

Dismetabolic disorders in patients with arterial hypertension and diabetes mellitus type 2

Objective — to study the peculiarities of dysmetabolic disorders in patients with arterial hypertension (AH) and type 2 diabetes mellitus (DM 2).

Materials and methods. 61 patients with stage II second degree AH without carbohydrate metabolism disorders were observed; 64 patients with combined course of AH and DM 2. The control group (n = 20) was the most comparable with observed patients in age and gender.

Results and discussion. Patients with combined course of AH and DM 2 had exceeding levels of LDL and triglycerides in the serum compared with the parameters of the 1st group and control group ($p < 0.05$). Decreased high-density lipoprotein cholesterol (HDL) in patients with AH and DM 2 observed significantly more frequent than in the comparison group (55.4 and 22.4 % respectively, $p < 0.05$). The combination of AH and DM 2 contributed to an increase in atherogenicity coefficient by 2.3 times against the control and by 1.2 times the comparison group. Analysis of insulin resistance in patients of both groups indicated that the maximum values of HOMA-IR, insulin and C-peptide index occurred in patients of the group 2 compared to the group 1 and control parameters. In both groups there was a significant increase in serum TNF- α level against the control group ($p < 0.05$). The greatest increase in the index by 2.5 times ($p < 0.001$) was observed in both AH and DM 2.

Conclusions. The mechanisms of metabolic disorders formation are analyzed in patients with both AH and DM 2. They are characterized by the progression of insulin resistance, the development of atherogenic dyslipidemia, increased markers of systemic inflammation, which most pronounced in patients with overweight and obesity, thus significantly increases the level of cardiovascular risk in patients with both AH and DM 2.

Key words:

arterial hypertension, diabetes mellitus type 2, carbohydrate disorders, insulin resistance, dyslipidemia.

Combined for arterial hypertension (AH) and diabetes mellitus type 2 (DM 2), contribute in the early stages of development of target organ damage and, consequently, increases the risk of cardiovascular events [2, 4].

The identification of insulin resistance (IR) effect on the incidence of cardiovascular events development in DM 2.

Studies of the last years established that high insulin level in the blood serum can accelerate the development of atherosclerotic processes [5, 8].

IR is considered not only as the main link in the development of DM 2 and its complications, but also a component which participate in the pathogenesis of atherosclerosis, hypertension and other diseases [1, 6].

The evidence from epidemiological studies indicate that approximately 80–90 % of patients with DM type 2 are overweight or obese. Thus, the presence of I degree obesity is 2 times increase the risk of developing DM 2, II degree — 5 times, III degrees — more than 10 times. A particular role is played by fat distribution [9]. Established that visceral fat accumulation is associated with impaired glucose tolerance and IR regardless of body weight [10].



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Adipose tissue is an endocrine organ that is the site of synthesis of a large number of hormones and bioactive peptides [3]. There is evidence that some substances synthesized by adipose tissue can impair insulin signal transduction and cause IR in early stages on the stage of pre-diabetes [7].

The aim of research – to study the features of metabolic disorders in patients with AH and DM 2.

Materials and methods

The study involved 125 patients with stage II hypertension and 2nd degree (62 men and 63 women). The average age of the patients was (52.4 ± 5.6) years. The patients divided into groups: group 1 ($n = 61$), patients with hypertension without type 2 diabetes; group 2 ($n = 64$) with comorbidity on AH and DM type 2. The control group ($n = 20$) was the most comparable in age and sex to the patients surveyed.

The examination for AH was performed according to the recommendations of the European Society of AH and the European Society of Cardiology (ESH/ESC, 2013), as well as Ukrainian Heart Association for the AH prevention and treatment (2013). Diagnosis of abdominal obesity (AO) was established in accordance with the basis of the criteria adopted by the WHO (1997), the anthropometric measurements were surveyed on calculation of body mass index (BMI) and the degree of obesity according to the IDF criteria (2015). The diagnosis of DM type 2 was based on the general recommendations of the European Association for the Study of Diabetes (EASD, 2013). The inclusion criteria in the research was subcompensated diabetes: fasting glycemia is not exceed 8.5 mmol/l, postprandial hyperglycemia not exceed 11 mmol/l and HbA_{1c} level to not more than 9 %.

