

European Journal of Biomedical and Life Sciences

№ 1 2017



«East West» Association for Advanced Studies and Higher Education GmbH

Vienna

2017

European Journal of Biomedical and Life Sciences

Scientific journal

№ 1 2017

ISSN 2310-5674

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European Journal of Biomedical and Life Sciences is an international, German/English/Russian language, peer-reviewed journal. It is published bimonthly with circulation of 1000 copies.

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Typeset in Berling by Ziegler Buchdruckerei, Linz, Austria.

Printed by «East West» Association for Advanced Studies and Higher Education GmbH, Vienna, Austria on acid-free paper.

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**THE PATHOGENETIC INTERRELATION OF METABOLIC
DISORDERS IN PATIENTS WITH ARTERIAL HYPERTENSION
AND TYPE 2 DIABETES MELLITUS**

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ABSTRACT

The article deals with the mechanisms of progression of metabolic disorders in patients with concomitant course of hypertension and diabetes mellitus type 2, the most important is the state of insulin resistance, carbohydrate metabolism disturbances, the development of atherogenic dyslipidemia and systemic inflammation in correlation with the imbalance of adipocytokines, which contributes to high risk cardiovascular.

Keywords: arterial hypertension, diabetes mellitus type 2, metabolic disorders, insulin resistance.

Combined for arterial hypertension (AH) and diabetes mellitus (DM) type 2, contribute in the early stages of development of target organ damage and, consequently, increases the risk of cardiovascular events [1, 2].

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

Studies of the last years established that high insulin level in the blood serum can accelerate the development of atherosclerotic processes [3, 4].

IR is considered not only as the main link in the development of DM type 2 and its complications, but also a component which participate in the pathogenesis of atherosclerosis, hypertension and other diseases [5, 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 type 2, II degree - 5 times, III degrees - more than 10 times. A particular role is played by fat distribution [7]. Established that visceral fat accumulation is associated with impaired glucose tolerance and IR regardless of body weight [8].

Adipose tissue is an endocrine organ that is the site of synthesis of a large number of hormones and bioactive peptides [9]. 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 [10].

Aim. To stud the features of metabolic disorders in patients with AH and DM type 2.

Materials and methods. The study involved 74 patients with AH and DM type 2: the 1st group consisted of 38 patients with AH, 2nd group - 36 patients with concomitant AH and DM type 2. The control group (n = 20) was the most comparable in age and sex to the patients surveyed. The average age of patients was $54,7 \pm 4,5$ years. Clinical examination of patients included an analysis of complaints, collection of medical anamnesis, physical monitoring and an evaluation of anthropometric indicators.

Diagnosis of hypertension was performed according to the recommendations of the European Society of Hypertension and the European Society of Cardiology (ESH / ESC, 2013), as well as Ukrainian Association of Cardiology on prevention and treatment of hypertension (2013). To study the anthropometric characteristics of

the course of AH and DM type 2, patients were grouped according to Body Mass Index (BMI). The diagnosis of DM type 2 were carried out according to the criteria of the International Diabetes Federation (IDF, 2015). The criteria for inclusion into study was subcompensated diabetes: Impaired fasting glycaemia (IFG) not exceeding 8.5 mmol / l, postprandial hyperglycemia not exceeding 11 mmol / l and HbA1c level not higher than 9%.

Lipid spectrum Indicators of blood serum total cholesterol (TC), triglycerides (TG), high-density lipoprotein - (HDL), low-density lipoprotein (LDL) was determined by an enzymatic colorimetric method using sets «Human» (Germany).

Insulin levels in blood serum were determined by enzyme-linked immunosorbent assay ELISA, «DRG» sets, (USA). Assessment of insulin resistance level was performed using HOMA (homeostasis model assessment) - homeostasis model assessment to insulin resistance by calculating the index (HOMA-IR) by the formula: $HOMA-IR = \frac{\text{insulin mcU/ml} \times \text{glucose, mmol / l}}{22.5}$. The concentration of glucose in fasting blood serum (FBS) was determined by glucose oxidation method, also was determined glucose tolerance.

The content of tumor necrosis factor- α (TNF- α) in the blood serum were determined by enzyme immunoassay using sets of «Protein contour» (St. Petersburg).

The content of C - reactive protein (CRP) was analyzed by using ELISA with «DRG» set of reagent (USA).

The statistical processing of the results the research carried out by means of the software package Statistica - 6.0 using Student's t-test and nonparametric statistical methods.

