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**An improvement of the child acute respiratory infection treatment program**

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*High morbidity rate, frequent development of severe complication forms, unfavorable remote effects for children’s health, insufficient efficacy of the used acute respiratory infection therapy schemes necessitate a treatment program improvement for this group of diseases. A complex clinical-laboratory examination of 72 3-6-year-old children with acute nasopharyngites and bronchites was conducted. Dependence of the disease’s clinical form and course peculiarities from the premorbid setting state and immune status changes’ intensity has been found. It has been established that the introduction of inosine pranobex in the complex treatment of acute respiratory infections in children favors rapid positive dynamics of clinical symptomatology and immune status parameters and is not accompanied by the development of side effects. Thus, high efficacy and safety of inosine pranobex’s use allow to recommend introducing this drug into the treatment program for children of 3 years of age and older with acute respiratory infections regardless of the disease form and immune status state.*

***Keywords:*** *acute respiratory infections, children, inosine pranobex.*

The problem of acute respiratory infections (ARI) remains one of the most actual for modern pediatrics and pediatric infectology. It is connected not only with high ARI morbidity in children, but also with unfavorable consequences of respiratory tract’s infections to child’s health and society in whole [1-3]. At present, ARI morbidity in children remains on a high level (65-70 thousand per 100 thousand) and exceeds the same index in adults 3-4 times [4]. The highest morbidity level is registered in the age group of 2-6 years [5]. Up to 90% of children’s diseases and up to 80% of medical help requests are due to ARI [3]. ARI in children often take a severe course and is accompanied by the development of complications in 20-30% of patients [3, 6]. Unfavorable ARI consequences are: secondary immunodeficiency state (SIS), dysbiosis of mucous tunics, child’s growth and development disorder, maturation of functional systems, chronic pathology of ENT-organs, lungs, kidneys, gastrointestinal tract, central nervous system (CNS) and allergic diseases [7]. ARI issue has not only medical, but also socioeconomic aspects. It is proved that children with recurrent ARI episodes relatively often develop social disadaptation, have worse school performance and lower quality of life not only of children themselves, but also of their parents. Economic loss to the state and the society in whole is rather high [1, 3].

That is why the tactics of therapeutic measures needs improvement; this is indicated by insufficient efficacy of the schemes applied, post-therapeutic increase in frequency of diseases, development of side effects, especially in case of polypragmasy [3, 6]. This necessitates the development of new approaches to treatment of ARI patients using highly efficient and safe complex ethiopathogenetic drugs.

Use of inosine pranobex (Isoprinosine, Teva Pharmaceutical Industries Ltd, Israel) seems to be a prospective area of ARI complex therapy improvement in children. This drug has complex antiviral, immunomodulatory and cytoprotective action. Inosine pranobex inhibits replication of a wide range of DNA- and RNA-containing viruses [8]. The drug’s antiviral action is caused by a change in ribosomal stereochemical structure by incorporating inosine-orotic acid into them [9]. This results in no attachment of adenylic acid to viral RNA and viral protein synthesis disorder. Experiments on cell cultures conducted by L.V. Osidak et al. proved antiviral action of inosine pranobex to ARI causative agents, including influenza, parainfluenzae and respiratory-syncytial viruses [10]. Influenza virus replication inhibition is noted both before the cell culture infection (preventive regimen) and after its infection (therapeutic regimen). Moreover, inosine pranobex use at experimental lethal influenzal infection in white mice led to the reduction in laboratory animals’ morbidity: unlike the control group, influenza virus titer reduction was noted in pulmonary tissue, which in authors’ opinion is the drug’s unquestionable advantage.

Moreover, inosine pranobex has immunocorrecting action [8, 9, 11, 12]. It modulates cellular immune response – increases functional activity of T helpers, type 1 (Th1), production of interleukin (IL) 2, interferon (IFN) γ, quickens the differentiation of T lymphocyte precursors into T helpers and cytotoxic CD8 lymphocytes. Cellular immune response intensification is also connected with the increase in chemotactic and phagocytic activity of macrophages, their IL 1 production. There is an improvement in functional activity of neutrophils and natural killer cells. Combination of direct virus replication inhibition and cellular immunity activation potentiate drug’s antiviral activity. Moreover, inosine pranobex affects humoral immune response. The drug assists in the differentiation of B lymphocytes into plasma cells and stimulates the production of immunoglobulins (Ig) A, M and G. It has also been established that inosine pranobex improves metabolic processes in affected cells.

There is an experience of using inosine pranobex at various infectious diseases – herpesviral infections, measles, epidemic parotitis, viral hepatites, papillomaviral infection, subacute sclerosing panencephalitis etc. [11, 12]. Thus, the study that we conducted established that there was a reduction in frequency of lymphoproliferative, toxic, infectious and cerebral syndromes and laboratory activity markers of Epstein-Barr virus (EBV) and positive dynamics of immunological parameters characterizing activation of immunocompetent cells, cellular and humoral cellular response and innate resistance factors when prescribing inosine pranobex to children with chronic Epstein-Barr viral infection [13]. The similar data were obtained by M.S. Savenkova et al., who used inosine pranobex in children with chronic herpesviral infection caused by EBV, cytomegalovirus and also mixed chlamydial-mycoplasmal infection [12]. Positive clinical symptomatology dynamics and reduction in the frequency of revealing laboratory indicators of infectious process’s activity has been noted in the setting of a treatment using this drug.

