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ДИФЕРЕНЦІЙНО-ДІАҐНОСТИЧНІ ОСОБЛИВОСТІ МЕТАБОЛІЧНОГО СИНДРОМУ З ОЖИРІННЯМ ПРИ НАЯВНОСТІ ТА ВІДСУТНОСТІ ХРОНІЧНОЇ ІШЕМІЧНОЇ ХВОРОБИ СЕРЦЯ З ВРАХУВАННЯМ СТАТІ

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Реферат

Мета. *У нашій праці з'ясовано відмінності між метаболічним синдромом (МС) з ожирінням, а також в поєднанні цього захворювання з коморбідною патологією (ХІХС).*

Матеріал і методи. *Обстежено 126 пацієнтів з МС: з них - 82 без ХІХС і 44 з ХІХС. Всім хворим визначали показники ліпідного обміну, рівні кортизолу, пролактину, тиреотропного гормону (ТТГ), вільного тироксину (fT4), глікозильованого гемоглобіну (HbAlc) і глюкози, з врахуванням при цьому ультрасонографії серця.*

Результати й обговорення. *При МС без ХІХС виявлено підвищення рівнів кортизолу (в обох статей), ТТГ та пролактину (тільки у жінок). Тоді як при МС з ХІХС спостерігали нормалізацію рівнів кортизолу та пролактину, одночасно з підвищенням вмісту ТТГ в обох статей, а рівень fT4 перебував в межах контрольних величин. У пацієнтів з МС та ХІХС, незалежно від статі, зміни даних параметрів супроводжувались підвищенням загального холестерину (ЗХС), тригліцеридів (ТГ), ліпопротеїдів низької щільності (ЛПНЩ), ліпопротеїдів дуже низької щільності (ЛПДНЩ) та зниженням ліпопротеїдів високої щільності (ЛПВЩ), тоді як при МС з ожирінням без ХІХС збільшувались тільки ТГ та ЛПДНЩ. При даній комор бідній патології збільшувалися товщини міжшлуночкової перегородки (МШП) та задньої стінки лівого шлуночка (ТЗС ЛШ), кінцево-діастолічний розмір лівого шлуночка (КДР ЛШ) та передньо-задній розмір лівого передсердя (ЛП) в обох статей, тоді як при МС відмічався лише ріст товщини МШП та розмір ЛП. Результативним при МС з ожирінням є підвищення у жінок пролактину і ТТГ, на відміну від чоловіків. При поєднаній патології незалежно від статі зберігається тільки високий рівень ТТГ.*

Висновок. *Таким чином, діагностичні особливості МС з ожирінням без ХІХС характеризуються гормональними зрушеннями у жінок, на відміну від чоловіків, тоді як при коморбідній патології ендокринні зрушення не мають гендерних особливостей.*

Ключові слова: *метаболічний синдром, ожиріння, пролактин, тиреотропний гормон*

Abstract

DIFFERENTIAL DIAGNOSTIC FEATURES OF METABOLIC SYNDROME WITH OBESITY IN THE PRESENCE OR ABSENCE OF CHRONIC CORONARY ARTERY DISEASE CONSIDERING GENDER DIFFERENCES

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Aim. *The differences between metabolic syndrome (MS) with obesity with or without comorbid pathology (chronic coronary artery disease i.e. CAD) were explicated in the research.*

Material and Methods. *126 patients with MS were examined. MS without chronic CAD was diagnosed in 82 patients and MS with chronic CAD was diagnosed in 44 patients. Levels of lipid spectrum, cortisol, prolactin, thyroid-stimulating hormone (TSH), free thyroxine (fT4), glycosylated hemoglobin (HbAlc), and glucose were determined in all patients. Ultrasonography of the heart was taken into account.*

Results and Discussion. *Increased levels of cortisol, TSH and prolactin (only in women) were observed in patients with MS without chronic CAD. Normal levels of cortisol and prolactin were observed in the patients with MS and chronic CAD simultaneously with increase of TSH levels in men and women the fT4 level was within normal limits. Changes in given parameters were accompanied by increase in total cholesterol (TCH), triglycerides (TG), low-density lipoprotein cholesterol (LDL CH) and very low-density lipoprotein cholesterol (VLDL CH) and decrease in high-density lipoprotein cholesterol (HDL CH) in patients with MS and chronic CAD regardless of gender, whereas only TG and VLDL CH were increased in patients with MS with obesity without chronic CAD. Interventricular septal thickness(IVST), left ventricular posterior wall thickness (LVPWT), left ventricular end-diastolic size (LVEDS) as well as left atrium anteroposterior dimension (LA) increased in men and women with comorbid pathology, whereas only IVST and LA were increased in MS. Increased prolactin and TSH in women in contrast to men in MS with obesity have been established. High levels of TSH were recorded in the presence of combined pathology regardless of gender.*

Conclusion. *Thus, diagnostic features of MS with obesity without chronic CAD are characterized by hormonal abnormalities in women, in contrast to men, whereas endocrine changes are not gender-specific in the presence of comorbid pathology.*

Keywords: *metabolic syndrome, obesity, prolactin, thyroid-stimulating hormone*

Introduction

The chronic coronary artery disease's morbidity requires thorough study; first of all, taking into account the pathogenesis of this pathology

combined with improvement of clinical features already at the premorbid stage [3, 13, 14].

