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STATE OF IMMUNE RESPONSE MEDIATORS IN CHILDREN WITH GASTRITY

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Annotation
98 (53.8%) children with HP-associated pathology and 84 (46.2%) with HP-negative pathology of the gastroduodenal zone were examined, in whom the content of cytokines IL-4, TNF-α was determined. Results: An increase in the production of the studied Th1-helper cytokines indicates the activation of Th1-type immunity in H. pylori-associated gastroduodenal pathology. At the same time, an increase in the concentration of cytokines in the blood serum more clearly reflects the dynamics of the pathological process.

Keywords: children, gastroduodenitis, peptic ulcer, immunology, Helicobacter pylori.

GASTRITI BO'LGAN BOLALARDA IMMUN JAVOB VOSITACHILARINING HOLATI

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Annotatciya:
HP bilan bog'liq patologiyasi bo'lgan 98 (53,8%) va gastroduodenal zonaning HP-salbiy patologiyasi bo'lgan 84 (46,2%) bolalar tekshirildi, ularda IL-4, TNF-a sitokinlarining tarkibi aniqlandi. Natijalar: o'rganilayotgan Th1-yordamchi sitokinlar ishlab chiqarishning ko'payishi H. pylori bilan bog'liq gastroduodenal patologiyada Th1 tipidagi immunitetning faollashishini ko'rsatadi. Shu bilan birga, qon zardobida sitokinlar kontsentratsiyasining ortishi patologik jarayonning dinamikasini yanada aniqroq aks ettiradi.

СОСТОЯНИЕ МЕДИАТОРОВ ИММУННОГО ОТВЕТА У ДЕТЕЙ С ГАСТРИТОМ

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Аннотация:
увеличение продукции изученных цитокинов Th1-хелперов свидетельствует об активации иммунитета по Th1 типу при H. pylori ассоциированной гастродуоденальной патологии. При этом увеличение концентрации цитокинов в сыворотке крови более выражено отражает динамику патологического процесса. Выводы: одним из факторов риска, развития язвенного процесса слизистой оболочки гастродуоденальной зоны у обследованных детей, является увеличение содержания TNF-α в периферической крови.

Ключевые слова: дети, гастродуоденит, язвенный болезнь, иммунология, Helicobacter pylori.

Introduction

The high prevalence of inflammatory diseases of the stomach and duodenum, their significant share in the structure of gastroenterological morbidity [1,2], recurrent and progressive course [3] determine the urgency of the problem of chronic gastroduodenitis in children. H. pylori (HP) infection is considered to be one of the main etiological factors of chronic inflammatory diseases of the stomach and duodenum in children [4]. At the same time, data on the role of this microbe in chronic gastroduodenitis in school-age patients are very contradictory and require further clarification [5-7]. In the pathogenesis of chronic gastroduodenitis, immunological mechanisms, including the role of cytokines, are least studied, and their diagnostic and prognostic significance is not determined [11]. Being the initial link in the activation of the immune response, cytokines determine the effectiveness and type of immunological response to infectious and non-infectious agents, and are directly involved in the development and regulation of local inflammatory and immune responses [11]. Studying the profile of proinflammatory cytokines synthesized directly in the focus of inflammation, in relation to the clinical course of gastroduodenitis, morphofunctional changes in the organs of the gastroduodenal system, indicators of local protection, and taking into account the leading etiological factor of the disease (infectious, allergic) will expand knowledge about the pathogenesis of inflammatory diseases of the stomach and duodenum, which will improve their diagnosis and treatment.

Research Objective

To study the prognostic significance of proinflammatory cytokines in children with H. pylori-associated gastroduodenal pathology.

Material and Methods

We examined 182 children (79 boys and 103 girls) aged 7-18 years with inflammatory diseases of the stomach and duodenum. Of these, 98 (53.8%) patients with HP-associated pathology and 84 (46.2%) patients with HP-negative pathology of the gastroduodenal zone. 28 (15.4%) of them had peptic ulcer disease, 154 (84.6%) – with 48 ISSN 2181-7812 www.tma-journals.uz Clinical medicine of chronic gastroduodenitis (CGD). The clinical diagnosis was verified according to the classifications of YABDPC and CHD accepted in pediatrics and the classification of A.V. Mazurin (1984). The content of cytokines was determined Cytokine test kit (St. Petersburg, Russia). The content of human IL-4 and TNF-α was determined using a set of ELISA reagents IL-4 and ELISA-TNF-α by solid-phase enzyme immunoassay. The results of an immunological study of blood serum were compared with similar indicators obtained by the Institute's employees during the examination of children without inflammatory changes in the gastric and duodenal mucosa, who formed the control group and were conditionally accepted as normal. The obtained results were processed on a Pentium IV personal computer (software package). Microsoft Office Excel 2012). Methods of variational parametric and nonparametric statistics were used to calculate the arithmetic mean parameter (M), mean square deviation (σ), standard error of the mean (m), and relative values (frequency, %). Statistical significance in the comparative analysis of average indicators was evaluated by Student's criterion (t). At the same time, the probability of error (p) was determined when checking the normality of the distribution (kurtosis criterion) and the equality of general variances F according to the Fisher criterion. Confidence level $P<0.005$ was taken as a static value.