In recent years there have been data on the efficacy of using inosine pranobex in children with ARI. Thus, the study conducted by L.V. Osidak et al. showed that there is reduction in the duration of ARI symptoms – fever, intoxication, catarrhal symptoms [10]. V.A. Bulgakova et al. studied the drug’s efficacy at ARI in children with atopic bronchial asthma [11]. It was established that inosine pranobex prescription favored reduction in the duration of ARI symptoms and prevented the development of bronchial asthma complications. The authors connect the drug’s efficacy with antiviral action, which is documented by the reduction in discharge of respiratory viruses from nasopharyngeal mucus and its immunomodulatory activity – immune response polarization towards Th1 and IFN γ and IL 2 production increase.

A range of inosine pranobex use aspects at ARI in children requires a more precise definition. Primarily, this concerns the drug’s use efficacy evaluation at different forms of acute respiratory pathology. Moreover, immunomodulatory activity of inosine pranobex also requires a study, including the drug’s influence on the IFN system. The aforementioned served as a prerequisite towards this clinical-immunological study.

The aim of the study is to evaluate the efficacy of inosine pranobex introduction into complex ARI therapy in children.

**Patients and methods**

72 3-6-year-old children with acute respiratory infection in forms of acute nasopharyngitis (38 children; 52.8%) and acute bronchitis (34 children; 47.2%) were examined. Patients were divided into 2 groups, comparable in terms of clinical laboratory parameters by the treatment beginning, by random sampling. Both group consisted of 36 children with 19 of them with acute nasopharyngitis and 17 – with acute bronchitis in each. The 1st group patients were prescribed standard treatment: disintoxication therapy, polyvitamins, local antiseptics, according to indications – antibiotics, mucolytics, antifebriles, antihistamines, inhalations etc. Along with standard therapy, 2nd group patients were prescribed inosine pranobex, 50 mcg/kg per day in 3-4 intakes, for 10 days.

Clinical immunological examination of patients was conducted before treatment and in 10 days. Determination of different types of immunocompetent cells was conducted by indirect immunofluorescence using the corresponding murine homogenous antibodies (“Sorbent LTD”, Russia): for T lymphocytes – CD3, for T helpers – CD4, for cytotoxic T lymphocytes – CD8, for cells in early activation state – CD25, for cells in late activation state – HLA-DR, for with apoptotic signal – CD95, for B lymphocytes – CD20, for natural killer cells – CD16. The results were accounted using laser flow cytofluorometer “Epix-XL” (“Coulter”, USA). Serum blood immunoglobulin A, M and G content was studied by radial immunodiffusion (1965) in gel using monospecific serums (“Imbio”, Russia). Blood serum content of circulating immune complexes (CIC) was studied by polyethylene glycol precipitation. Intensity of oxygen-dependent neutrophilic metabolism was assessed in spontaneous and stimulated tests of nitro blue tetrazolium recovery (NBT sp., NBT st.). NBT-test stimulation coefficient (NBT st. c.) was calculated using the following formula:

St. c. = NBT st. / NBT sp.

Interferon status study included the flow cytofluorimetry determination of ratio of cells with CD199-receptors to IFN γ using monoclonal antibodies (“Caltag”, EU). Serum content, spontaneous and stimulated IFN α and IFN γ production were studied by immune-enzyme analysis technique using test-systems “Vector-Best” (Russia). Spontaneous and phytohemagglutinin (5 mcg/ml) stimulated IFN γ and IFN α production was evaluated by cytokine content in peripheral blood’s mononuclear supernatant obtained throughout the 48-hour test in CO2-incubator at 37oС. IFN γ and IFN α production stimulation coefficient was calculated using the following formula:

St. c. = Stimulated IFN production / Spontaneous IFN production

Immunofluorescence test of nasal mucous tunic’s impression smears was used for ARI etiological deciphering. 30 1st health group children of the same age were examined to generate immune status standards.

Significance of differences for absolute value parameters was evaluated using Mann-Whitney and Wilcoxon tests, for relative value parameters – Fisher's exact test. Statistical data manipulation was conducted using software “OpenOffice.Calc”.

**Study results and their discussion**

Analysis of life anamnesis data revealed compromised premorbid background in all the examine patients. However, patients with acute bronchitis more often than patients with acute nasopharyngitis had history of gestosis (52.9 and 26.3, accordingly; p<0.05) and threatened miscarriage (35.3 and 13.2%, accordingly; p<0.05) , physical development delay (26.5 and 7.9%, accordingly; p<0.05), perinatal CNS affection (41.2 and 13.2%, accordingly; p<0.05), suppurative-septic diseases in children (32.4 and 10.5%, accordingly; p<0.05).

