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Research Article

MODERN APPROACHES TO THE STUDY OF THE STATE OF THE IMMUNE SYSTEM OF CHILDREN WITH PAPILLOMATOSIS OF THE LARYNX ON THE BACKGROUND OF ANTIVIRAL THERAPY

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Sh.A. Makhamadaminova
Tashkent Medical Academy, Uzbekistan

ABSTRACT

The goal was to study the state of the immune system of children with laryngeal papillomatosis depending on the clinical course of the disease in the dynamics of antiviral therapy. A comparative analysis of immunological parameters was carried out in the dynamics of standard therapy (before and after), and after standard + immunotropic therapy. For this purpose, 252 children with laryngeal papillomatosis aged 3 to 9 years were examined. All children were examined and treated in the surgical department of otolaryngology of TMA. In order to determine the effectiveness of the treatment of children, the following division into groups was carried out: Group I - children with a continuously recurrent course of papillomatosis of the larynx were divided into two subgroups: Subgroup I - the comparison group received standard treatment surgery + IFN preparations (reaferon) - one course per 28 days; Subgroup I - study group surgery + IFN preparations (alpha-IFN / inosine) - according to the scheme for 1 year. Group II - children with a frequently relapsing course of PH: II a subgroup - received standard treatment surgery + IFN preparations (reaferon) - one course for 28 days; II in the subgroup - surgery + IFN preparations (alpha-IFN / inosine) - according to the scheme for 6 months. Group III - children with a rarely recurrent course of PH: III a group - surgery; III in group - surgery + likopid. Unidirectional changes in the state of the immune response in papillomatosis of the larynx were revealed, which were most pronounced in the group of children with a continuously recurrent form of papillomatosis of the larynx. In the dynamics of therapy, improvements in the indicators of cellular and humoral immunity were found;

KEYWORDS

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papillomatosis of the larynx in children, interferons, interferon inducers, cellular and humoral parameters of immunity.

INTRODUCTION

As is known from the literature, the diagnosis of laryngeal papillomatosis, being a benign consequence of a viral process, requires immunological studies, ranging from cellular to molecular [2,4,16]. It has been established that children with laryngeal papillomatosis are characterized by dysfunction in the state of the cellular and humoral parts of the immune system, which are probably due to defects in one or more immune response mechanisms. Thus, the presence of a secondary immunodeficiency state is substantiated. As is known, immunodeficiencies are independent syndromes, characterized by a lack of immunity [1,6], which is characterized by a tendency to acyclic course, recurrence of the disease and the occurrence of oncological pathology [10]. The very first and main syndrome of the secondary immunodeficiency state is the infectious syndrome, which is characterized by chronic recurrent infection. Among all existing syndromes of secondary immunodeficiency, the infectious syndrome is the leading one, and in a laboratory study, the infectious syndrome is characterized by its own algorithm of immunological changes, including defects in the state of cellular and humoral immunity factors [1,6,10,11]. As it is already clear, laryngeal papillomatosis refers to an infectious syndrome of a secondary immunodeficiency state, which is distinguished by all the signs of immunodeficiency characteristic of it, and therefore attracts great attention from researchers. In this case, the theoretical justification was the previously identified imbalance in the immune system and deficiency in the system of functioning of the main interferons of the immune system [9,12]. As for treatment, it should be noted that, in general, the evaluation of treatment results presents great difficulties, which are primarily due to the diversity of the clinical course of laryngeal papillomatosis in children. According to the data obtained, it is known that during the course of papillomatosis of the larynx in children, spontaneous long-term remissions can be observed, as well as rapid growth, which forms frequently recurrent forms of the disease [1,2,5,7,14]. As for the immune status, there is a pronounced imbalance in the populations of lymphocytes of the immune system and immunodeficiency in the cellular link of immunity [11,12,18].

In connection with the foregoing, we set a goal to study the state of the immune system of children with laryngeal papillomatosis, depending on the clinical course of the disease in the dynamics of antiviral therapy. In connection with the above, we carried out a comparative analysis of immunological parameters in

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the dynamics of standard therapy (before and after), and after standard + immunotropic therapy.

