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INTERMEDIATE ANALYSIS OF LABORATORY-BIOCHEMICAL ANALYSIS IN CHILDREN INFECTED WITH CHRONIC VIRUS HEPATITIS V ON THE DEGREE OF DISEASE PASSAGE

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ABSTRACT: In this article, the average analysis of the laboratory-biochemical analyzes of the disease course in children with chronic viral hepatitis V and the development of the complications of acute otitis media developed against the background of SVGV are highlighted.

Changes in the functional state of the middle ear are more evident when acute otitis media in children occurs against the background of chronic viral hepatitis B. When acute otitis media in children developed against the background of chronic viral hepatitis B, the clinical course of acute otitis media was specific, significantly severe and prolonged. According to the results of biochemical analyzes in the blood of sick children, it was found that as the activity of ALT increased, the clinical signs of acute otitis media in sick children also increased.
Keywords: acute otitis media; chronic viral hepatitis B; children; immune system.
АННОТАЦИЯ: В статье освещен средний анализ лабораторно-биохимических анализов течения заболевания у детей с хроническим вирусным гепатитом В и развитие осложнений острого среднего отита, развившегося на фоне СВГВ.

Изменения функционального состояния среднего уха более выражены при остром среднем отите у детей, протекающем на фоне хронического вирусного гепатита В. При развитии острого среднего отита у детей на фоне хронического вирусного гепатита В клиническое течение острого среднего отита было специфичным, значительно тяжелым и затяжным. По результатам биохимических анализов в крови больных детей установлено, что по мере повышения активности АЛТ усиливаются и клинические признаки острого среднего отита у больных детей.
Ключевые слова: острый средний отит; хронический вирусный гепатит В; дети; иммунная система.
АННОТАЦИЯ: Уш бу мақолада сурункали вирусли гепатит в билан касалланган бемор болаларда лаборатор-биокимёвий таҳлилларнинг касалликнинг кечиш даражаси бўйича ўртача таҳлиллари ва СВГВ фонида ривожланган ўткир ўрта отит касаллигида авж олувчи асоратларининг ривожланиши ёритиб ўтилган.

Болаларда ўткир ўрта отит сурункали вирусли гепатит В фонида кечганда ўрта қулоқнинг функционал ҳолатларидаги ўзгаришлар яққолроқ намоён бўлади. Болаларда ўткир ўрта отит сурункали вирусли гепатит В фонида ривожланганида ўткир ўрта отитнинг клиник кечиши ўзига хос бўлиб, сезиларли даражада оғир ва узоқ давом этди. Бемор болаларнинг

қонидаги биохимик таҳлилллар натижасига кўра АЛТ активлиги ошиб борган сари бемор болалардаги ўткир ўрта отитнинг клиник белгилар ҳам кучайиб борганлиги аниқланди.

Калит сўзлар: ўткир ўрта отит; сурункали вирусли гепатит В; болалар; иммун тизим.

Relevance. Despite the achievements of world science, the treatment and prevention of acute otitis media, which develops in children against the background of chronic viral hepatitis B, remains one of the unsolved problems of modern medicine. It is known that chronic viral hepatitis B affects the liver and many organs and systems, and accordingly affects the growth and development of the child. Chronic viral hepatitis B significantly changes the clinical picture of acute otitis media, aggravates the course of the disease and, in parallel, increases the risk of developing meningoencephalitic complications that lead to an unfavorable outcome of the disease. According to the statistics of the Republic, acute otitis media occupies 32.7% of all ear diseases in children in Uzbekistan. Although these diseases do not threaten human life, they lead to deterioration of the quality of life of patients.

Acute otitis media in children occurs in most cases (88-98% of patients) against the background of other somatic diseases in the body. The link between acute otitis media and chronic viral hepatitis B is of interest to any researcher. It is known that chronic viral hepatitis B is a multifaceted disease that affects the activity of several organs and causes existing chronic diseases in the body or creates conditions for the emergence of certain diseases in individual cases. The organic relationship between acute otitis media in children and chronic viral hepatitis B is of interest to any researcher. Based on the above, it can be said that when acute otitis media in children is accompanied by liver dysfunction, timely diagnosis, development and justification of the optimal treatment scheme is an urgent task for the practical healthcare system.

