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THE DEPENDENCE OF THE CYTOKINE HOMEOSTASIS STATE ON THE CYTOTOXICITY OF H. PYLORI STRAINS IN PATIENTS WITH PEPTIC GASTRIC AND DUODENAL ULCER COMBINED WITH HYPERTENSION AND TYPE 2 DIABETES MELLITUS

Abstract. *The article demonstrates the prevalence of CagA+, VacA+ strains and their combinations in patients with peptic gastric and duodenal ulcer combined with arterial hypertension and type 2 diabetes mellitus. The changes in the state of the cytokine homeostasis have been revealed. The changes are accompanied with an increase in the IL-6, IL-12, IL-18 content and a decrease in the IL-10 content, which parameters depend on the presence of H.pylori (CagA+, VacA+) strains and their combinations.*

Key words: *gastric ulcer, IL-12, IL-10, IL-6, IL-18, diabetes mellitus 2, arterial hypertension, cytokine homeostasis.*

Introduction. The wide spread and increasing incidence of gastric and duodenal ulcer, high probability of development of severe complications, increase in mortality and disability of patients justify the urgency of search for new pathogenic mechanisms of the disease. In recent years, the numerous data appeared, which show that chronic inflammation is due not only features of the H. pylori pathogen persistence and its damaging effects on the mucosa, but also due to the development of immunodeficiency state or immunopathological aggression [1,2]. Changes in the content of IL-6, IL-10, IL-12, IL-18 is a diagnostic criterion of the frequency of relapses and the disease stage.

Objective: to study the dependence of the state of the cytokine homeostasis on the H. pylori toxic strains in patients with peptic gastric and duodenal ulcer combined with hypertension and type 2 diabetes mellitus.

Materials and methods. 71 patients were examined (33 patients with PGU and PDU (18 patients with H.pylori-associated diseases with CagA+VacA+ toxigenic strains (group1a), 15 patients with H.pylori-associated diseases with CagA+VacA-/CagA-VacA+ toxigenic strains (group 2a) and 38 patients with peptic gastric

(PGU) and duodenal ulcer (PDU) combined with arterial hypertension (AH) and type 2 diabetes mellitus (DM2) (22 patients with H.pylori-associated diseases with CagA+VacA+ toxigenic strains (group 1b), 16 patients with H.pylori-associated diseases with CagA+VacA+/CagA-VacA+ toxigenic strains (group 2b) and 20 apparently healthy people (AHP). The criteria for inclusion of the patient in the study were the following: Hp-associated peptic gastric and duodenal ulcer; AH of I and II stage, of 1st and 2nd degree; DM2 of low severity, compensated, of medium severity, and subcompensated. CagA, VacA H. pylori strains in the biopsies were determined using the PCR reagents "Khelikopol" ("Litekh", Russia). Cytokine series was determined by ELISA using the reagents IL-6, IL-10, IL-12, IL-18 (Benher MedSystems GmbH, Austria).

Results and discussion. As a result of the study of H. pylori strains it was found out that there is a presence of (SagA + VacA +) in 18 patients with PGU and PDU (54.54%) (group 1a), and a presence of (SagA + VacA- / SagA-VacA +) in 15 patients (45.45%) (group1b). In the group of patients with PGU and PDU combined with AH and DM2 the results are similar: (SagA + VacA +) is observed in 22 patients (57.89%) (group 1b),

(SagA + VacA- / SagA-VacA +) is observed in 16 patients (42.11%) (group 2b). It is proved that the presence of CagA and VacA is an additional risk factor for chronic gastritis, PGU and PDU, gastric cancer in patients infected with H. pylori. The combination of VacA and SagA strains is a marker of the disease severity [3].

Evaluating the state of the cytokine homeostasis (Table 1) it was established that in patients with PGU and PDU with the presence of CagA+VacA+ H. pylori strains there is a significant increase in the IL-6 content in 2.3 times, in the IL-12 content - in 3.88 times, in the IL-18 content - in 2.3 times and a decrease in the IL-10 content in 1.37 times compared with the

group of AHP. In groups 1b, 2a, 2b there is an increase in the IL-6 content in 5.23 times, in 8.2 times, in 9.91 times accordingly compared with the group of AHP; the IL-12 content increases in 2.13 times, in 2.95 times and in 9.71 times in groups 1b, 2a, 2b accordingly compared with the group of AHP; the IL-18 content increases in 2.11 times, in 9.74 times and in 3.37 times in groups 1b, 2a, 2b accordingly compared with the group of AHP; and in groups 1b, 2a, 2b there is a decrease in the IL-10 content of 16.11%, in 3.4 times and in 1.92 times accordingly.