The analysis of lipid metabolism: the total cholesterol concentration in blood serum, high density lipoproteins (HDL), triglycerides (TG) have been identified by using an enzymatic colorimetric method with a set of «Human» (Germany). The cholesterol concentration in the low-density lipoprotein (LDL) determined by the formula Friedewald W.T.: $LDL (mmol/l) = total\ cholesterol - (HDL + TG/2.22)$.

The level of glycated hemoglobin (HbA_{1c}) in whole blood was analyzed by using the test-system of the firm «Reagent» (Ukraine). The insulin resistance index (HOMA-IR) was calculated using the formula: $HOMA-IR = insulin\ (fasting\ insulin\ (mcU/ml) \times fasting\ glucose\ (mmol/l) / 22.5$. With the index of HOMA-IR > 2.77 was considered insulin-resistant patients.

The immunoenzyme method identified fasting blood glucose and insulin concentration in blood

serum (FBG) by using «DRG» sets (USA). The tumor necrosis factor – (TNF- α) and C-peptide concentration in blood serum is researched by using immunoenzyme method with reagents set «DRG» (USA).

Statistical analysis of the research results performed by using Statistica software package – 8.0.

Results and discussion

The analysis for revealed trophological status indetified characteristics for both groups. Patients with a BMI in the range of 18.5–24.9 kg/m² (6 patients) have been identified in the group of progressing isolated hypertension, obesity III degree (BMI exceed 40.0 kg/m²) was observed in two patients with hypertension and 8 patients with combined AH and DM 2. The predominant majority of patients having isolated and combined course of the disease (65.6 and 57.7 %, accordingly) has been identified with BMI in the range of 30–34,9 kg/m². In addition, men prevail among the patients with AH BMI 30–34,9 kg/m², and with a BMI within 35–39,9 kg/m² and a little larger-women (74.6 %).

Serum lipid abnormalities has been identified statistically higher in patients with concomitant AH and DM 2 (65.6 and 44.9 %, respectively; $p < 0.05$). The level of triglycerides in the blood serum of patients with AH and DM 2 is 1.1 times as many ($p < 0.05$) as in patients of the first group and 2.2 times- the control group indexes ($p < 0.05$).

Lowering levels of HDL in patients with AH and DM 2 was observed more commonly compared to the meaning of this index in comparison group (53.1 and 24.0 %, accordingly; $p < 0.05$) (Table 1). Patients in group 2 with the BMI within 30–34,9 kg/m² has been identified as having lower levels of HDL compared to the value of this indicator in the comparison group ($p < 0.05$). Progression of lipid disorders in patients with concomitant course of the disease depended on BMI: maximum indexes of total cholesterol and TG levels have been observed in BMI within 35–40 kg/m² ($p = 0.246$; $p = 0.067$, accordingly), and HDL concentration in blood serum was the lowest ($p = 0.046$).

The combination of AH and DM 2 promoted an increase in the coefficient of atherogenic by 2.3 times in comparison with the control and by 1.2 times with the comparison group, which indicated the progression of atherosclerotic changes in the vessels.

Analysis of the HOMA-IR index in patients of both groups testified that the maximum values of the HOMA-IR index, insulin and C-peptide has been identified in patients of the group 2 comparatively to indicators of the 1st group and the control

Table 1. Characteristics of the lipid spectrum in the examined patients (M ± SD)

Indexes	Control (n = 20)	AH (n = 61)	AH + DM 2 (n = 64)	p
Total cholesterol, mmol/l	5,3 ± 2,2	5,5 ± 2,3	5,8 ± 2,8	p ₁₋₂ = 0,46 p ₁₋₃ = 0,32 p ₂₋₃ = 0,72
HDL, mmol/l	1,3 ± 0,6	1,2 ± 0,7	0,7 ± 0,42	p ₁₋₂ = 0,53 p ₁₋₃ = 0,003 p ₂₋₃ = 0,009
TG, mmol/l	1,8 ± 0,8	1,7 ± 1,1	2,9 ± 1,2	p ₁₋₂ = 0,73 p ₁₋₃ = 0,002 p ₂₋₃ = 0,0002
LDL, mmol/l	3,2 ± 1,54	3,64 ± 1,6	4,07 ± 3,0	p ₁₋₂ = 0,27 p ₁₋₃ = 0,054 p ₂₋₃ = 0,34