Results and discussion. The analysis of the trophological status identified characteristics for both groups. Patients with BMI in the range 18.5-24.9 kg / m² (5 patients) identified in the group with progression of isolated AH. However, III degree of obesity (BMI exceed 40.0 kg / m²) was observed in two patients with AH and in 6 patients with concomitant AH and DM type 2. The predominant majority of patients with isolated and combined course of the disease (67.5% and 55.1%, respectively)

had a BMI in the range 30-34,9 kg / m². Thus, in patients with AH and BMI 30-34,9 kg / m² prevail men (72.4%), and with a BMI 35-39,9 kg / m² and more - women (74.6%).

Indicators of the lipid levels in patients with comorbid hypertension and DM type 2, characterized by the progression of an atherogenic dyslipidemia. The triglyceride levels in blood serum of patients with AH and DM type 2 is 1.5 times ($p < 0,05$) higher than in patients of the 1st group and 2.2 times higher- indicators of the control group ($p < 0,05$). Reducing HDL levels in patients with AH and DM type 2 was observed significantly more frequently than in the control group (55.2% and 23.5%, respectively; $p < 0,05$). In patients with comorbidities BMI 30-34,9 kg / m² had lower HDL levels compared with the value of this indicator in the comparison group ($p < 0,05$). Progression of lipid disorders in patients with concomitant course of the disease depending on BMI: maximum values of TC and TG were observed with BMI 35-40 kg / m² ($p = 0.242$, $p = 0.052$, respectively), and the concentration of HDL in blood serum had the lowest value.

The concomitant and DM type 2 caused to increase in the ratio of an atherogenic index (AI) in 2.3 times in comparison with the control and 1.2 times with the comparison group, indicating the progression of atherosclerotic lesions in blood vessels.

Analysis of the insulin resistance (IR) indicators in patients of both groups testified that the maximum values of HOMA-IR index, insulin and C-peptide were patients in the 2nd group in comparison with indicators of the 1st group and the control ($p = 0.000$; $p = 0.008$; $p = 0.004$, respectively), indicating that the progression of in hyperinsulinemia conditions associated with the presence of DM type 2.

HOMA-IR index exceeded the control indicators by 2.1 times in the group of patients with isolated course of disease and 2.4 times was significantly higher in patients with concomitant AH and DM type 2 ($p = 0.004$).

Identified statistically significant relationship between glucose levels ($r = 0,52$; $p = 0.04$), C-peptide ($r = 0,64$; $p = 0.0001$), BMI ($r = 0,56$; $p = 0,0052$) and the level of TC ($r = 0,62$; $p = 0.054$) confirms the hypothesis that IR influence on the

development of dyslipidemia and associated with inflammation in patients with concomitant AH and DM type 2.

Impaired glucose tolerance (IGT) in patients with AH was observed in 9.5% of cases ($p < 0.05$), whereas patients of 2nd group in 96.7% ($p < 0.05$). A significant increase of HbA1c observed in patients of 2nd group compared to control ($p < 0.05$) confirms the negative impact of excess weight on carbohydrate metabolism and unsatisfactory compensation of carbohydrate metabolism, which increases the metabolic disorders and cause the atherosclerotic vascular lesion, patients of the 1st group 1 (7.6%) has been observed a significant increase in FBG levels compared to the control group ($p < 0.05$), which is explained by the presence of abdominal obesity, because excess body weight is one of the cause for IR progression, the maximum value of this indicator has been reached in patients with concomitant AH and DM type 2 ($p < 0.05$).

In both groups, there was observed a significant increase of TNF- α in blood serum comparatively to the control group ($p < 0.05$). The largest increase in 2.5 times ($p < 0.001$) was observed in concomitant course of AH and DM type 2.

CRP levels in blood serum exceed the reference values in both groups of surveyed patients ($p < 0.05$). The greatest increase for CRP indicators (in 2.2 times) was observed in patients with comorbidity ($p < 0.05$) and correlated with BMI ($r = 0,43$; $p < 0.001$), FBG level ($r = 0,48$; $p < 0.001$) and TG levels ($r = 0,37$; $p < 0.04$), index of HOMA-IR ($r = 0,46$; $p < 0.001$).

Conclusion. It was found that the mechanisms of metabolic disorders in patients with concomitant AH and DM type 2, characterized by insulin resistance and progression of the development of atherogenic dyslipidemia, an increase in markers of systemic inflammation are most pronounced in patients with overweight and obesity.

Thus, a comprehensive diagnosis of AH and DM type 2, will contribute to the individualization of preventive and therapeutic measures, as well as the establishment of control for the progression of atherosclerosis and reduce cardiovascular risk.

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