Purpose of work: It consists in the study of clinical-laboratory and immunoreactivity characteristics, diagnosis and assessment of the state of the immune system in children affected by acute otitis media developed against the background of chronic viral hepatitis B.

Material and research methods. 114 children between the ages of 3 and 18 who were treated in the hepatology department of the Bukhara Regional Children's Hospital for Infectious Diseases, were infected with AOM developed on the background of ChVHB, and were treated with acute otitis media in the ENT department of VBKTTM. All control patients underwent extensive continuous examination, including clinical and laboratory, biochemical, immunological studies. In this regard, attention is focused on their complaints, past and concomitant diseases, premorbid appearance, causes of the disease, duration of the disease, and the effect of early treatment measures.

In order to study the immunological reactivity of the child's organism in dynamics, 50 children were involved in this study, of which 25 children affected by AOM developed on the background of ChVHB were treated conventionally, while 25 children affected by AOM developed on the background of ChVHB were children who received traditional and immunostimulating therapy.

According to the results of the study, 700 children affected by AOM developed on the background of ChVHB were retrospectively analyzed, 114 of them were prospectively analyzed, and all of them formed the main group of our study. 76 of our main group were children living in rural areas, and 38 were children living in urban areas.

The diagnosis of acute otitis media was made based on the complaints of children, clinical signs, results of otoscopic and endoscopic examination, medical history, peripheral blood parameters and the amount of eosinophils in the nasal septum, and the results of x-ray examination of the

nasal cavities. Liver status was assessed based on blood biochemical analysis, blood pigments (total, bound and unbound bilirubin) and enzymes (ALT-ACT).

The statistical development of the research results was carried out using general statistical methods. Data acquisition was performed on a PC with Intel(R) Core(TM)2 Quad CPU and OS Windows7. The STATISTICA 6.0 program was used in the study.

Results and analyses. In all patient children taken for the study, T-cell immune system parameters CD3+ (T-lymphocytes), CD4+ (T-helper/inducers) and CD8+ (T-cytotoxic lymphocytes) antigen expression, as well as CD4+/CD8+ ratio (immunoregulatory index - IRI) value was determined. The values of B-lymphocytes and the concentration of the main immunoglobulins in the peripheral blood serum were studied in children affected by AOM developed on the background of CHVHB. In addition to the basic cellular parameters of the immune system, signs of early and late activation of lymphocytes, which are of great diagnostic and prognostic value in the interpretation of the results, were studied.

Analyzing the results of the T-cell level of immunity in children with AOM developed on the background of CHVHB, it was shown that the average amount of the total number of leukocytes in children with an infectious inflammatory process expressed in the body was higher compared to the values of the control group. It seems that the leukocytosis we detected was an indication of the presence of systemic inflammation.

The relative amount of leukocytes in the peripheral blood tended to decrease, but was not clearly differentiated. The absolute value of lymphocytes was significantly higher in children with secondary otitis media than in the control group due to the observed increase in the number of leukocytes.

The results of the analysis of the immune system T-cell junction showed that the relative amount of CD3+ T-lymphocytes in children affected by O'O'O developed on the background of CHVHB was lower than the values of the control group. For example, in the control group, the value of CD3+ was 53.10±2.47%, and in the children of the main group, this indicator was on average 47.40±1.05%, which was a real difference. In the main group of children, the absolute values of T-lymphocytes were not significantly different.

n the analysis of the subpopulation composition of the T-cell junction, which includes the description of lymphocyte subpopulations, such as CD4+ and CD4+, a 1.2-fold decrease in the amount of T-helper/inducers (CD4+) was found in the children of the main group. Due to the high values of leukocytes, the absolute number of CD4+ lymphocytes tended to increase. This appears to be due to an adequate presence of leukocytes, including lymphocytes, but suppression of the T-helper/inducer subpopulation, which plays a key regulatory role in immune status. Therefore, the relative amount of T-helpers/inducers in the main group of children was actually lower than the data of the control group.