Table 2. Characteristics of insulin resistance in examined patients studied (M ± SD)

Indexes	Control (n = 20)	AH (n = 61)	AH + DM 2 (n = 64)	p
HOMA-IR	1,64 ± 0,52	4,42 ± 2,4	5,6 ± 3,3	p ₁₋₂ = 0,00001 p ₁₋₃ = 0,00001 p ₂₋₃ = 0,12
Insulin mcU / ml	5,52 ± 2,3	11,2 ± 5,7	13,6 ± 7,5	p ₁₋₂ = 0,0005 p ₁₋₃ = 0,0002 p ₂₋₃ = 0,045
C-peptide ng/ml	0,48 ± 0,23	0,97 ± 0,52	1,3 ± 0,78	p ₁₋₂ = 0,0004 p ₁₋₃ = 0,0001 p ₂₋₃ = 0,058

Table 3. Characteristics of carbohydrate metabolism in examined patients (M ± SD)

Indexes	Control (n = 20)	AH (n = 61)	AH + DM 2 (n = 64)	p
Glucose, mmol/l	4,26 ± 2,32	6,24 ± 3,73	7,73 ± 3,94	p ₁₋₂ = 0,032 p ₁₋₃ = 0,0002 p ₂₋₃ = 0,075
HbA _{1c} (%)	4,2 ± 2,5	6,4 ± 3,62	8,5 ± 4,17	p ₁₋₂ = 0,0965 p ₁₋₃ = 0,0001 p ₂₋₃ = 0,0052

(Table 2), this indicate the progression of insulin resistance into hyperinsulinemia associated with the cases of DM 2.

The set statistically significant interaction between HOMA-IR levels and glucose levels ($r = 0.46$; $p = 0.07$), C-peptide ($r = 0.58$; $p = 0.0001$), BMI ($r = 0.56$; $p = 0.0054$) and cholesterol levels ($r = 0.64$; $p = 0.053$) confirms the hypothesis about the key importance of IR in the development and progression of metabolic changes that are correlated with hyperinsulinemia and dyslipidemia and is associated with inflammation and the development of atherosclerotic lesions of the vascular wall in patients with concomitant AH and DM 2.

A significant increase of HbA_{1c} in patients the group 2 compared to control ($p < 0.05$) testified about the negative impact of excess weight on carbohydrate metabolism and carbohydrate metabolism unsatisfactory compensation (Table 3). Patients in the group 1 in 6.3 % had a significant increase of glucose in the fasting blood serum (FBG) comparatively to the

control group ($p < 0.05$), that is explained by the abdominal obesity, because excess body weight is one of the reasons for the development of the IR, the maximum value of this indicator was in patients with concomitant AH and DM 2 ($p < 0.05$).

A significant increase of TNF- α in blood serum has been observed in both groups comparatively to the control group ($p < 0.05$). The largest increase in the 2.4 – fold ($p < 0.001$) was observed with comorbid AH and DM 2. C-peptide levels in the blood serum exceed the reference values in both groups of the examined patients ($p < 0.05$). The greatest increase (2.3–fold) was observed in patients with comorbid AH and DM 2 ($p < 0.05$) and correlated with BMI ($r = 0.48$; $p < 0.001$), FBG levels ($r = 0.48$; $p < 0.001$), TG levels ($r = 0.42$; $p < 0.05$), HOMA-IR ($r = 0.46$; $p < 0.001$).

Conclusions

The mechanisms of metabolic disorders formation were analyzed in patients with concomitant course

of AH and DM 2, which are characterized by the progression of IR and the development of atherogenic dyslipidemia (reduced HDL, increasing LDL

and TG), the increase in systemic inflammation markers and most observed in patients with overweight and obesity.

There are no conflicts of interest.

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Дисметаболически порушення у пацієнтів з артеріальною гіпертензією та цукровим діабетом 2 типу

Мета роботи — вивчити особливості дисметаболических порушень у пацієнтів з артеріальною гіпертензією (АГ) та цукровим діабетом (ЦД) 2 типу.

Матеріали та методи. Обстежено 61 пацієнт з АГ II стадії та 2-го ступеня без порушень вуглеводного обміну; 64 пацієнта з поєднаним перебігом АГ та субкомпенсованим ЦД 2 типу. Контрольна група (n = 20) була максимально порівняна за віком та статтю з обстежуваними хворими.