MATERIAL AND RESEARCH METHODS

We conducted immunological studies in 252 children with larynx papillomatosis aged 3 to 9 years. All children were examined and treated in the surgical department of otolaryngology of the Tashkent Medical Academy (TMA). In order to determine the effectiveness of the treatment of children, the following division into groups was carried out: Group I - children with a continuously recurrent course of papillomatosis of the larynx were divided into two subgroups: Subgroup I - the comparison group received standard treatment surgery + IFN preparations (reaferon) - one course per 28 days; Subgroup I - study group surgery + IFN preparations (alpha-IFN / inosine) - according to the scheme for 1 year. Group II - children with a frequently relapsing course of PH: II a subgroup - received standard treatment surgery + IFN preparations (reaferon) - one course for 28 days; II in the subgroup - surgery + IFN preparations (alpha-IFN / inosine) - according to the scheme for 6 months. Group III - children with a rarely recurrent course of PH: III a group - surgery; III in group - surgery + licopid . The control group was represented by 29 practically healthy children of the same age and gender.

Immunological studies of children were carried out on the basis of clinical, laboratory and instrumental methods of research before the appointment of treatment, and during therapy after surgical removal at 6 months of therapy. Immunological studies were carried out at the NDC "Immunogen-test" at the RNCI of the Ministry of Health of the Republic of Uzbekistan on the basis of a scientific agreement. Determination of cellular, humoral immunity, as well as identification of activation markers CD 38+, CD 95+ was carried out using mAb in accordance with the methodological recommendations developed by the Institute of Immunology of the Russian Federation and the Institute of Immunology of the Academy of Sciences of the Republic of Uzbekistan [9]. The following research methods were carried out: determination of the number of leukocytes and lymphocytes, determination of subpopulations of lymphocytes by determining CD 4+ - T-helpers, CD 8+ - T-cytotoxic lymphocytes, CD 16+ - natural killer cells, CD 20+ - B-lymphocytes, C D 38+ - precursors of T- and B-lymphocytes, C D 95+ - lymphocytes with a receptor for physiological apoptosis, determination of the level of immunoglobulins of the main classes in blood serum and determination of circulating immune complexes of various sizes (CIC) by ELISA method.

The results obtained and their discussion. As mentioned above, it is customary to consider papillomatosis of the larynx in children as an

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immunodeficiency state, and in the literature it is described as a disease related to secondary immunodeficiencies in pathogenesis, due to the fact that papillomatosis is a chronic recurrent virus-induced process [7,8]. Therefore, the study of the state of immunoreactivity in children with laryngeal papillomatosis is an important factor necessary to establish the depth and extent of the formation of immunodeficiency, predict the disease, and most importantly, identify the most radical ways of therapy, including immunotropic therapy. In this regard, the study of quantitative and functional factors of the immune system, i.e. cellular and humoral parameters of immunity in the dynamics of therapy is a global problem in medicine [7,10,11,12,17]. Therefore, based on the foregoing, we assessed the cellular and humoral factors of the immune system in children with laryngeal papillomatosis, depending on various forms of the course of the disease in the dynamics of antiviral and immunotropic therapy. Table 1 presents the results of a comparative analysis of the immune status of children with laryngeal papillomatosis in the course of therapy. According to the data presented in the table, in a comparative analysis of the cellular composition of populations and subpopulations, certain changes are observed between groups 1a and 1c. So, for children of group 1c, where inosine was added in the complex, when compared with the data of children of group 1a, an increase in the expression of CD 3+ on lymphocytes by 1.14 times, CD 4+ - by 1.15 times, a decrease in CD 8+ - by 1.14 times, IRI increased by 1.3 times, CD 16+ was slightly reduced, but significantly. The study of humoral factors of immunity revealed that immunoglobulin A in peripheral blood serum was reduced by 1.7 times, CIC3% was reduced by 1.7 times, CIC4% was reduced by 2.4 times. The differences identified were all significant. Obviously, the decrease in the total pool of T-lymphocytes (CD 3+) was observed mainly due to the suppression of the number of T-lymphocytes that express CD 4+. It was found that the lowest content of T-lymphocytes was found in the group of children with continuously recurrent papillomatosis of the larynx before treatment. At the same time, during therapy, an increase in the total pool of T-lymphocytes is observed, which positively affects the state of T-cell immunodeficiency. Further, the content of the main regulatory cell of immunity, T-helpers/inducers, was studied. The CD 4+ T cell response to viral proteins is an important mechanism of host defense, since CD 4+ T helpers stimulate the production of antibodies by B lymphocytes and activate CD 8+ T lymphocytes specific for virus-infected cells [10]. The analysis revealed that, during therapy, there was also a significant increase in the expression of CD 4+ on T-lymphocytes compared with the values of the control group and the group before treatment ($p<0.05$). So it is known that cytotoxic CD 8+ T-lymphocytes play an important role in the pathogenesis of viral and proliferative diseases [9,10]. Analysis of the expression of CD 8+ on T-lymphocytes showed that during treatment there is a