Results and Discussion

The content of interleukins in the blood serum depends on their entry into the blood and the involvement of systemic immune responses in the inflammatory response. The concentration of cytokines in the bloodstream is influenced by the duration of the disease and the frequency of relapses. When assessing the cytokine status of children aged 7 to 14 years, it was found that the level of interleukin-1b was significantly higher, and in children with H. pylori " + " gastroduodenal pathology, it exceeded the control by 2.2 times (47.9±0.96 and 21.6 ±0.86 pg/ml, respectively, $P<0.001$. and in almost 1.3 times this indicator in children with GDPN without HP (37.3±0.80, $P<0.001$) According to J. Bauditz (1999), M. M. D'ellios (2007), and S. Futagami (1998), microbial products lead to lymphoid infiltration of the gastric mucosa and the production of Th1 cytokines [8]. Based on the conditions of IL-1b expression and the mechanism of action, an increased interleukin content can be justified.

On the one hand, this is a possible damage to the gastric and duodenal mucosa, on the other hand, a decrease in the influence of other adverse factors and participation in the reparative processes of the gastroduodenal mucosa, which is consistent with the data of R. A. Akdogan (2014). This is an important function, since the quality of mucosal recovery depends on the probability of relapse of the disease [9]. Elevated serum IL-1b in children with H. pylori " + " gastroduodenal pathology is explained by the fact that H. pylori plays a significant role in the development of acid-dependent diseases of the gastrointestinal tract. When this pathogen is exposed to the gastric and duodenal mucosa, IL-1b is the first to be involved in the body's defense response and plays a leading role in both the development and regulation of non-specific infection. protection and specific immunity, i.e., in response to H. pylori infection, the synthesis of cytokines in the cells of the gastric mucosa increases. However, it is important to take into account the fact that with a prolonged inflammatory process, instead of limiting the growth of the pathogen, its own cells die, and the risk of developing atrophic gastritis, metaplasia, and stomach cancer increases. TNF-α is a pluripotent cytokine that is mainly produced by monocytes and macrophages and performs critical functions. During the period of triggering inflammation, it activates the endothelium, increases the expression of adhesion molecules on endothelial cells and promotes the adhesion of leukocytes to the endothelium, activates white blood cells (granulocytes, monocytes, lymphocytes), and induces the production of other pro-inflammatory cytokines that have a synergistic effect with TNF-α, in particular IL-1β [10]. Analysis of TNF-α data showed the same dynamics. Its level in blood serum in sick children was higher, with the maximum value in H. pylori " + " (52.4±083 and control 23.8 ±0.83 pg / ml, $p<0.001$).

According to the mechanism described after infection of the gastric mucosa, HP triggers a cytokine cascade, which primarily leads to increased expression of IL-1b, and it first activates neutrophils (increases chemotaxis and phagocytosis). Normally, neutrophils are the first to migrate to the focus of inflammation under the action of HP-induced chemoattractants and destroy bacteria by phagocytosis. However, a bacterial infection of HP can change the direction of the immune response, which leads to the pathogen's departure from immunological surveillance and imperfection of the immune response, therefore, to inefficiency the work of a non-specific link of immunity. Hyperproduction of IL-1b can lead to inhibition of the production of hydrochloric acid in the stomach, which contributes to the colonization of HP. Prolonged hypersecretion of cytokine causes depletion of the reserve capacity of producing cells and subsequently immunodeficiency, which contributes to the formation of a focus of chronic inflammation. At elevated levels of TNF-α, Th1 cells also activate macrophages, which, due to the production of bactericidal components (nitric oxide and oxygen radicals), destroy foreign antigens.

Since the HP bacterium is an extracellular pathogen, consequently, the body's immune system in the" face " of macrophages should activate the humoral immune response, i.e., the formation of antibodies. Therefore, in this case, the activation of the cellular immune response is "defective" and contributes to the persistence of the pathogen. HP is able to inhibit the action of macrophages due to their neutralization by catalase and superoxide dismutase, which contributes to its survival, i.e. the elimination of the bacterium does not occur.

Thus, the study of the state of the immune system in children with gastroduodenal pathology, depending on infection, revealed the focus of the study. immune shifts and their severity, which indicates an important pathogenetic role of immune mechanisms in the development and progression of changes in the state of the immune system of children with diseases of the digestive system. An increase in the production of the studied Th1 helper cytokines indicates the activation of Th1-type immunity in H. pylori-associated gastroduodenal pathology. At the same time, an increase in the concentration of cytokines in the blood serum more clearly reflects the dynamics of the pathological process.

Conclusion

The results of the study showed that an increase in the level of IL-1b is a prognostically unfavorable sign, which indicates the progression of gastroduodenal pathology. One of the risk factors for the development of ulcerative process of the gastroduodenal mucosa in the examined children is an increase in the content of TNF-α in the peripheral blood.

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