In the group of patients with PGU and PDU combined with AH and DM2 there is a statistically significant increase in the IL-6,

Table 1

The dependence of the cytokine homeostasis state in patients with peptic gastric and duodenal ulcer combined with hypertension and type 2 diabetes mellitus on the H. pylori toxic strains

Parameters	PGU and PDU (group 1) (n=33)		PGU and PDU combined with AH and DM2 (group 2) (n=38)		AHP (group 3) (n=20)
	CagA+ VacA+ (group 1a) (n=18)	CagA+ VacA- /CagA- VacA+ (group 1b) (n=15)	CagA+ VacA+ (group 2a) (n=2a)	CagA+ VacA- /CagA- VacA+ (group 2b) (n=16)	
IL-6	28.72±0.59 p ₁ ≤0.001	28.67±0.71 p ₁ ≤0.05	66.36±3.68 p ₁ ≤0.001 p ₂ ≤0.001 p ₃ ≤0.001	54.31±1.35 p ₁ ≤0.001 p ₂ ≤0.001 p ₄ ≤0.05	5.48±0.22
IL-10	1.49±0.11 p ₁ ≤0.001	1.78±0.11 p ₁ ≤0.001 p ₂ ≤0.05	0.6±0.6 p ₁ ≤0.001 p ₂ ≤0.001 p ₃ ≤0.05	1.06±0.04 p ₁ ≤0.001 p ₂ ≤0.05 p ₃ ≤0.05 p ₄ ≤0.05	2.04±0.12
IL-12	6.17±0.2 p ₁ ≤0.001	3.39±0.33 p ₁ ≤0.001 p ₂ ≤0.05	53.89±11.02 p ₁ ≤0.001 p ₂ ≤0.001 p ₃ ≤0.001	16.36±3.05 p ₁ ≤0.001 p ₂ ≤0.05 p ₃ ≤0.05 p ₄ ≤0.001	1.59±0.19
IL-18	163.17±9.58 p ₁ ≤0.05	146.67±17.6 p ₁ ≤0.001	678.41±101.69 p ₁ ≤0.001 p ₂ ≤0.05 p ₃ ≤0.05	235±23.14 p ₁ ≤0.001 p ₂ ≤0.05 p ₃ ≤0.05 p ₄ ≤0.05	69.63±4.72

Note. p₁ – the parameters are statistically significant compared with the group of healthy persons; p₂ – the parameters are statistically significant compared with the group 1a; p₃ – the parameters are statistically significant compared with the group 1b; p₄ – the parameters are statistically significant compared with the group 2a.

IL-12 and IL-18 content and a decrease in the IL-10 content at the presence of the CagA+VacA+ strains in 1.22 times, in 3.29 times, in 2.89 times and in 1.77 times accordingly compared with the group of patients with PGU and PDU combined with AH and DM2 at the presence of combination of CagA+VacA-/ CagA-VacA+ strains.

Conclusion. 1. In patients with peptic gastric and duodenal ulcer combined with arterial hypertension and type 2 diabetes mellitus there is a higher prevalence of strains CagA+VacA+ and the lower prevalence of combinations of strains CagA+VacA-/ CagA-VacA+.

2. The presence of CagA+VacA+ *H. pylori* strains in patients with peptic gastric and duodenal ulcer is accompanied by the violation of the state of the cytokine homeostasis (an increase in the IL-6 content ($p \geq 0.001$, $p \geq 0.05$), the IL-12 content ($p \geq 0.001$, $p \geq 0.05$), the IL-18 content ($p \geq 0.001$, $p \geq 0.05$) and a decrease in the IL-10 content ($p \geq 0.001$, $p \geq 0.05$) and

combination of this pathology with arterial hypertension and type 2 diabetes mellitus complicates the course of the underlying disease, diagnostic criteria and treatment.

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