Obesity is one of the risk factors of chronic CAD. Development of this condition is associated with metabolic abnormalities at different levels of integration [9, 10, 15].

At the same time, in our opinion, neuroendocrine effects begin playing the leading role. They are realized by metabolic changes. These abnormalities are the clinical basis and are confirmed in several studies [7, 8, 11, 12]. The problem of combination of obesity with the development of chronic CAD needs further improvement to prevent its progression in relation with MS in different levels of integration in the clinic [15]. Pathogenetic and clinical features of chronic CAD in MS with obesity, differently for men and women, have not been studied thoroughly. It needs further refinement to better understand the prognosis, taking into account gender features. In our opinion, determination of morbidity of chronic CAD is questionable without regard of gender [1, 2, 4, 5].

The aim of the study. To determine diagnostic parameters for MS with obesity, and for MS with chronic CAD, which could be common specific criteria for predicting features of development of this pathology considering gender.

Material and Methods

126 patients with obesity II-III degree were examined. MS was diagnosed in 82 patients (23 men (28.05%), and 59 (71.95%) women). Chronic CAD with MS was diagnosed in 44 patients (men - 17 (38.64%) women - 27 (61.36%). The control group consisted of 40 virtually healthy individuals aged 27.55±1.28 years (men - 17 (42.5%), women - 23 (57.5%)).

Anthropometric parameters such as height, body weight, and waist circumference (WC) were measured in the patients. The presence of obesity was defined by body mass index (BMI), according to the WHO (1997). Obesity of II-III degree was diagnosed in patients. Blood glucose level and glycosylated hemoglobin (HbAlc) were determined. The total cholesterol level (TCH), triglycerides (TG), high and very low density lipoprotein cholesterol (HDL CH, LDL CH) were determined by colorimetric method. Low density lipoprotein cholesterol (LDL CH) was calculated according to the WT.Friedewald formula (1972), and the coefficient of atherosclerosis (CA) - by the AN Klimova formula.

The lipid profile was evaluated in accordance with the recommendations of the European Society of Cardiology (ESC) and European Society of Atherosclerosis (EAS) for 2016.

Levels of free thyroxine (fT4), thyroid-stimulating hormone (TSH), prolactin, and cortisol were studied by method of immunoassay analysis. Blood glucose content was determined by colorimetry.

The ultrasonography of heart was performed on the Acusson Cypres apparatus. The interventricular septal thickness (IVST), left ventricular posterior wall thickness (LVPWT), dimensions of the ascending aorta, left ventricular end-diastolic size (LVEDS), right ventricular anteroposterior dimension (RV), left atrium anteroposterior dimension (LA), and ejection fraction (EF) were determined.

The criteria for inclusion of patients with chronic CHD were as follows: stable angina I - II functional class (according to NYHA); cardiovascular insufficiency stage I defined according to the recommendations of the European Society of Cardiologists and the Association of Cardiologists of Ukraine.

Exclusion criteria included pregnancy, endocrine pathology, chronic diseases at the stage of sub- and decompensation, and cardiovascular insufficiency stages II-III.

The diagnosis of MS was established according to the diagnostic criteria of the International Federation of Diabetes (IDF 2005) [6].

Statistical analysis was performed using T-Student test and Mann-Whitney U-criterion. The strength of relationship between variables was determined by the Pearson correlation coefficient (r).

Results and Discussion

The level of blood glucose equaled 5.67±0.16 mg/l in patients with MS, and 5.61±0.19 mg/l in patients with chronic CAD at MS, i.e. was increasing compared to the control group, which was a sign of impaired glucose tolerance and is included in the criteria of MS. Similar changes were observed in

