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ВПЛИВ АНТИХЕЛІКОБАКТЕРНОЇ ТЕРАПІЇ НА СТАН ЦИТОКІНОВОГО ЗВ'ЯЗКУ У ХВОРИХ НА ВИРАЗКОВУ ХВОРОБУ ШЛУНКА ТА ДВАНАДЦЯТИПАЛОЇ КИШКИ В ПОЄДНАННІ З АРТЕРІАЛЬНОЮ ГІПЕРТЕНЗІЄЮ ТА ЦУКРОВИМ ДІАБЕТОМ 2 ТИПУ

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INFLUENCE OF ANTIHELICOBACTER THERAPY ON THE STATE OF CYTOKINE LINK IN PATIENTS WITH PEPTIC ULCER OF THE STOMACH AND DUODENUM IN COMBINATION WITH ARTERIAL HYPERTENSION AND TYPE 2 DIABETES MELLITUS

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Анотація

У статті представлено зміни цитокінового профілю, а саме ІЛ-6, ІЛ-10, ІЛ-12, ІЛ-18. Усіх обстежених пацієнтів було розподілено на 2 групи: 33 хворих на виразкову хворобу шлунка (ВХШ) та дванадцятипалої кишки (ДПК) у поєднанні з артеріальною гіпертензією (АГ) та цукровим діабетом 2 типу (ЦД 2 типу) (1 група); 30 хворих на ЯБД та виразкову хворобу дванадцятипалої кишки (2 група) та 30 практично здорових осіб (ПОЗ) (3 група)).

У групі хворих на ПАП та ПСХ у поєднанні з АГ та ЦД 2 типу проводили наступну терапію: 1а (7 пацієнтів) отримували вісмуту субцитрат 120 мг 4 рази на день, тетрациклін 500 мг 4 рази на день, метронідазол 500 мг 3 рази на день. на 10 днів; 1б (9 пацієнтів) отримували вісмуту субцитрат 120 мг 4 р. д., тетрациклін 500 мг 4 р. д., метронідазол 500 мг 3 р. д. на 10 днів і Лаціум по 1 пакетику 2 р.д. на 1 місяць. група 1в (9 осіб) - езомепразол 20 мг 2 р., амоксицилін 1,0 г 2 р. протягом 5 днів, езомепразол 20 мг 2 р., кларитроміцин 500 мг 2 р., тинідазол 500 мг 2 р. наступні 5 днів; 1г (8 осіб) - езомепразол 20 мг 2 р., амоксицилін 1.0 г 2-й раз протягом 5 днів, езомепразол 20 мг 2-й раз, кларитроміцин 500 мг 2-й раз, тинідазол 500 мг 2-й раз протягом наступних 5 днів і Лаціум по 1 пакетику 2-й раз протягом 1 місяця.

Після лікування покращився цитокіновий профіль (наприклад, у групах 1а, 1с після запропонованих схем лікування рівень ІЛ-6 вірогідно знизився на 13,50% (42,24±1,27) ($p<0,05$), на 15,40% (41,31±1,29) ($p<0,05$)). Проте найкращі результати виявлено в групах із додатковим комбінованим пробіотиком (значне зниження ІЛ-6 (на 26,66% (35,81±1,01) $p<0,05$), у 1,8 раза (27,06±0,69) ($p<0,05$)).

Висновок. Вплив як токсигенної, так і супутньої патології на перебіг ПВД та виразкової хвороби ДПК супроводжується значним цитокіновим дисбалансом (збільшенням концентрації прозапальних (ІЛ-6, ІЛ-12, ІЛ-18) та зниженням вмісту протизапальних цитокінів (IL-10) у сироватці крові пацієнтів), порушується рівень ДЕК, що призводить до тяжкої ендотеліальної дисфункції та має взаємно обтяжений перебіг.

Abstract

The article presents changes in the cytokine profile, namely IL-6, IL-10, IL-12, IL-18. All examined patients were divided into 2 groups: 33 patients with peptic ulcer of the stomach (PUD) and duodenum (duodenal ulcer) in combination with arterial hypertension (AH) and type 2 diabetes mellitus (T2DM) (group 1); 30 patients with PUD and duodenal ulcer (group 2) and 30 practically healthy individuals (PHI) (group 3)).