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decrease in their expression, which confirms the improvement in cellular immunity and a decrease in suppression against the background of immunostimulation. It should be noted that, according to the literature, the virus is able to persist even in the presence of CD 8+ lymphocytes, which becomes the main mechanism of disease progression [8,10]. The immunoregulatory index (IRI), which is the ratio of the number of CD 4+T-helpers/inducers to the number of CD 8+T-lymphocytes, is essential in secondary infectious immunodeficiency states . Obviously, the suppression of CD 4+T-helpers/inducers against the background of an increase in the number of CD 8+T-lymphocytes leads to a decrease in IRI. The smallest reduced value of IRI is noted in the group of children with a continuously recurrent form of laryngeal papillomatosis compared with the values of the two groups of children studied, and amounted to 0.8 ± 0.03 in the group of children with continuously recurrent laryngeal papillomatosis, and in the control group - 1.49 ± 0.02 ($p<0.05$). Obviously, a decrease in IRI is an important criterion for the depth of T-cell immunodeficiency in children with laryngeal papillomatosis. Again, against the background of therapy, the value of IRI increases significantly and is reliably distinguishable.

Table 1.

The immune status of children with laryngeal papillomatosis in the dynamics of therapy depending on the clinical features of the disease (continuously relapsing group), M± m , %

Immunity parameters	Norm (n= 29)	Before treatment (n= 34)	Group 1a (standard + IFN drug) (n = 28)	Group 1c (standard + IFN + inosine pranobex) (n =26)
Leukocytes	6050±128.0	5910±114.5*	7200.5±165.8	8190.7±142.8
Lymphocytes	32.5±0.84	37.2±1.32*	41.5±0.92*^	42.8±1.12*#
CD 3+	58.4±1.25	42.4±0.98*	47.9±1.52* ^	54.6±1.42* #$
CD4+	38.3±1.25	30.5±1.33*	32.48±0.83* ^	37.5±1.34* #$
CD8+	18.8±0.54	33.80±1.18*	28.4±1.26* ^	24.80±0.88* #$

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IRI	1.65±0.05	0.72±0.02*	1.04±0.04 *^	1.32±0.02 *#$
CD 16+ _	18.2 1.0 ±3 _	28.4±0.14*	24.3±0.21*	22.02±0.42* #$
CD20+	19.9 ±0.83	2 6.6 ±1.26 *	2 3.5 ±1.2 2* ^	2 1, 4 ±1, 31* #
CD38 + _	22.4±0.86	27.8±1.24*	25.2±1.11*	22.8±1.30* #
CD95 + _	23.5±1.26	32.9 ±1.45*	27.3 ±1.42* ^	23.2 ±1.25* #
IgG	1260.0 ±21.60	1390.4±26.2*	1325.2±30.2*	1295.0±20.4* #
IgA	122.0 ±3.21	160.8 ±4.68*	152.4 ±2.85 ^	130.4 ±1.94 #$
IgM	112 ±2.1	138.4 ±1.61*	127.5 ±1.70 ^	119.2 ±1.46 #
CEC3%	8.58±1.34	198.2 ±3.72	145.4 ±2.28 ^	85.60 ±3.65 #$
CEC4%	14.22±1.51	158.5 ±2.45* ^	109.4 ±2.55* ^	45.80 ±3.15* #$

Note: * - significance of differences with the data of the control group, ^ - differences of group 1a with values before treatment; # - differences in group 1b with values before treatment; $ - differences between 1a and 1c groups.