Table 1

Blood pressure levels and ultrasonographic parameters of heart in studied groups

Parameters	Control	MS	Chronic CAD with MS
Right ventricular anteroposterior dimension (RV)	2.0[1.8; 2.2]	2.2 [1.8;2.3]	2.05 [1.7;2.6]
Dimensions of the ascending aorta	2.8[2.45; 3.15]	3.0 [2.6;3.25]	3.2 [3.1;3.3]
Interventricular septal thickness (IVST),	0.9[0.9 ;1.0]	1.1 [0.85;1.2] p1<0.05 p2<0.05	1.2 [1.1;1.13] p2<0.05 p3<0.05
Left ventricular posterior wall thickness (LVPWT)	0.9[0.9; 1.0]	1.0 [0.8;1.15] p2<0.05	1.2 [1.1;1.3] p2<0.05 p3<0.05
Left ventricular end-diastolic dimension (LVEDD),	4.7[4.35; 4.95]	4.4 [4.15;4.75] p2<0.05	4.95 [4.65;5.1] p2<0.05 p3<0.05
Ejection fraction (EF). %	62[60; 65]	64.5 [61.0;66.5]	62.0[60.0;65.5]
Left atrium anteroposterior dimension (LA) см	3.1[2.9; 3.4]	3.75[3.4;4.1] p1<0.05	4.15 [3.5;4.35] p3<0.05
Systolic blood pressure, (SBP) mmHg	109.25±2.21	148.7±2.17 p1<0.05 p2<0.05	160.3±3.89 p2<0.05 p3<0.05
Diastolic blood pressure, (DBP) mmHg	68±1.43	93.9±1.49 p1<0.05 p2<0.05	98.44±1.42 p2<0.05 p3<0.05

p1 - significant difference between control and MS
p2 - significant difference between MS and chronic CHD with MS
p3 - significant difference between control and chronic CHD with MS

dimension of HbAlc which was at the level 5.6 [5.41;6.1] in patients with MS and with obesity, compared to 5.85 [5.5;6.1] in patients with chronic CAD in MS which was reliably higher compared to healthy individuals - 4.57 [4.05;5.21].

Regarding anthropometric indicators, body mass - 97±1.57 kg, height-164.3±1.21 cm, WC(m) 106.05±1.21 cm, WC(w) - 97.41±0.86 cm, body mass index(BMI) - 36.2±0.3 kg/m^2 were observed in patients with MS and with obesity, while patients with chronic CAD at MS were characterized by indicators such as body mass - 118.7±1.48 kg, height - 167.05±2.14 cm, WC(m) 116.17±1.1 cm, WC(w) 112.2±1.38 cm, body mass index(BMI) 42.99±1.25 kg/m^2. These anthropometric indicators confirmed obesity in patients.

According to the results of our studies presented in Table 1, increase of LA is a general shift in both groups, while the increase of IVST-1.2 [1.1; 1.13], LVPWT - 1.2 [1.1; 1.3] and LVEDD - 4.95 [4.65; 5.1] were observed in patients with chronic CAD at MS in comparison to patients with MS and with control group. At the same time, these parameters were similar for men and women. It should be noted that EF and RV did not change in the studied groups.

Thus, according to results of echocardiography, increase in LA and IVST are common shifts in ultrasonography of heart dimensions in patients with MS and chronic CAD with MS with obesity compared to virtually healthy individuals. Besides, the comorbid pathology is characterized by the increase in LVPWT and LVEDD.

As we can see from Table 2, increased levels of TG 1.9 [1.73, 2.21] mmol/l and VLDL CH 0.86 [0.79, 1.0] mmol/L, were observed in patients with MS with obesity.

Levels of TCH 5.41 [4.995; 6.51] mmol/L, LDL CH 3,9 [3.24; 4.56] mmol/L, CA 5, 11 [3.85, 6.78], TG - 1.95 [1.38; 2.48] mmol/L, and VLDL CH 0.89 [0.63; 1.13] mmol/L are increased in patients with chronic CHD and MS. HDL CH level 0.89 [0.8; 1.02] mmol/L is decreased in this pathology.

Consequently, lipid metabolism is affected at the levels of VLDL CH and TG already in patients with MS with obesity, whereas, patients with MS and chronic CAD with obesity are characterized by changes at the level of lipid spectrum parameters studied, regardless of the gender.

Gender specifics that were found in the process of studying hormones are presented in Table 3. Thus, increased level of prolactin 24.27±2.61 ng/ml and TSH level - 4.32±0.45 μU/dl were observed in women in comparison to men with MS with obesity

Table 2

Parameters of lipid spectrum in patients with chronic CAD with MS at obesity, MS with obesity and control

Parameters	control	MS	Chronic CAD with MS
TCH, mmol/l	4.8[3.89; 5.19]	5.04 [4.43;5.5] p2<0.05	5.41[4.995;6.51] p2<0.05 p3 <0.05
TG, mmol/l	0.85[0.69; 0.94]	1.9[1.73;2.21] p1 <0.05	1.95[1.38;2.48] p3 <0.05
HDL CH, mmol/l	1.25[1.03; 1.54]	1.20[0.98;1.39] p2<0.05	0.89[0.8;1.02] p2<0.05 p3 <0.05
LDL CH, mmol/l	3.24[1.87; 3.54]	3.0[2.54;3.29] p2<0.05	3.9[3.24;4.56] p2<0.05 p3 <0.05
VLDL CH, mmol/l	0.39[0.31; 0.43]	0.86 [0.79;1.0] p1 <0.05	0.89[0.63;1.13] p3 <0.05
CA	2.3[1.41; 3.42]	3.3[3.01;3.3] p1 <0.05 p2<0.05	5.11[3.85;6.78] p2<0.05 p3 <0.05

p1- significant difference between control and MS
p2 - significant difference between MS and chronic CHD with MS
p3 - significant difference between control and chronic CHD with MS

and with the control group. Cortisol level is equally elevated in these two groups (women and men with MS at obesity) compared to control group.