In the group of patients with PAP and PSC in combination with hypertension and T2DM, the following therapy was performed: 1a (7 patients) received bismuth subcitrate 120 mg 4 p.d., tetracycline 500 mg 4 p.d., metronidazole 500 mg 3 p.d. for 10 days; 1b (9 patients) received bismuth subcitrate 120 mg 4 p.d., tetracycline 500 mg 4 p.d., metronidazole 500 mg 3 p.d. for 10 days and Lacium 1 sachet 2 p.d. for 1 month. group 1c (9 people) - esomeprazole 20 mg 2 rd, amoxicillin 1.0 g 2 rd for 5 days, esomeprazole 20 mg 2 rd, clarithromycin 500 mg 2 rd, tinidazole 500 mg 2 rd for the next 5 days; 1g (8 people) - esomeprazole 20 mg 2 rd, amoxicillin 1.0 g 2 rd for 5 days, esomeprazole 20 mg 2 rd, clarithromycin 500 mg 2 rd, tinidazole 500 mg 2 rd for the next 5 days and Lacium 1 sachet 2 rd for 1 month.

After treatment, the cytokine profile improved (e.g., in groups 1a, 1c, after the proposed treatment regimens, IL-6 levels significantly decreased by 13.50% (42.24±1.27) (p<0.05), by 15.40% (41.31±1.29) (p<0.05)). However, the best results were found in the groups with additional combined probiotic (a significant decrease in IL-6 (by 26.66% (35.81±1.01) p<0.05), 1.8 times (27.06±0.69) (p<0.05)).

Conclusion. The effect of both toxigenic and concomitant pathologies on the course of PVD and duodenal ulcers is accompanied by a significant cytokine imbalance (increased concentration of proinflammatory (IL-6, IL-12, IL-18) and decreased content of anti-inflammatory cytokines (IL-10) in the serum of patients), impaired DEC levels, which leads to severe endothelial dysfunction and has a mutually aggravated course.

Ключові слова: Виразкова хвороба, цукровий діабет, антихелікобактерна терапія.

Keywords: Peptic ulcer, diabetes, anti-helicobacter therapy.

Relevance. Antihelicobacterial therapy is the gold standard for the treatment of peptic ulcer of the stomach and duodenum associated with H. pylori [1]. It is known that Helicobacter pylori directly affects the lipid profile of the blood. It increases the levels of total cholesterol (TC), low-density lipoprotein (LDL) and atherogenicity index (AI) (TC/LDL), and stimulates the production of proinflammatory cytokines (IL-1β, IL-2, IL-6, IL-12, IL-18, TNF-α, etc.), which is probably one of the risk factors for the development of hypertension and atherosclerosis [1,2,3]. The studied changes in the polymorphisms of the genes IL-1β, TNF-α, IL-6, IL-8, IL-10, IL-12, IL-18 indicate the development of gastric atrophy, hypochlorhydria, and non-cardiac gastric cancer [1,4,5].

The biological effects of IL-6 are associated with the temporary development of atherosclerosis, realized through the activation of endothelial cells, proliferation and migration of smooth muscle cells. Various studies indicate the expression of IL-6 in areas of the vascular bed that are prone to metabolic damage (coronary arteries, cerebral vessels, peripheral arteries) [3].

Therefore, the aim of our work is to evaluate the effect of toxigenic strains (CagA, VacA) of H. pylori and their combinations on the cytokine link in patients with peptic ulcer of the stomach and duodenum in combination with arterial hypertension and type 2 diabetes mellitus.

Materials and methods of the study. We examined 33 patients with peptic ulcer of the stomach (PUD) and duodenum (duodenal ulcer) in combination with arterial hypertension (AH) and type 2 diabetes mellitus (T2DM) (group 1); 30 patients with PUD and duodenal ulcer (group 2) and 30 practically healthy individuals (PHI) (group 3)).