The analysis of the CD4+/CD8+ ratio (immunoregulatory index - IRI) showed its true decrease compared to the indicators of the control group ($R<0.05$). Differences in individual indicators of IRI in the main group of children varied to some extent, but most of the patients had IRI values lower than 1.0. Such a change in IRI was observed due to a decrease in CD4+ lymphocytes against the background of unrealistic changes in the value of CD8+ lymphocytes. We found that the number of CD8+ lymphocytes was not significantly different from the values of the control group. It appears to be related to the immunodeficient state in children, which is exacerbated by the presence of an infectious process and an inappropriate response to the pathogen.

Thus, in this case, the deficiency of the T-lymphocyte population in children of the main group is associated with a predominant reduction of CD4+ T-helpers/inducers, which are necessary for the regulation and formation of an adequate pathological process.

Therefore, the severe deficiency of T-cells in the children of the main group was associated with the deficiency of immunoregulatory subpopulations of T-lymphocytes, manifested by a clear deficiency in the number of CD4+ T-cells and CD8+ T-cytotoxic lymphocytes.

Currently, cytokines have been identified as a new independent system of regulating the main functions of the body, primarily related to the maintenance of homeostasis during the introduction of pathogens and disruption of tissue integrity. It is known that cytokines are a group of polypeptide mediators involved in the formation and regulation of the body's defense reactions. Studying the level of cytokines provides information about the functional activity of different types of immunocompetent cells; severity of the inflammatory process, its transition to the systemic level and prognosis, activation of type 1 and 2 T-helper provides information for the course of the process. To determine the level of cytokines, in particular, evaluation using immunoenzyme diagnostic test systems allows a new approach to studying the state of the body's immune system in clinical practice.

Pro-inflammatory and anti-inflammatory cytokines control inflammatory processes. Cytokines such as IFN-γ and IL-4 are involved in the regulation of the specific immune response, regulating the amplitude and duration of inflammatory and immune responses.

IFN-γ is a source of activated T-lymphocytes and natural killers. Among T-lymphocytes, pro-inflammatory cytokine producers are both cytotoxic CD8+ and helper CD4+ cells, but when they differentiate into Th1 and Th2, only Th1 cells retain the ability to produce pro-inflammatory cytokines. The most important function of pro-inflammatory cytokines is to mediate the relationship between lymphocytes and macrophages and participate in the regulation of the ratio of cellular and humoral components of the immune response. Pro-inflammatory cytokine, which is the main product of Th1-cells, reduces the secretory activity of Th2-cells. Thus, the pro-inflammatory cytokine is the main cytokine of the cellular immune response and the inhibitor of the humoral immune response, playing an important role in immunoregulation.

IFN-γ has been described as a V-lymphocyte-stimulating factor because it induces V-cell proliferation. The main producers of IL-4 are T-helpers of class 2. IL-4 is synthesized by mast cells and cells of the V-cell lineage. IL-4 reduces the functions of macrophages and their secretion of IL-1, TNF and IL-6, has an anti-inflammatory effect. Thus, IL-4 is the main product of Th2 cells and stimulates their differentiation. It causes the differentiation of B- and T-lymphocytes, affects the development of hematopoietic cells, macrophages, natural killers, basophils, which are functional antagonists of cytokines produced by Tx1 cells. IL-4 helps in the development of allergic reactions, has a clear anti-inflammatory effect.

We studied the nature of anti-inflammatory cytokines in children with AOM developed on the background of CHVHB. The obtained data are presented in Figure 1.