Normalization of prolactin level in women is 13.05±1.05 ng/ml and cortisol level in both groups (women and men) were observed in patients with chronic CAD with MS with obesity. The TSH level is increased in men 9.08±3.35 μD/dl and in women 6.18 ±1.8 μS/dl. The level of free thyroxine remains at the same degree in all studied patients.

As a result, it was found that several hormonal changes studied in the research are gender specific. Consequently, hormonal changes in MS are characterized by increased TSH and prolactin in women, whereas, elevated level of TSH with normal prolactin levels are maintained in MS with chronic CAD and obesity, both for men and women. The cortisol level does not depend on gender in studied patients in both groups.

Correlation analysis has been used to confirm the results of the research.

Correlation between ultrasonographic

Table 3

Indicators of laboratory parameters in patients with chronic CAD with MS and obesity in comparison with MS and obesity and control group

Parameters	control	MS	chronic CAD with MS
Prolactin (women), ng / ml	11.34±1.17	24.27±2.61 p1<0.05 p2<0.05	13.05±1.05 p2<0.05
Prolactin (men), ng/ml	7.9±0.59	12.83±1.46	9.45±0.53
TSH, mkOd/dl (women)	1.95±0.27	4.32±0.45 p1<0.05 p2<0.05	6.18±1.8 p2<0.05 p3<0.05
TSH (men), mkOd/dl	2.05±0.25	2.53±0.66 p2<0.05	9.08±3.35 p2<0.05 p3<0.05
fT4, (women), ng/dg	1.35±0.06	1.4±0.11	1.395±0.07
fT4, (men), ng/dg	1.37±0.06	1.47±0.09	1.38±0.06
Cortisol, ng/ml (women)	152.33±10.06	243.4±16.3 p1<0.05 p2<0.05	164.2±20.5 p2<0.05
Cortisol, (men), ng/ml	158.85±15.8	237.17±13.6 p1<0.05 p2<0.05	169.78±18.77 p2<0.05

p1 - significant difference between control and MS
p2 - significant difference between MS and chronic CAD with MS
p3 - significant difference between control and chronic CAD with MS

parameters was found in the patients with chronic CAD with MS.

Thus, the IVST positively correlates with the LVEDS (r=0.72), LA (r=0.70), LVPWT and negatively correlates with EF (r=-0.69). Similarly, positive correlation is observed between RV, LVEDS, LVPWT, and LA with a negative correlation with EF. Systolic blood pressure positively correlates with the LA(r=0.31).

As for parameters of lipid spectrum, a positive correlation between TCH, TG, VLDL CH, and the LA, LVEDS, and the level of systolic blood pressure were found.

Negative correlation between cortisol and prolactin (r=-0.4) in women in studied groups has been found. It should be noted that there is a positive correlation between TSH and VLDL CH (r=0.36), as well as between TSH and TG (r=0.35) in patients with chronic CAD and MS. In addition, a direct correlation between TSH and LVEDS (r=0.41) and inverse correlation of cortisol level to the IVST(r=-0.75), LVPWT (r=-0.75), LA (r=-0.59), and LVEDS(r=-0.56) were investigated.

Conclusions

As a result of the research, it can be argued that MS with obesity is characterized by initial changes in lipid metabolism, namely an increase in the level of TG and VLDL CH that is accompanied by the growth of the IVST and LA.

The increase in TCH, LDL CH and decrease in HDL CH are joined with the above changes in the chronic CAD with MS with obesity that leads to changes in LVEDS and LVPWT. These parameters were not gender specific in all patients.

In this case, the gender features of hormonal shifts in individuals of both groups are clearly traced. First of all, these features are characterized by increased prolactin and TSH levels in women with MS with obesity, whereas these parameters were within the normal limits in men. Prolactin level reaches its control level in women with comorbid pathology. Level of TSH is increased, but fT4 is within its normal limits in men and women with chronic CAD with MS with obesity. These abnormalities may indicate subclinical hypothyroidism, regardless of the gender. The content of cortisol in patients with chronic CAD with MS with obesity decreases to the level of healthy individuals. Thus, the shifts of prolactin and TSH metabolism are specific criteria of this comorbid pathology, indicating the pathogenetic features of the development of chronic CAD with MS in women.

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