In the group of patients with PAP and PSC in combination with hypertension and T2DM, the following therapy was performed: 1a (7 patients) received bismuth subcitrate 120 mg 4 p.d., tetracycline 500 mg 4 p.d., metronidazole 500 mg 3 p.d. for 10 days; 1b (9 patients) received bismuth subcitrate 120 mg 4 p.d., tetracycline 500 mg 4 p.d., metronidazole 500 mg 3 p.d. for 10 days and Lacium 1 sachet 2 p.d. for 1 month. group 1c (9 people) - esomeprazole 20 mg 2 rd, amoxicillin 1.0 g 2 rd for 5 days, esomeprazole 20 mg 2 rd, clarithromycin 500 mg 2 rd, tinidazole 500 mg 2 rd for the next 5 days; 1g (8 people) - esomeprazole 20 mg 2 rd, amoxicillin 1.0 g 2 rd for 5 days, esomeprazole 20 mg 2 rd, clarithromycin 500 mg 2 rd, tinidazole 500 mg 2 rd for the next 5 days and Lacium 1 sachet 2 rd for 1 month.

The state of the cytokine link was assessed by ELISA by determining IL-10, IL-12 p70, IL-18 Bender MedSystems GmbH (Austria), IL-6 "Cytokin" (St. Petersburg).

Results of the study. Investigating the level of interleukins in the blood, it was found that in group 1 the content of IL-6 was (48.83±1.61), IL-12 - (19.6±0.25), IL-18 - (240.17±9.56) against the background of a decrease in IL-10 (0.85±0.03). A similar situation was observed in group 2 (increase in IL-16 (24.32±1.21), IL-12 (9.61±0.36), IL-18 (98.11±7.36) against a decrease in IL-10 (1.35±0.23)). Comparing the state of the cytokine link in the presence of concomitant pathology, it was found that the highest rate was found in the group of patients with PAP and duodenal ulcers in combination with hypertension and T2DM.

With the proposed treatment regimens, it was found that in the groups of patients 1a, 1c after the proposed treatment regimens, the level of IL-6 significantly decreased by 13.50% (42.24±1.27) (p<0.05), by 15.40% (41.31±1.29) (p<0.05), respectively; IL-12 level – by 13.37% (16.98±0.43) (p<0.05), by 18.16% (16.04±0.85) (p<0.05), respectively; IL-18 level – by 35.79% (154.22±7.61) (p<0.05), by 32.56% (161.97±4.1) (p<0.05), against the background of IL-10 increase by 43.33% (1.5±0.05) (p<0.05), by 44.81% (1.54±0.14) (p<0.05), respectively, in the groups. However, in the groups of patients treated with the combined probiotic “Lacium”, the state of the cytokine link improved with a significant decrease in IL-6 (by 26.66% (35.81±1.01) p<0.05), 1.8 times (27.06±0.69) (p<0.05)), IL-12 (by 20.46% (15.59±0.84) (p<0.05), by 23.88% (14.92±0.63) (p<0.05),), IL-18 (1.99 times (120.44±2.78) (p<0.05), 2.04 times (117.88±3.24) (p<0, 05),) against the background of increased IL-10 (1.91 times (1.62±0.06) (p<0.05), 1.96 times (1.67±0.15) (p<0.05),) according to the groups.

Discussion of results. IL-10 plays an important role. The activation of its production and imbalance leads to the release of catecholamines and glucocorticoids as a response to stress induced by bacterial aggression [2,4]. A significant increase in IL-10 secretion suppresses the synthesis and secretion of cytokines by Th1 lymphocytes, activated monocytes, and natural killer cells and decreases the production of antibodies by plasma cells. At the same time, a reduced level of IL-10 leads to an increase in T-lymphocyte secretion. However, increased sensitivity of Th1 cells leads to negative regulation of IL-10 [5,6].

IL-12 is a key cytokine for enhancing the cell-mediated immune response and initiating effective de-

fense. The protective effects of IL-12 enhance the production of nitric oxide metabolites and T-cell infiltration, increase the expression of adhesive molecules and chemokine production, and stimulate the cytotoxic activity of natural killer cells and cytotoxic lymphocytes [6,7].

Several lines of evidence support the tight association of IL-18 with MS and its components and its predictive role in cardiovascular events. However, it should be emphasized that the exact role of IL-18 in the pathogenesis of these conditions requires further careful study at the clinical level [1,2,8].

Conclusion. The effect of both toxicogenic and concomitant pathologies on the course of PVD and PDA is accompanied by a significant cytokine imbalance (increased concentration of proinflammatory (IL-6, IL-12, IL-18) and decreased content of anti-inflammatory cytokines (IL-10) in the serum of patients), impaired DEC levels, which leads to severe endothelial dysfunction and has a mutually burdened course.

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