THE ROLE OF ADIPOCYTOKINES IN THE PATHOGENESIS OF INSULIN RESISTANCE IN PATIENTS WITH DIABETES MELLITUS TYPE 2 AND NON-ALCOHOLIC FATTY LIVER DISEASE

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Introduction. The combination of diabetes mellitus type 2 (DM 2) with non-alcoholic fatty liver disease (NAFLD) and obesity is of scientific interest in the key of understanding the pathogenesis of the metabolic syndrome (MS), because liver dysfunction exacerbates insulin resistance (IR) which is a leading factor in the development of these diseases.

Aim: to evaluate the relationship of adipocytokines imbalance with the progression of hepatic steatosis and indicators of IR in patients with combined course of diabetes mellitus type 2 and non-alcoholic fatty liver disease.

Methods. 40 patients (17 men, aged 54.5 ± 4.5 years) with DM 2 and NAFLD and 20 healthy persons matched for age and sex were examined. The plasma concentration of adipocytokines (leptin (LN) and adiponectin (AN)), the level of tumor necrosis factor-alpha (TNF-α) and C-reactive protein (CRP) were investigated by ELISA followed by evaluation of the results in relation to the serum lipid spectrum, IR index HOMA-IR and the content of fat in the liver. Visceral fat area (VFA) was determined by magnetic resonance imaging of abdominal area at the level of L4.

Results. Disorders of body weight were observed in 94.5% of patients, including obesity 1st degree at 55.8%, 2nd degree at 33.8% and 4.9% - obesity 3rd degree. AN level was reduced compared with the control ($p<0.05$) and correlated with the degree of obesity ($p<0.05$). There was a negative relationship between the level AN and BMI ($r=-0.36$; $p<0.01$), waist circumference (WC) ($r=-0.34$; $p<0.05$), triglycerides (TG) ($r=-0.44$; $p<0.001$) and CRP ($r=-0.38$; $p<0.001$), severity of hepatic steatosis ($r=-0.54$; $p<0.001$), as well as the positive relationship between the level AN and the content of high density lipoprotein (HDLP) ($r=0.44$; $p<0.001$). An inverse relationship between the level of AN and insulin ($r=-0.34$; $p<0.05$), glucose ($r=-0.36$; $p<0.05$), index HOMA-IR ($r=-0.46$; $p<0.001$), alanine aminotransferase ($r=-0.44$;

$p<0.05$) was determined. The level of serum LN in obese patients of 3rd degree was higher than in patients with obesity 1st and 2nd degree ($p<0.01$). The level of LN correlated with BMI ($r=0.42$; $p<0.001$), WC ($r=0.41$; $p<0.001$), index HOMA-IR ($r=0.44$; $p<0.001$). The level of TNF-α was in 4.5 times higher compared to the control ($p<0.05$), was in negative correlation with the level of HDLP ($r=-0.36$; $p<0.05$) and in positive with WC ($r=0.38$; $p<0.05$) and index HOMA-IR ($r=0.38$; $p<0.05$). CRP level in the serum was in 1.5 times over the control values ($p<0.001$) and correlated with BMI ($r=0.47$; $p<0.001$), WC ($r=0.54$; $p<0.001$), glucose level ($r=0.44$; $p<0.001$), level of TG ($r=0.34$; $p<0.04$), insulin ($r=0.36$; $p<0.001$), index HOMA-IR ($r=0.48$; $p<0.001$). There was a correlation of VFA with WC ($r=0.48$; $p=0.002$), glucose ($r=0.36$; $p=0.02$), HOMA-IR ($r=0.36$; $p=0.02$), CRP ($r=0.31$; $p=0.04$) and the level of LN ($r=0.28$; $p=0.04$).

Conclusions. It was found that an imbalance of hormone production in adipose tissue (hypoadiponektinemia, hyperleptinemia, increased level of tumor necrosis factor-alpha) and markers of the acute phase of inflammation are involved in the pathogenesis of insulin resistance in patients with diabetes mellitus type 2 and non-alcoholic fatty liver disease and correlate with the severity of hepatic steatosis. The secretion of these substances correlates with obesity and is optional factor in the progression of metabolic disorders in the liver, which contributes to insulin resistance, closing the "vicious circle".