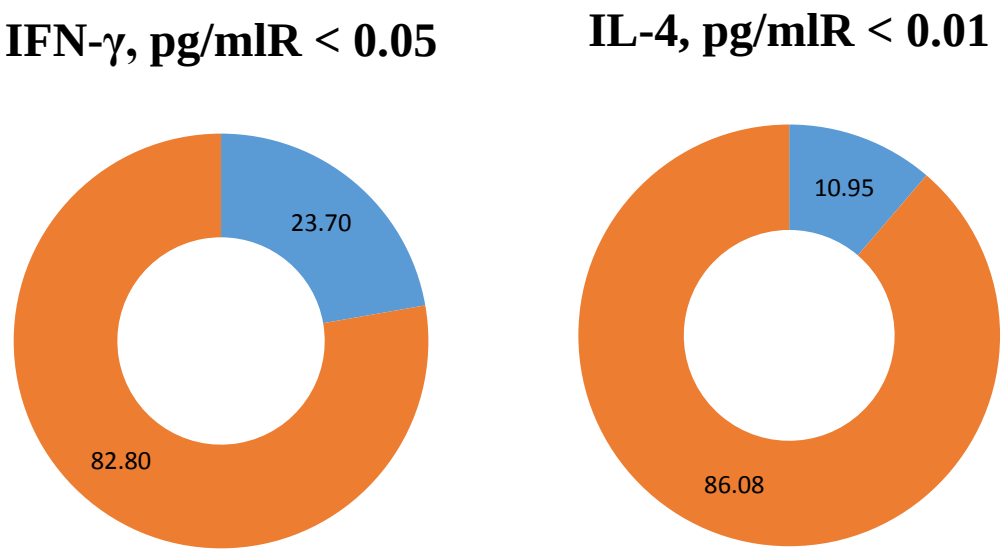

Figure 2. The patient with AOM developed on the background of CHVHB received inflammation and the status of anti-inflammatory cytokines in children

We studied inflammation and the type of pro-inflammatory cytokines in children with AOM developed on the background of strongly expressed CHVHB. The analysis of the obtained results revealed real differences between the values of the children of the control group and the main group. For example, the level of IFN-γ in healthy children was 23.70±5.38 pg/ml, while in children of the main group this indicator was 82.80±25.07 pg/ml. Thus, the level of IFN-γ increased by 3.5 times in children in the main group, which indicated the intensity of the inflammatory process.

When studying the level of IFN-g in the children of the control group, it was 10.95±3.65 pg/ml, and in the children of the main group, it was 86.08±25.72 pg/ml. In this case, the level of the anti-inflammatory cytokine IL-4 increased by 7.9 times.

A comparative analysis of the cytokine profile showed that the ratio of IFN-γ /IL-4 (pro-inflammatory/anti-inflammatory cytokines or Tx1/Tx2) was 2.2 in the group of healthy children. In the presence of a strong inflammatory process, as in the main group, this indicator was equal to 0.96. It seems that we observed a strongly expressed imbalance in the state of the main regulatory cytokines, which was expressed in a sharp increase in anti-inflammatory cytokines, which are the main regulators of acute inflammatory conditions, and a decrease in pro-inflammatory cytokines in children with CHVHB-infected AOM.

Thus, a patient affected by AOM developed against the background of CHVHB is characterized by the development of clinical symptoms depending on the severity of the main disease in children and the strengthening of these clinical symptoms at the stage of the disease. Enlargement of the liver and spleen was evident in this pathology. The clinical course of the disease in children with AOM developed against the background of CHVHB and the clinical manifestations of the disease are characterized by a decrease in the indicators of the cellular and humoral systems of the immune system in the body, and a sharp increase in anti-inflammatory cytokines, which are the main regulators of acute inflammatory conditions, and a decrease in pro-inflammatory cytokines.

CONCLUSION. Immunological studies conducted in patients affected by acute otitis media developed against the background of chronic viral hepatitis V in children before treatment with

immunotropic drugs and after treatment with normalization of the main immune system to identify some changes or features characterized by severe immunodeficiency, and the introduction of an immunotropic drug into the treatment complex leads to a positive clinical and immunodiagnosis of the disease helped and led to normalization of cellular, humoral and cytokine indicators in the body. In the study of the immune status in children, it was proved that there is a correlation between the cellular, humoral and cytokine indicators of the immune system.

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