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THE ROLE OF QUINAPRIL IN THE CORRECTION OF THE ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH PEPTIC ULCER OF THE STOMACH AND DUODENUM, COMBINED WITH DIABETES MELLITUS

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Summary. The indices of the functioning of the endothelium in patients with peptic ulcer of the stomach and duodenum, combined with diabetes mellitus, have been analyzed and a marked vasculoendothelial dysfunction has been established. A correction of the revealed disturbances by means of the quinapril has been proposed.
Key words: endothelial dysfunction, peptic ulcer, diabetes mellitus, quinapril, treatment.

Introduction. Significant changes of homeostasis in diabetes mellitus (DM), including hiperhlikememiya, hyperlipidemia directly modulate the expression of endothelial receptors in response to numerous biologically active compounds. In addition, prolonged and excessive influence of metabolic disorders in endothelial and smooth muscle cells of blood vessels can cause atherogenesis and other morphological changes that indirectly affect the release and action of endothelin-1 (ET-1) for different target organs [1, 2]. Also the role of Helicobacter pylori (Hp) in causing of endothelial dysfunction has been shown [3]. But the mechanisms of recurrence and progression of PU are not found out in the presence of diabetes.

The aim of the study. To investigate the functional state of the endothelium in patients with PU, combined with DM and to develop improved methods of treatment.

Material and methods. Using a set for definition of endothelin-1 (Biomedica, Austria) on immunoassay analyzer (ELISA) the level of endothelin-1 (ET-1) was found. The concentration of NO metabolites in the serum was determined using Gris reagent on spectrophotometer SF-46 [4]. The study involved 11 patients with PU (group I), 11 diabetic patients (group II), 30 patients with PU, combined with DM (group III) and 8 healthy individuals.

Also, the functional state of endothelium was assessed by tests result in reactive hyperemia using blood vessels color Doppler of the upper extremity. The study involved 24 patients with PU, combined with DM (group II), 8 diabetic patients (group I) and 8 healthy individuals.

Results and discussion. Analysis of the survey results showed (table 1), in patients of group I ET-1 levels in 2.6 times higher, in group II in 3.3 times and in the third group in 4.4 times ($p<0.05$) higher compared with the healthy individuals. In group I patients experienced NO reduction in 1.14 times, in group II – increased in 1.1 times and in the third group of patients – increased in 1.2 times ($p<0.05$).

It was found after the Doppler study that patients with PU, combined with DM and in diabetic patients a significant increase of the diameter of blood vessels at rest (D0) compared with healthy individuals ($p<0,05$) observed. Despite the larger diameter vessels, blood flow velocity did not differ significantly in any of the groups (table 2).

Shear stress on the endothelium at rest was high in healthy individuals and lower in other groups. In response to the test with reactive hyperemia in patients with diabetes there was insufficient increase of both diameter and shear stress on the endothelium, but the tendency to vasodilatation remained.

Sensitivity of the artery to the shear stress (K) in the group I was significantly ($p<0.05$) lower (0.18±0.02), than in the group of healthy individuals (0.44±0.13). There is a violation of endothelium dependent vasodilatation in patients with DM. In the group of patients with PU, combined with DM, test with reactive hyperemia caused an ambiguous reaction.

The diameter of the vessels on average has not changed, but the percentage observed in three patients (18%) complete lack of response in the test (completely broken vasoregulation), 6 people (37%) revealed a paradoxical reaction (vasoconstriction) and 7 people (45%) found positive growth diameter (expected vasodilatation). Indicators $\Delta\tau_1$ and K_1 in group III is the lowest ($p<0.05$) and make up 12.17±1.85 and 0.11±0.03 in accordance. Thus, in patients with PU, combined with DM expressed abuse of endothelial dependent vasodilatation was found.

Analysis of nitroglycerin test showed that diabetic patients do not develop violation of the endothelial independent vasodilatation, but the response of the vessels to the nitrate drug was less than in healthy individuals ($p<0.05$). Namely, τ_2 reduced in 1.17 times, $\Delta\tau_2$ in 2 times, the rate of sensitivity of the artery to the shear stress in 3,38 times. In the group of patients with PU, combined with DM, expressed abuse of endothelial independent vasodilatation was found.

Marked endothelial dysfunction in patients with PU, combined with DM, which manifested by increased levels of ET-1 and NO in the blood, as well as violation of endothelial dependent vasodilatation and endothelial independent vasodilatation was established. Probably pathogenetic links of the detected violations are HP persistence and performance of high concentration of glucose in tissue. High concentrations of NO in plasma of patients with PU, combined with DM, do not cause vasodilatation, but rather leads to vasoconstriction in 37% of subjects. Taking into account the results of tests with nitroglycerin, we can provide specific violation of endothelial independent vasodilatation in these patients, including disorders due to the receptor system.

In view of the foregoing, the third group was divided into 2 groups: control (Ia) and primary (Ib). To correct the detected changes, with the basic treatment

Table 1

Indicators of endothelin-1 and NO in patients with peptic ulcer, combined with diabetes mellitus, during the exacerbation (M ± m)

Data	Healthy individuals n=8	Group I n=11	Group II n=11	Group III n=30
ET-1, fmol/ml	0.38±0.06	0.98±0.08*	1.26±0.07*/**	1.66±0.09*/**/***
NO, mmol/l	19.05±0.77	16.67±0.76*	21.15±0.55*/**	22.87±0.42*/**/***

Note: * Significant changes compared to the data of the healthy individuals (p<0.05); ** Significant changes compared to the data of patients with PU (p<0.05); *** Significant changes compared with the data of the diabetic patients (p<0.05).

