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GENDER FEATURES IN THE ASSESSMENT OF INSULIN RESISTANCE IN PATIENTS WITH TYPE 2 DIABETES AND ITS COMBINATION WITH METABOLIC SYNDROME

Abstract: This article presents the results of a comparative analysis of insulin resistance indicators (HOMAIR, HOMAb, and QUICKI) in men and women suffering from type 2 diabetes (DM-2) and a combination of DM-2 with metabolic syndrome (MS). It has been shown that in patients with diabetes-2, an aggravated combination with MS, pathological changes in the indices reflecting tissue insulin resistance are revealed to a greater degree, which seems to confirm the role of estrogen protection in women.

Thus, a certain significance of gender differences in the formation of insulin resistance disorders in patients with DM-2, regardless of the presence of MS, was demonstrated.

Key words: diabetes mellitus type 2, metabolic syndrome, insulin resistance, insulin sensitivity, gender differences.

Language: English

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Introduction

According to the WHO assessment, DM-2 is a disease characterized by impaired carbohydrate metabolism and caused by predominant insulin resistance (IR) and relative insulin deficiency, or a predominant defect of insulin secretion with or without IR [1;16]. Thus, the formation of DM-2 occurs due to 2 major defects: IR and dysfunction of the β -cells of the pancreas that produce insulin [3].

The majority of patients with DM-2 have a primary (inherited) defect, manifested in a decrease in tissue sensitivity to insulin. As a result, insulin producing β -cells have to produce more insulin, and when this ability decreases, hyperglycemia also develops, which is especially characteristic of MS [11].

At the present stage, a number of structural mathematical models have been developed, the socalled IR indices [6], of which the $HOMA_{IR}$ (Homeostasis Model Assessment), reflecting the resistance to insulin, HOMA_B, reflecting secretor activity of b-cell, and QUICKI index (quantitative insulin sensitivity check index), a quantitative index of insulin sensitivity, is quite informative and widely used [10; 13].

In recent years, a certain importance has been given to gender differences in the defeat of atherosclerosis, coronary heart disease and other pathological conditions in the hormonal and biochemical profile [4; 5; 14], which is mainly associated with the protective effect of estrogen in women [7; 9].

In the light of the above, in the present article we attempted to clarify possible sex differences in the development of IR and the level of insulin secretion by conducting a comparative analysis of data obtained from male and female patients diagnosed with DM-2 and a combination of DM-2 with MS.

MATHERIALS AND METHODS

147 patients (87 men and 60 women) who were on an outpatient examination. The average age of patients was $58,97 \pm 0.93$ years. During the clinical examination, height, heart rate, blood pressure, Quetelet's index (body mass index, BMI) were measured. The diagnosis of DM-2 and MS was



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established on the basis of the recommendations of the ADA and WHO [1; 11; 16].

Inclusion criteria were: the presence of DM-2 of different variants of the clinical course and compensation, combined with MS or without it.

Exclusion criteria were: symptomatic arterial hypertension, oncological diseases (found at the time of treatment or in history), tuberculosis, HIV infection, viral hepatitis, mental illness, decompensated cardiovascular diseases, hormonal drugs, pregnancy, lactation.

From 73 patients with DM-2 without MS in 33 (22,45%) was mild, in 40 (27,21%) – moderate clinics of DM-2. In 47 (31,97%) DM-2 was in compensated (HbA1c<7%), in 26 (17,69%) – insub-compensatedstage (HbA1c<7,5%).

From 74 patients with DM-2 combined with MS in 28 (19,05%) was mild, in 46 (31,29%) – moderate clinicsof DM-2. In31 (21,09%) DM-2 wasincompensated (HbA1c<7%), in 43 (29,25%) – insub-compensatedstage (HbA1c<7,5%).

Of the 73 patients we examined in the DM-2 subgroup without MS, mild DM-2 was observed in 33 (22.45%), and DM-2 of moderate severity was observed in 40 (27.21%) patients; in 47 (31.97%) DM-2 was in the compensation phase (HbA1c <7%), in 26 (17.69%) - in the subcompensation phase (HbA1c <7.5%).

Of the 74 patients examined in the DM-2+MS subgroup, 28 (19.05%) had a mild course of DM-2, and 46 (31.29%) patients had moderate-type DM-2; in 31 (21.09%) patients DM-2 was in the compensation phase (HbA1c <7%), in 43 (29.25%) - in the subcompensation phase (HbA1c <7.5%).

Laboratory examination included:

1. Determination of fasting blood glucose and insulin levels on a fully automated robotic analyzer BS 200 E by MINDRAY (USA-China) for laboratory determination of glycemia using the appropriate Human Diagnostic reagents (Germany);

2. Glycated hemoglobin (HbA1c) using portable disposable cartridges on the analyzer A1cCare (USA) byWHO recommendations [17];

3. HOMA1-IR, HOMA-b and QUICKI indices were calculated using suggested formulas [10;13].

Statistical analysis were performed using Microsoft Excel 7.0 and ANOVA.

The results and discussion.

As can be seen from the data presented in the table 1, in the DM-2 subgroup without concomitant MS, there was a significant trend towards an increase in the level of glucose and glycated hemoglobin (HbA1c) in the blood of men, reaching $9,6 \pm 0,25$ and

 $7,69 \pm 0,15$ compared with women in the subgroup of $8,68 \pm 0,24$ and $7,2 \pm 0,15$ (p = 0,009819; p = 0,023849, respectively). At the same time, the level of insulin in the blood in the same subgroup was higher for women: 19,94 ± 2,22 versus 10,83 ± 0,89 (p = 0,000297). The above-described differences by gender resulted in significantly higher values IR of HOMA_{IR}, HOMA β and QUICKI insulin resistance indexes in women who made up the subgroup.