Результати та обговорення. У пацієнтів з поєднаним перебігом АГ і ЦД 2 типу рівні холестерину ліпопротеїнів низької щільності (ЛПНЩ) і тригліцеридів в сироватці крові перевищував показники пацієнтів 1-ї групи і групи контролю (p < 0,05). Зниження рівня холестерину ліпопротеїнів високої щільності (ЛПВЩ) у хворих з АГ і ЦД 2 типу спостерігалось значно частіше, ніж в групі порівняння (55,4 і 22,4 % відповідно; p < 0,05). Поєднання АГ і ЦД 2 типу сприяло збільшенню коефіцієнта атерогенності в 2,3 рази в порівнянні з контролем і в 1,2 рази з групою порівняння. Аналіз показників стану інсулінорезистентності у пацієнтів обох груп свідчив про те, що максимальні значення індексу НОМА-IR, інсуліну та С-пептиду мали місце у пацієнтів 2-ї групи в порівнянні з показниками 1-ї групи і контролем. В обох групах спостерігалось достовірне підвищення рівня ФНП-α в сироватці крові в порівнянні з контрольною групою (p < 0,05). Найбільше збільшення показника в 2,5 рази (p < 0,001) спостерігалось при поєднанні АГ і ЦД 2 типу.

Висновки. Проаналізовано механізми формування метаболічних порушень у пацієнтів з поєднаним перебігом АГ і ЦД 2 типу, вони характеризуються прогресуванням інсулінорезистентності, розвитком атерогенної дисліпідемії, підвищенням маркерів системного запалення, які найбільш виражені у пацієнтів з надмірною масою тіла та ожирінням, що значно підвищує кардіоваскулярний ризик.

Ключові слова: артеріальна гіпертензія, цукровий діабет 2 типу, вуглеводні порушення, інсулінорезистентність, дисліпідемія

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Дисметаболические нарушения у больных с артериальной гипертензией и сахарным диабетом 2 типа

Цель работы — изучить особенности дисметаболических нарушений у пациентов с артериальной гипертензией (АГ) и сахарным диабетом (СД) 2 типа.

Материалы и методы. Обследованы 61 пациент с АГ II стадии и 2-й степени без нарушений углеводного обмена, а также 64 пациента с сочетанным течением АГ и СД 2 типа. Контрольная группа ($n = 20$) была максимально сопоставима по возрасту и полу с обследуемыми больными.

Результаты и обсуждение. У пациентов с сочетанным течением АГ и СД 2 типа уровень холестерина липопротеинов низкой плотности (ЛПНП) и триглицеридов в сыворотке крови превышал показатели пациентов первой группы и группы контроля ($p < 0,05$). Снижение уровня холестерина липопротеинов высокой плотности (ЛПВП) у больных с АГ и СД 2 типа наблюдалось значительно чаще, чем в группе сравнения (55,4 и 22,4 % соответственно; $p < 0,05$). Сочетание АГ и СД 2 типа способствовало увеличению коэффициента атерогенности в 2,3 раза в сравнении с контролем и в 1,2 раза — с группой сравнения. Анализ показателей состояния инсулинорезистентности у пациентов обеих групп свидетельствовал о том, что максимальные значения индекса НОМА-IR, инсулина и С-пептида имели место у пациентов второй группы в сравнении с показателями первой группы и контролем. В обеих группах наблюдалось достоверное повышение уровня ФНО- α в сыворотке крови в сравнении с контрольной группой ($p < 0,05$). Наибольшее увеличение показателя — в 2,5 раза ($p < 0,001$) наблюдалось при сочетании АГ и СД 2 типа.

Выводы. Проанализированы механизмы формирования метаболических нарушений у пациентов с сочетанным течением АГ и СД 2 типа. Они характеризуются прогрессированием инсулинорезистентности, развитием атерогенной дислипидемии, повышением маркеров системного воспаления, которые наиболее выражены у пациентов с избыточной массой тела и ожирением, что значительно повышает кардиоваскулярный риск.

Ключевые слова: артериальная гипертензия, сахарный диабет 2 типа, углеводные нарушения, инсулинорезистентность, дислипидемия.