Table 2

Indicators of the brachial artery sensitivity to the shear stress on the endothelium in patients with peptic ulcer, combined with diabetes mellitus, during the exacerbation (M ± m)

Data	Healthy individuals n=8	Group I n=8	Group II n=16
D_0, sm	0.33±0.02	0.39±0.01*	0.41±0.01*
V_0	84.63±1.70	83.13±2.43	82.62±2.48
τ_0 din/sm^2	52.30±2.47	43.20±2.21*	40.61±1.72*
D_1, sm	0.38±0.02	0.41±0.02	0.42±0.02
V_1	134.63±2.58	123.63±4.41	112.63±3.24*
τ_1 din/sm^2	72.46±2.93	61.36±3.01*	52.79±2.11*/**
$\Delta\tau_1$	20.16±1.45	16.15±1.76	12.17±1.85*/**
K_1	0.44±0.13	0.18±0.02*	0.11±0.03*/**
Vasodilatation, %	14.78±2.51	6.36±0.49*	0.90±0.37*/**
D_2, sm	0.42±0.02	0.46±0.02	0.45±0.02
V_2	136.25±2.88	123.13±2.84*	104.19±4.79*/**
τ_2 din/sm^2	65.07±2.40	53.77±2.69*	45.97±2.34*/**
$\Delta\tau_2$	12.77±0.88	10.57±1.46	5.35±1.33*/**
K_2	1.29±0.22	0.98±0.23	0.29±0.07*/**
Vasodilatation, %	29.26±2.96	20.17±2.08*	9.39±3.37*/**

Note: * Significant changes compared to the data of the healthy individuals (p<0.05); ** Significant changes compared with the data of the diabetic patients (p<0.05).

(rabeprazole – 20 mg twice daily, amoxicillin – 1000 mg twice daily, clarithromycin – 500 mg twice daily for 14 days) for patients of the primary group quinapril drug at a dose of 2.5 mg 1 time per day in the morning under the control of hemodynamic parameters within a week, with the transition to 5 mg once daily in the morning for three weeks. Repeated studies conducted 4-6 weeks after treatment.

Analyzing the data of the functional state of the endothelium in patients with PU, combined with DM (table 3), it was found that the level of ET-1 decreased slightly in case of the basic treatment (36%), but the highest reduction observed in the group of patients who received quinapril (in 3.2 times).

Table 3

Indicators of endothelin-1 and NO in patients with peptic ulcer, combined with diabetes mellitus, dynamics of treatment (M ± m)

Data	Healthy individuals n=8	Group Ia n=10		Group Ib n=10	
		Before treatment	After treatment	Before treatment	After treatment
ET-1, fmol/ml	0.38±0.06	1.52±0.08	1.12±0.07*/**	1.64±0.11	0.51±0.05**/***
NO, mmol/l	19.05±0.77	23.01±0.34	21.64±0.52*/**	22.98±0.42	20.01±0.21**/***

Note. * Significant changes compared to the data of the healthy individuals (p<0.05); ** Significant changes compared with the data in the subgroup before and after treatment (p<0.05); *** Significant changes compared with the data in the subgroup Ia after treatment (p<0.05).

After the treatment, the results tend to set Doppler reducing of the diameter of blood vessels in the group Ib (0.40±0.02) and diameter unchanged in group Ia (0.41±0.02). According to the literature, and ACE-causing effect on the diameter of the vessel can be found after combined treatment duration of 6 months. Also the tendency to improve blood flow velocity at rest (3%) and shear stress at rest (8%) was showed. However a significant increase in the rate of 11% and the shear stress in response to reactive hyperemia test with 13% compared with before treatment revealed ($p<0.05$). Patients who received basic treatment had no significant differences in data.

These changes were confirmed by sensitivity index of brachial artery to the shear stress which in the patients of group Ib increased by 58%, and vasodilatation, which increased by 6%.

Conclusions:

1. The disease HP-associated peptic ulcer of the stomach and duodenum, combined with diabetes mellitus, is characterized by marked vascular endothelial dysfunction.

2. Application of quinapril with basic therapy results in significant positive indicators of endothelial function, namely the reduction of endothelin-1 levels and NO, which is also confirmed by the shear stress changes and sensitivity of the brachial artery to the shear stress during reactive hyperemia tests.

Prospects for further research. It is advisable to study the impact of the proposed treatment on the other pathogenic links in case of peptic ulcer of the stomach and duodenum, combined with diabetes mellitus.

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PROBLEM OF HIV TRANSMISSION TO CHILDREN THROUGH BREASTFEEDING IN THE REPUBLIC OF CRIMEA

ПРОБЛЕМА ИНФИЦИРОВАНИЯ ДЕТЕЙ ВИЧ ЧЕРЕЗ ГРУДНОЕ ВСКАРМЛИВАНИЕ В РЕСПУБЛИКЕ КРЫМ

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