Next, we studied the number of natural killer cells (NKCs), which are the third population of lymphocytes that ensure the maintenance of genetic homeostasis, which are phenotypically and functionally significantly different from T- and B-lymphocytes [8,10]. We have studied ECCs with CD 16+ phenotypes. Revealed a significant increase in the relative number of CD 16+ ECC in laryngeal papillomatosis, with the largest number of ECC found in the group of children with continuously recurrent form of laryngeal papillomatosis ($p<0.05$). Thus, in the group of children with a continuously recurrent form of papillomatosis of the larynx, the relative number of CD 16+ ECC was 28.4±1.3%, while in the control group it was 18.6-1.24 ±%. According to the data in Table 1, against the background of standard treatment, the number of ECC decreased, and with the addition of an IFN inductor, a significant decrease in ECC was observed and was close to the normal values. The level of B-lymphocytes, the main regulatory cells of the immune system, which is important in the development of humoral immunity, showed that the number of B-lymphocytes by the expression of CD 20+ receptors involved in the activation of B-lymphocytes was significantly increased

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in the group of children with a continuously recurrent form of papillomatosis larynx in comparison with the values of the control group ($p<0.05$). Moreover, it was found that the highest content of B-lymphocytes was also found in this group of children and amounted to 26.6 ± 1.2%, and in the control group - 19.4 ±0.72%, and the lowest value of B-lymphocytes was found in the group children with a rare recurrent form of papillomatosis of the larynx. It is obvious that the increased expression of CD 20+ on B-lymphocytes in laryngeal papillomatosis indicates the active participation of B-lymphocytes in the antiviral immune response, but it should be noted that the protective efficacy under conditions of virus persistence is limited [3,6,10]. Despite this, the study of the content of B-lymphocytes is an important criterion for assessing the depth of immunodeficiency and determining the next steps in terms of diagnosis and treatment of laryngeal papillomatosis in children. During therapy, a gradual decrease in the number of B-lymphocytes is observed, especially in the group of children against the background of adding an IFN inducer to the treatment regimen. It is known that immunoglobulins play an important function of mediators in the cascade development of the immune response and can partially determine the effectiveness of the final, effector reactions of cellular immunity in inactivation and elimination of viral antigens [1,10]. Also, it is known that circulating antibodies are one of the effector factors of immunity, providing antigen-specific protection [4,10,12]. Serum concentrations of the main immunoglobulins IgG, IgA, IgM were analyzed in children with laryngeal papillomatosis depending on the clinical course of the disease and in the dynamics of therapy. Depletion of IgG was revealed in the group of children with laryngeal papillomatosis with a continuously recurrent form, the content of IgM was significantly reduced in the group of children with a continuously recurrent form compared with the data of the control group and data of other groups. Analysis of the IgA content revealed the presence of a significant increase in IgA in the blood serum of all children with laryngeal papillomatosis. Moreover, a pronounced increase in IgA was noted in the group of children with a frequently recurrent form of laryngeal papillomatosis. Consequently, the death link of immunity was characterized by an increase in serum concentrations of Ig G and Ig A in the group of children with laryngeal papillomatosis. Moreover, in the dynamics of treatment, an improvement in immunoglobulin parameters is observed, which once again confirms the formation of an adequate humoral immune response against the background of the use of IFN preparations and IFN inducers.

From the available literature data, it can be seen that the study of activation markers of lymphocytes is of great scientific and practical importance, especially in infectious diseases. analysis of activation markers of lymphocytes makes it possible to study the processes

