP) were revealed between the groups of patients with AH and patients with AH associated with OB compared to healthy people (P < 0.05).

The results of biochemical studies of patients with AH are presented in the *Table 2*. The study of lipid metabolism in patients of the first and second groups showed the following results: on the background of obesity we observed a tendency to increase in all main indices of lipid metabolism, but no significant differences when dividing the study subjects by gender were detected (*Table 2*).

Comparing the fasting glucose levels of men and women within the same group did not differ significantly, but test results demonstrated differences when compared women of the first and the second groups (P < 0.05). Insulin levels in blood serum in the fasted state statistically differed between female and male patients with AH and OB and also when compared the female patients of the first and second groups (P < 0.05). The presence of AH associated with OB resulted in a significant increase in the HOMA index on the grounds of gender identity, and also when compared women of the first and second groups and men of the first and second groups.

Vaspin concentration in the blood serum differed significantly between both women and men in the first group, and between the genders in the second group (AH+OB) (p < 0.05).

Correlation analysis revealed significant relationships of vaspin levels only in men with AH, with OB or without it. For example, vaspin levels in men of the first group correlated with BMI (r = 0.420; P < 0.05), (r = 0.592; P < 0.05), HOMA (r = 0.410; P = 0.0002). In men and women with AH associated with obesity, vaspin level correlated with insulin levels (r = 0.710, P < 0.05). In case of combined pathology in men correlation relationships found between the vaspin levels and BMI indices (r = 0.510; P < 0.05) and HOMA indexes (r = 0.52; P < 0.05). Changes in correlation of vaspin levels with IR may be due to visceral fat weight, accumulation of which is a major risk factor of IR.

Thus, the analysis of gender differences between the groups of men and women suffering from AH and combined pathology (AH + OB) showed that waist circumference and BMI of women were significantly reduced; also women were characterized by lower levels of insulin and HOMA index. Other indicators of carbohydrate and lipid metabolism, as well as the constitutional symptoms between the groups did not differ significantly. Vaspin levels correlated with parameters of the visceral fat distribution and insulin levels, especially in men with combined pathology.

OB is considered as one of the main factors of AH. The relationship between OB and AH has been confirmed in the Framingham study (Framingham Heart Study), which demonstrated that increasing body mass significantly increased prevalence of AH in different age groups in both sexes [7]. Patients with AH often have the OB component of MS, which is important for both women and men. In the modern view adipose tissue performs endocrine function. A change in the content of adipocytokines in the adipose tissue can inhibit the insulin action at the receptor and intracellular level. It is assumed that the induction of mRNA expression of human vaspin in the adipose tissue is regulated by BMI and may be associated with IR and the change in glucose metabolism. In addition, it has been found that the concentration of circulating vaspin is increased in healthy women compared with men. However, the association of vaspin levels with sex, age, and BMI in patients with OB, metabolic and cardiovascular diseases has shown conflicting results [8].

It has been shown in our study that the gender differences are found in BMI values and waist circumference in the first group (Table 1). The differences in other anthropometric indicators between men and women with AH and with combined pathology (AH + OB) have not been found. Attention should also be paid to the lack of gender differences in lipid metabolism in patients of the first and second (AH + OB) groups. However, reliable gender differences have been demonstrated between the insulin levels in patients with AH.

Vaspin levels were significantly higher in women than in men in both study groups (Table 2). Women demonstrated lower levels of fasting insulin and HOMA, compared to men. This is probably connected with protective effect of estrogen, which provides a lower risk of cardiovascular disease in women of younger age groups [1]. Estrogens have a regulatory effect on the renin-angiotensin system activity, inhibiting the conversion of angiotensin I to angiotensin II. Lower BP in women of reproductive age could be attributed to direct vascular effect of estrogens – decrease in cardiac output in combination with vasodilatation. In addition, estrogens have the ability to reduce IR [1].

Vaspin levels correlated with BMI, waist circumference and male sex in patients with OB and AH, which is coherent with the results of authors studying gender characteristics of other proinflammatory adipocytokines [9]. Comparing changes in the concentrations of vaspin in men and women, it should be noted that when OB is as an additional factor of the metabolic syndrome it increases the significance of changes in carbohydrate metabolism, which is consistent with the results of other authors [10]. Vaspin is adipokine, which correlates with OB, visceral fat distribution, metabolic and cardiovascular diseases, although our results contradict the data obtained by other authors [1]. The increase of vaspin in serum reflects the process of AH formation primarily due to metabolic disorders. In the presence of OB complicated by AH vaspin level in the serum increases with the development of AH prior to the formation of life-threatening heart failure, dilated cardiomyopathy, etc.

Conclusions

1. The study showed that the increase of the studied parameters of carbohydrate and lipid metabolism and vaspin levels was observed in men and women with AH associated with OB and without it.

2. However, gender differences were found in vaspin levels and the degree of IR only in males of both study groups. The parameters of vaspin and IR significantly correlated with anthropometric indices (BMI, $r = 0.42$ to $r = 0.592$, $P < 0.005$, respectively) and insulin levels ($r = 0.710$, $P < 0.005$), and HOMA ($r = 0.52$, $P < 0.005$) in men. Perhaps, gender characteristics should be taken into account in the treatment tactics choice of patients with hypertension and obesity.

The perspective of further scientific research includes design of new strategies of obese patients with AH therapy considering gender.

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Конфлікт інтересів: відсутній.

Conflicts of Interest: authors have no conflict of interest to declare.

Надійшло до редакції / Received: 15.05.2017

Після доопрацювання / Revised: 03.07.2017

Прийнято до друку / Accepted: 06.07.2017