



IL-1  $\alpha$  content analysis revealed its significant predominance in group 2 patients ( $48,94 \pm 7,05$  vs  $22,43 \pm 3,41$  pg/ml (group 1),  $p < 0,01$ ). IL-6 level was markedly higher in group 2 patients as well ( $51,63 \pm 7,86$  vs  $16,84 \pm 3,94$  pg/ml,  $p < 0,01$ ), and level of anti-inflammatory cytokine IL-10 was some less in group 2 patients comparing group 1 ( $2,45 \pm 0,51$  vs  $4,03 \pm 0,73$  pg/ml,  $p > 0,05$ ).

Tumor-necrotizing factor (TNF) and neopterin (Np) levels analysis in groups indicates significant predominance of these both values in group 2 patients comparing group 1:  $63,41 \pm 3,78$  vs  $43,1 \pm 2,62$  pg/ml for TNF ( $p < 0,01$ ) and  $24,28 \pm 4,32$  vs  $15,08 \pm 1,76$  nmol/l for Np ( $p < 0,05$ ).

Elder patients age, higher class of ALVF, presence of DM and CHF, anterior localization of AMI, smoking and obesity, EF low then 40% are independent predictors of lethal event development in patients with AMI and ALVF. Besides, increase in pro-inflammatory cytokines level (IL-1 $\alpha$ , IL-6, TNF and Np) parallel to worsening of EchoCG EF results in favor of increase of lethal event onset probability in the mentioned category of patients.

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### **CHANGES OF THE IMMUNE DEFENCE IN DIABETIC PATIENTS WITH PYOINFLAMMATORY PROCESSES**

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The immune system disorders in diabetic patients lead to a significant decrease in non-specific and specific immune anti-infectious defense by inhibiting phagocytic function of polymorphonuclear leukocytes, lowering of complement system activity, lysozyme, interferons, bactericidal activity of blood serum.

Diabetic patients with pyoinflammatory processes treated by traditional methods ( $n=40$ ); diabetic patients with pyoinflammatory processes treated by ozonotherapy along with traditional treatment ( $n=53$ ). The obtained results confirm changes in the absolute and relative number of immune cells in the peripheral blood of DM patients associated with pyoinflammatory processes. A relative number of lymphocytes decreases in these patients, at the same time a tendency to growth in the absolute number of the total pool of lymphocytes is formed. The research of the immune disorders degree confirmed that therapeutic measures, including ozonotherapy, against pyoinflammatory processes in patients with DM show their effectiveness. On admission 65,0% of patients were diagnosed with the I-II degree of immune disorders, which required immunorehabilitation; after pyoinflammatory processes therapy only 55,0% of diabetic patients were left. Special efficiency is shown in the III stage of immune disorders.

Pyoinflammatory processes in patients with diabetes occur on the background of decrease in the appropriate number of lymphocytes; increase in the absolute and relative number of monocytes, the absolute number of leukocytes due to the increase in the relative amount of neutrophilic polymorphonuclear leukocytes, as well as decrease in the absolute number of eosinophils, erythrocytes and hemoglobin.

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### **METFORMIN IMPROVES ENDOTHELIAL VASCULAR REACTIVITY IN FIRST-DEGREE RELATIVES OF TYPE 2 DIABETIC PATIENTS**

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Endothelial dysfunction is an early marker of atherosclerosis seen in type 2 diabetic subjects. Metformin is commonly used in the treatment of type 2 diabetes and has besides hypoglycemic, a known vascular protective effect. We aimed to investigate the vascular effects of metformin in first-degree relatives with metabolic syndrome of type 2 diabetic patients.

The study included 43 subjects (age  $38,3 \pm 7,6$  years and BMI  $36,3 \pm 5,2$  kg/m<sup>2</sup>), who were first-degree relatives of type 2 diabetic patients and who had metabolic syndrome and normal glucose tolerance. The subjects were randomly assigned 1:1 in a double-blind fashion to receive placebo ( $n = 13$ ) or metformin ( $n = 30$ ). Endothelial function was assessed by venous occlusion plethysmography, measuring forearm blood flow (FBF) and vascular resistance responses to three intra-arterial infusions of endothelium-dependent (acetylcholine 7,5, 15, and 30  $\mu$ g/min) and independent (sodium nitroprusside 2, 4, and 8  $\mu$ g/min) vasodilators. Weight, BMI, systolic and diastolic blood pressure, waist, and laboratory parameters (lipid profile and fasting plasma glucose [FPG]) were assessed before and after treatment.

The metformin and placebo groups did not differ in anthropometric, clinical, laboratory, and vascular measurements at the beginning of the research. The metformin group had decreased weight, BMI, systolic blood pressure, and FPG and improved lipid profile. Endothelium-dependent FBF responses were also improved, without any effect on endothelium-independent responses. There was no correlation between the improvement on FBF responses and the observed changes on anthropometric, clinical and laboratory parameters.