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of activation, proliferation, differentiation and apoptosis of immunocompetent cells and characterizes the cell cycles associated with these processes [6,9,10]. Thus, we studied lymphocyte markers, such as CD38+ and CD 95+. It is known that CD 38+ is an activation marker represented by a transmembrane glycoprotein, which is considered as a multifunctional protein [10]. CD38+ is the precursor of plasma cells. It is expressed on immature T-lymphocytes and B-lymphocytes, activated T-lymphocytes, and plasma cells [6,10,12]. Analysis of the study of CD38+ expression on lymphocytes revealed a significant increase in this marker in groups of children with larynx papillomatosis in comparison with the data of the control group ($p<0.05$). Moreover, the difference in the expression of this marker was significant in all groups of children. Thus, the expression of CD38+ in the continuously relapsing form of papillomatosis was 27.8±1.14%, and in the group with the frequently relapsing form it was 29.2±1.40%, in the group with the rarely relapsing form it was 31.4±1. 20%, while the norm was equal to 23.4±0.58%. Thus, it can be seen that the expression of CD38+ on lymphocytes differed between the studied groups of children ($p<0.05$). Therefore, the analysis showed that an increase in the expression of CD38+ activation markers in children with laryngeal papillomatosis indicates the presence of activation of both cellular and humoral inflammatory factors. Moreover, this factor indicates the depletion of the cellular link of immunity in a continuously recurrent form of larynx papilomatosis and vice versa, the presence of an inflammatory potential of lymphocytes in frequently and rarely recurrent forms of larynx papilomatosis. During treatment, a decrease in the expression of CD 38+ is observed, which indicates the presence of an anti-inflammatory effect of therapy, especially when an IFN inducer is added to therapy. According to the literature data, there is information about the role of APO -1/ Fas (CD95+) receptors in the process of apoptosis, and its degree is a reflection of the level of lymphocyte apoptosis. It has been established that an increase in the expression of CD95+ receptors on lymphocytes indicates an excessive and inefficient process of stimulation of blood lymphocytes, which indicates an apoptotic pathway of lymphocyte death [11]. Thus, a slightly increased expression of CD 95+ on peripheral blood lymphocytes was found in groups of children with laryngeal papillomatosis. It was found that the highest expression of CD 95+ was typical for children with a continuously recurrent form of laryngeal papillomatosis, amounted to 3 2.9±1.3%, and in the control group 22.4±0.5%. Expression of CD 95+ in other forms of larynx papilomatosis was intermediate and did not differ significantly from the values of the control group ($p>0.05$). Obviously, excessive apoptosis in combination with activation of the humoral link of immunity and deep T-cell immunodeficiency contributes to the progression of the disease. During treatment, a decrease in the

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expression of CD95+ is observed. Therefore, the analysis of activation markers of lymphocytes indicates a confirmed important role of activation markers of lymphocytes in the immune response during long-term viral processes. Thus, the analysis of the results obtained in laryngeal papillomatosis, depending on the clinical course of the disease and observation in the dynamics of treatment, showed that it was possible to identify pronounced changes both in the cellular link of immunity, which are manifested by suppression of CD 3 + T-lymphocytes, CD 4 + T - helpers , IRI , an increase in the number of CD 8 + T-lymphocytes, CD 16 + cells, and in the humoral immunity - an increase in serum concentrations of IgG and IgA , increased expression of CD38+ and CD95+. Moreover, against the background of standard therapy with the use of IFN, especially with the use of IFN inducers, there is an improvement in immunological parameters, which is reflected in a decrease in the number of relapses of the disease.

It has been established that one of the most important biological functions of immunoglobulins is antigen binding and the formation of circulating immune complexes (CIC) [10] . An important characteristic of the CEC is their size. It was revealed that with papillomatosis of the larynx there is an increased content of circulating immune complexes. There is an increase in the average CEC values of 3% (large values) and 4% (small values). We found that the highest average value of small and large CECs was typical for patients with a continuously recurrent form of laryngeal papillomatosis. In other types of papillomatosis of the larynx, there is also a significant increase in the CEC of small and large. It is known that CEC 3%, formed with an excess of antibodies, although they are able to bind complement, are large, insoluble, rapidly phagocytosed and have low pathogenicity [10] . Soluble immune complexes of small sizes, which were formed with an excess of antigen, have the greatest pathological potential [10] . A high level of CEC at can be due not only to the activation of the immune response to viral antigens, but also to the suppression of the mechanisms of their elimination. The latter, apparently, is associated with a weakening of the function of cells of the monocyte-macrophage system - cells that absorb and disintegrate immune complexes [10,12] . Consequently, there is an activation of the humoral link of immunity along with a pronounced depression of the cellular link of immunity. Thus, based on the results obtained, it can be seen that with a long-term chronic course with relapses of laryngeal papillomatosis, a pronounced imbalance of the cellular and humoral parts of the immune system is observed. Moreover, the imbalance in the cellular link of immunity was expressed in the suppression of IRI due to a decrease in the number of T-helpers/inducers and an increase in T-cytotoxic lymphocytes. Circulating immune complexes of large and small values were increased, however, the greatest increase in the CEC was observed with a continuously recurrent form of