It should be noted that in the DM-2+MS subgroup, in which DM-2 was combined with MS, there were no significant differences depending on the se[of any of the parameters studied.

It is known that gender differencis definitely associated with mortality [15], and such diseases as atherosclerosis that occurs in men early enough (at about 30 years of age), and in women only after menopause. In this case, it is believed that female sex hormones, primarily estrogens, play a key role in antiatherosclerotic protection [12]. In basic research, however, the mechanism of the atheroprotective action of estrogens, the morphological differences between the endothelium of the intima and the arteries of men and women have not been studied sufficiently[8;18].

Insulin resistance is associated with certain components of the pathophysiological mechanisms underlying the development of obesity and MS. It was shown that the ratio of the basal level of insulin and glucose, being a reflection of their interaction in the feedback loop, is largely correlated with the assessment of insulin resistance.

The insulin resistance indexes we studied come from various mathematical homeostatic models for assessing insulin resistance and are based on the ratio of fasting glucose and insulin concentrations in blood plasma. HOMA_{IR} (Homeostasis Model Assessment of Insulin Resistance) values above 2,86 indicate insulin resistance.

The HOMA_{β} index reflects the functional activity of the cells of the pancreas and its increase reflects an increase in the activity of the cells of the activity of the pancreas [2].

We discovered the determined differences in male and women in the sensitivity and finally in resistance to insulin, which partly can be associated with some components of pathophysiological mechanisms lying in the basis of MS developing in women. Possibly this paths can be involved in the absence of gender dependent differences in patients with combination of DM-2 with MS, which possibly can decrease the meaning of above mentioned defending role of hormones in women.



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Table. The average values of some of the indicators used to assess insulin resistance in men and women suffering from DM-2 and DM-2 with concomitant MS

Indicators	All	Male	Female	Р
DM-2 without MS				
	(n = 73)	(n = 49)	(n = 24)	P*
Glucose, mmol/l	9,3 ± 0,19	9,6 ± 0,25*	8,68 ± 0,24*	0,009819*
	(6,3 - 12,2)	(6,3 - 12,2)	(7,4 - 11,3)	
Insulin, mcU/ml	$13,83 \pm 1,06$	$10,83 \pm 0,89*$	19,94 ± 2,22*	0,000297*
	(7,6 - 39,8)	(7,6 - 38,9)	(8,6 - 39,8)	
HbA1c, %	$7,53 \pm 0,11$	$7,69 \pm 0,15*$	7,2 ± 0,15*	0,023849*
	(6,2 - 8,9)	(6,2 - 8,9)	(6,2 - 8,9)	
HOMA _{IR}	$5,6 \pm 0,42$	4,63 ± 0,41*	$7,59 \pm 0,83*$	0,002082*
	(2,67 - 19,1)	(2,67 - 19,1)	(3,12 - 15,24)	
HOMA _b	$52,62 \pm 4,65$	$38,64 \pm 3,52*$	$81,16 \pm 10,01*$	0,000151*
	(18,54 - 185,12)	(18,54 - 158,78)	(27,37 - 185,12)	
QUICKI	$0,98 \pm 0,008$	$0,98 \pm 0,01*$	$0,1 \pm 0,01*$	0,0000001*
	(0,87 - 1,17)	(0,87 - 1,17)	(0,89 - 1,08)	
DM-2 + MS				
	(n = 74)	(n = 38)	(n = 36)	P*
Glucose, mmol/l	8,44 ± 0,31	$8,6 \pm 0,47$	$8,28 \pm 0,4$	>0,05
	(4,3 - 16,49)	(4,3 - 16,49)	(5,4 - 15,9)	
Insulin, mcU/ml	$14,43 \pm 0,39$	$15,02 \pm 0,47$	$13,8 \pm 0,63$	>0,05
	(6,8 - 19,8)	(6,9 - 18,3)	(6,8 - 19,8)	
HbA1c, %	$7,99 \pm 0,11$	$7,92 \pm 0,15$	$8,06 \pm 0,16$	>0,05
	(6,3 - 8,9)	(6,7 - 8,9)	(6,3 - 8,9)	
HOMA _{IR}	$5,39 \pm 0,26$	$5,69 \pm 0,35$	$5,07 \pm 0,37$	>0,05
	(1,67 - 13,12)	(1,67 - 13,12)	(1,99 - 12,51)	
HOMA _b	81,47 ± 7,44	89,36 ± 12,95	$73,14 \pm 6,67$	>0,05
	(17,22 - 407,5)	(22,53 - 407,5)	(17,22 - 159,0)	
QUICKI	$1,05 \pm 0,02$	$1,05 \pm 0,03$	$1,05 \pm 0,02$	>0,05
	(0,78 - 1,43)	(0,78 - 1,43)	(0,79 - 1,26)	

FINDINGS:

1. In men, compared with women suffering from DM-2 (without concomitant MS), there is a significantly higher level of glucose and HbA1c and a significantly lower level of insulinemia, which is combined with significantly higher values of the HOMAIR, HOMA β and QUICKI indices, reflecting comparatively higher degree of insulin resistance.

2. Adherence to diabetes mellitus-2 MS significantly erases gender differences, reflecting about the same degree of insulin resistance regardless of gender and indirectly indicating the addition of the effect of additional pathogenic factors characteristic of MS and leveling certain protective mechanisms inherent in the female body.

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