We concluded that metformin improved vascular endothelial reactivity in first-degree relatives with metabolic syndrome of type 2 diabetic patients, regardless of its known antihyperglycemic effects. Accelerated atherosclerosis seen in type 2 diabetes raised the question about pathogenetic factors that initiate the development of vascular disorders in the pre-diabetic population. Metabolic syndrome, a pre-diabetic state, includes a number of cardiovascular risk factors such as abdominal obesity, dyslipidemia, hypertension, impaired glucose tolerance, and insulin resistance.



Insulin resistance, the central abnormality for the pathogenesis of metabolic syndrome, is considered an independent risk factor for cardiovascular mortality in general and in the diabetic population in particular. Metformin exerts an antihyperglycemic effect, with minimal risk of hypoglycemia, and has been recently used to prevent type 2 diabetes with a 31% reduction in incidence.

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### **L-ARGININE CHLORIDE AND ENDOTHELIAL DYSFUNCTION**

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Nowadays hypertonic disease (HD) is considered as an endothelium dysfunction condition, accompanied by constriction of vascular smooth muscles which is related with insulin resistance development (IR). The accumulated experimental, epidemiological and clinical researches, showed the increase of insulin level in patients with HD, indicating that IR is an important pathogenic factor of HD.

All the patients with HD of stage II received basic therapy of lisinopril, amlodipine and atorvastatin as control group. Then we took 30 people of the group and gave them besides the basic therapy an infusion of 100 ml of 4,2% solution of L-arginine chloride over the period of 12-14 days as inpatient and then as outpatients orally 20 ml of 4 grams twice a day 40 minutes before the meal, for the duration of 3 months.

After 3 months, in patients with basic therapy plus L-arginine the improvement of endothelium dependent vasodilation (EDV) was 97,9 % and endothelium not dependent vasodilation hypertonic disease (ENDV) was 0% and the speed of blood flow in the brachial artery V in dynamics with reactive hyperemia test was (V-RHT) 17,1 % compared to improvement only of (EDV) 63,1%, (ENDV) 2,2 %, (V-RHT) 6,2 % in the group with basic therapy.

Combination of antihypertensive and hypolipidemic therapy and gradual including of L-arginine by intravenous-oral way showed significant improvement of endothelium dependent vasodilatation, compared with control group in hypertonic patients with concomitant insulin resistance.

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### **FIBRINOLYTIC ACTIVITY FEATURES OF BLOOD PLASMA AND MORPHOFUNCTIONAL STATE OF ERYTHROCYTES INFLUENCED BY PEPSANE AND QUERCETIN IN PATIENTS WITH EROSIIVE FORM OF GASTROESOPHAGEAL REFLUX DISEASE AGAINST DIABETES MELLITUS TYPE 2**

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Gastroesophageal reflux disease (GERD) is a global problem today due to the features of its course and treatment.

The aim of our study is to evaluate the efficiency of drugs "Pepsane" and "Quercetin" while adding them to a standard treatment regimen for the erosive form of GERD (EGERD) in patients with concomitant diabetes mellitus (DM) type 2.

The study involved 29 patients with EGERD, combined with DM type 2, from 40 to 74 years old and 20 practically healthy individuals (PII), who were divided into the following groups: group 1 was represented by 7 patients with EGERD who were administered basic therapy; group 2 included 13 patients with EGERD who took Pepsane alongside with the basic therapy; group 3 included 9 patients with EGERD who were administered "Pepsane" and "Quercetin" within 28 days as an addition to the standard treatment. The patients from PHI made up the fourth (reference) group. Fibrinolysis system in the blood plasma was studied by N.Tits techniques. The relative viscosity of erythrocyte suspension (RVES) and index of erythrocyte deformability (IED) were determined by Z.D. Fiodorova and M.O. Kotovshchykova techniques.

It has been established that exposure to basic treatment and "Pepsane" and to standard treatment combined with taking "Pepsane" and "Quercetin" leads to a significant correction process of fibrinolysis, which manifested itself with a potential decrease ( $p < 0,05$ ). And the patients who only received a basic therapy had better fibrinolysis indicators too, but these changes were less significant compared to the group who used combination therapy ( $p > 0,05$ ), with an obvious inter-group difference ( $p < 0,05$ ).

Comprehensive treatment with "Pepsane" and "Quercetin" was likely to contribute to a higher degree of increase (by 22,0% ( $p < 0,05$ ) in group 3) and normalization of IED value compared to that before the treatment, a significant decrease of RVES (by 16,4% ( $p < 0,05$ )) in the dynamics of treatment in contrast to the first one, where IED increased by 10,8% ( $p > 0,05$ ), and RVES decreased by 12,1% ( $p < 0,05$ ) obviously differing from those which were before the treatment.

Thus, the addition of "Pepsane" and "Quercetin" to a standard treatment in patients with EGERD, combined with DM type 2, helps to achieve more effective results, and may be recommended for using in clinical practice.