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laryngeal papillomatosis. Obviously, in this pathology T - cellular immune response is significantly weak and directed against a smaller number of epitopes, which suggests clonal depletion of T-lymphocytes. In turn, reduced immunoreactivity of the T-cell link in laryngeal papillomatosis can be considered as a result of a violation of antigen presentation to immune system cells, as well as a violation of the function of T-cells themselves [9]. In the dynamics of treatment, there is an improvement in the indicators of cellular and humoral immunity. Especially, pronounced changes are observed in the group of children taking IFN inducers in the complex of antiviral therapy, which contribute to the disclosure of their own potential or reserve of IFN alpha, beta and gamma, which play an important role in organizing an adequate antiviral and antitumor immune response.

Next, we analyzed the results of the analysis of children with a frequently recurrent form of laryngeal papillomatosis. The data obtained are presented in Table 2. On the part of the cellular factors of the adaptive immune response, when compared with the data before treatment, it was found that in the group of children i.e. the 2c group of children was characterized by an increase in the expression of CD 4+ on lymphocytes by 1.4 times, and in the 2nd group - by 1.2 times, a decrease in the expression of C D 8+ on lymphocytes in the 2nd group - by 1.4 times, and in 2a group - 1.1 times, increase in IRI in 2nd group - 1.5 times, and in group 2a - 1.24 times, CD 38+ decreased in 2nd group - 1.21 times, and in group 2a - 1.1 times, CD 95+ is reduced in group 2 - 1.22 times, and in group 2a - 1.1 times, immunoglobulin A is reduced in group 2 - 1.25 times, in group 2a - in 1.2 times; once. The revealed differences were all significant with the values of the group before treatment and among themselves.

Table 2.

The immune status of children with laryngeal papillomatosis depending on the clinical features of the disease (frequently relapsing group) in the dynamics of treatment, M ± m , %

Immunity parameters	Norm (n= 29)	Before treatment (n= 32)	Group 2a (standard + IFN) (n =25)	Group 2c (standard + IFN + inosine pranobex) (n =28)

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Leukocytes	6050±128.0	6100±112.7*	7350.5±145.5	7500.0±125.2
Lymphocytes	32.5±0.84	42.5±1.52*	40.2±0.94*^	42.4±1.15*
CD 3+	58.4±1.25	45.7±0.82*	5 1.8 ±1.50*	5 2 .2±0.9* #
CD4+	38.3±1.25	32.6±1.41*	39.40±0.94* ^	44.1±1.23* #$
CD8+	18.8±0.54	32.9±1.15*	29.42±1.42* ^	23.40±1.21* #$
IRI	1.65±0.05	0.92±0.04*	1.14±0.03 *	1.3 8 ±0.0 1*#$
CD 16+ _	18.2 1.0 ±3 _	21.9±0.24*	20.3± 0.6 0* ^	19.30± 0.84 * #
CD20+	19.9 ±0.83	2 4.6 ±1.16 *	2 3, 3 ±1.1 3* ^	22.1 ±1.16 *
CD38 + _	22.4±0.86	24.4±1.22*	22, 1 0±1.4 1 *	2 0, 2± 0.96 * $
CD95 + _	23.5±1.26	28.8 ±1.21*	26.3 ±0.72*	23.6 ±0.95* #$
IgG	1260.0 ±21.60	1341.2±26.2*	1300.4±25.4* ^	1272.0±19.6 #
IgA	122.0 ±3.21	161.4 ±2.6*	1 38 .0 ±2.20 ^	129.4 ±1.32 #$
IgM	112 ±2.1	140.4 ±1.32*	128.61.35 ^ _ ±_	11 5.4 ±0.84 #$
CEC3%	8.58±1.34	116.2 ±2.80	8 2 , 6 ±1.4 4*	36.5 ±0.86 #$
CEC4%	14.22±1.51	85.65 ±2.44*	48.64 ±0.68 *^	20.54 ±0.60* #$

Note: * - significance of differences with the data of the control group, ^ - differences of group 2a with values before treatment; # - differences in group 2 with values before treatment; $ - differences between 2a and 2b groups.

We analyzed the results of the immunological analysis of children with a rare-recurrent form of laryngeal papillomatosis. The data obtained are presented in Table 3. On the part of the cellular factors of the adaptive immune response , when compared with the data before treatment, it was found that almost many values were close to the normal values, however, significantly different values were found when

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compared with the results before treatment. These include, against the backdrop of an integrated approach, i.e. in group 3c, there is an increase in CD 3+ by 1.14 times, an increase in CD 4+ - by 1.14 times, a decrease in C D 8+ by 1.4 times, an increase in IRI - by 1.4 times, a decrease in CD 38+ and CD 95+, decrease in immunoglobulin A by 1.2 times, decrease in CIC3% - by 2.6 times, decrease in CIC4% - by 2.2 times. The differences found were all significant with pre-treatment group values.

Table 3

The immune status of children with laryngeal papillomatosis in the course of treatment depending on the clinical features of the disease (rarely relapsing group), M ± m , %

Immunity parameters	Norm (n= 29)	Before treatment (n= 30)	Group 3a (standard + IFN) (n =24)	Group 3c (standard + IFN + inosine pranobex) (n= 25)
Leukocytes	6050±128.0	8200.6±92.5*	7120.5±135.8	6500.3±158.2
Lymphocytes	32.5±0.84	34.2±0.68	33.5±0.84	32.6±1.15
CD3+	58.4±1.25	46.40±0.82*	48.5±1.24*	52.82±1.29 *#$
CD4+	38.3±1.25	34.30±0.68*	36.9±0.84 ^	39.2±0.55 #$
CD8+	18.8±0.54	29.40±0.65*	24.5±0.75* ^	20.5±1.2 #$
IRI	1.65±0.05	0.98±0.03*	1.22±0.04 *^	1.35±0.03 *#$
CD 16+ _	18.2 1.0 ±3 _	24.2±0.32*	21.20±0.52* ^	20.4±0.25*
CD20+	19.9 ±0.83	2 3.2 ±0.86*	2 1.4 ±0.6	2 0.8 ±0.22
CD38 + _	22.4±0.86	26.2±1.24*	24.3±0.52*	22.9±0.62 #
CD95 + _	23.5±1.26	28.40 ±1.12*	24.40 ±0.38 ^	22.8 ±1.02 #
IgG	1260.0 ±21.60	1355.4±23.7	1280.5±1.86*	1265.5±1.99

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IgA	122.0 ±3.21	146.0 ±2.94*	134.2 ±0.92 ^	126.9 ±1.42 #$
IgM	112 ±2.1	139.2 ±0.74	12 4 , 3 ±2.1 0^	1 19 .5 ±2, 2 1
CEC3%	8.58±1.34	52.20 ±0.84	3 1 , 6 0 ±0, 6 6 ^	19 .8 0 ±0.58 * # $
CEC4%	14.22±1.51	29.50 ±1.82*	19.5 5 ±0.80 *^	13 , 24 ±0, 48 * #

Note: * - significance of differences with the data of the control group, ^ - differences of group 3a with values before treatment; # - differences in group 3c with values before treatment; $ - differences between groups 3a and 3b.

CONCLUSION

Thus, unidirectional changes in the state of the immune response in laryngeal papillomatosis were revealed, which were most pronounced in the group of children with a continuously recurrent form of laryngeal papillomatosis. An etiopathogenetic approach was used in the treatment of laryngeal papillomatosis in children, which consisted in the inclusion of an interferon inducer and licopid in the complex therapy . Against this background, in addition to improving the performance of cellular and humoral immunity, there is an improvement in the clinical condition of children and a decrease in the frequency of relapses in the dynamics of treatment of children with laryngeal papillomatosis. On the part of immunological parameters, activation of cellular parameters of immunity, a decrease in activation markers of lymphocytes and activation of humoral immunity factors were observed, which indicated the anti-inflammatory effect of therapy.

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