Clinical examination before treatment revealed in all patients a combination of general infectious and catarrhal syndromes. Most patients with acute nasopharyngitis entered the inpatient department in moderate condition (76.3%), with complaints about body temperature rise up to subfebrile figures (73.7%), moderate intoxication symptoms (76.3%), pronounced rhinorrhea (78.9%) and dry cough (100%).

Patients with acute bronchitis entered the inpatient department in severe condition more often than children with acute nasopharyngitis (47.1 and 23.7%, accordingly; p<0.05). Temperature up to febrile figures and pronounced intoxication symptoms were observed in almost a half of the patients (47.1%). Cough was productive in 1/3 of patients (32.4%), in other children it was dry. Dry rales were sounded in all patients at auscultation in the setting of rough respiration; in 1/3 of patients (35.3%) the rales were coarse and medium moist. Children with acute bronchitis developed complications more often than patients with acute nasopharyngitis (32.4 and 10.5%, accordingly; p<0.05).

ARI etiological structure study by immunofluorescence test showed that antigens of influenza virus were observed in 27.8% of patients, of parainfluenzae virus – in 15.3%, of adenoviruses – in 13.8%, of respiratory-syncytial virus – in 4.2%; disease etiology remained undeciphered in 38.9% of patients.

Unidirectional changes were revealed in all patients regardless of ARI form when analyzing immune status before treatment (tb. 1). Reduction in the number of T lymphocytes and T helpers was observed on the part of the T-cellular level. There also was a derangement in the activation process of immunocompetent cells indicated by a reduction in the number of lymphocytes with markers of early activation (CD25), readiness to apoptosis (CD95) and an increase in the expression of late activation molecules (HLA-DR). An increase in IgM and CIC was revealed analyzing B-cellular level in the setting of reduction in the number of CD20 lymphocytes. An increase in the number of CD16 cells and oxygen-dependent neutrophilic metabolism inhibition (NBT sp.) was revealed on the part of innate resistance factors. Considerable changes were revealed in IFN system – reduction in the number of CD119 cells, increase in spontaneous production and serum content of IFN γ and IFN α, inhibition of stimulated generation of these cytokines.

It should be noted that immune status alterations were more pronounced in patients with acute bronchitis. There was a significant reduction in the number of T lymphocytes and T helpers. Unlike patients with acute nasopharyngitis, they experienced a reduction in cytotoxic CD8 lymphocyte content. Expression increase of late activation marker (HLA-DR) and CD16 lymphocytes was more pronounced than at acute nasopharyngitis. IFN-status peculiarities were a considerable reduction in the amount of CD119 cells, moderate increase in spontaneous production, serum content of IFN γ and IFN α, pronounced inhibition of stimulated IFN γ generation.

Juxtaposition of ARI symptoms’ duration with account of therapy scheme showed that fever, intoxication, rhinorrhea, cough, oropharyngeal mucous tunic’s hyperemia, rough pulmonary respiration and pulmonary rales in children disappeared earlier in patients receiving inosine pranobex than in those who received standard therapy (tb. 2). The drug proved its efficacy in 94.4% of patients. There were no side effects at inosine pranobex use.

Immune status disorders remained and progressed in patients with acute nasopharyngitis in the setting of the standard therapy (tb. 3). The amount of T lymphocytes and T helpers continued its decrease, CD8 cells did not increase in number at the same time. Reduction of CD25- and CD95 lymphocytes remained; steady increase in the amount of HLA-DR-positive cells was observed. There were no alterations in terms of B-cellular level: reduction in CD20 lymphocytes and increase in the content of IgM and CIC at normal level of IgA and IgG. There was a tendency to the reduction in the number of CD16 cells, stable inhibition of oxygen-dependent neutrophilic metabolism. Increase in spontaneous production, serum content of IFN γ and IFN α, depression of stimulated generation of this cytokines remained on the part of IFN-status in the setting of further reduction in the amount of CD119 lymphocytes.

On the contrary, introduction of inosine pranobex into comprehensive treatment of patients with acute nasopharyngitis favored positive dynamics of cellular and humoral immune response parameters and of innate resistance factors. Normalization of the amount of T lymphocytes, T helpers and increase in the amount of CD8 cells also took place. There was a tendency to restoring the number of CD20 cells, increase in IgA content, immunoglobulin synthesis shift from class M to class G, CIC level normalization. Further increase in the amount of CD16 lymphocytes and a tendency to restoring the neutrophilic metabolism activity were observed. There was a tendency towards the normalization of CD199 receptor expression and restoration of IFN γ and IFN α generation stimulation coefficient.

Examination of patients with acute bronchitis in disease dynamics showed that patients receiving standard therapy also experienced intensification T-cellular level disorders – further reduction in CD3- and CD8 lymphocytes (tb. 4). Changes of immunocompetent cell activation parameters remained – reduction in CD25- and CD95 lymphocytes, increase in HLA-DR cells. There were profound changes on B-cellular level – CD20 reduction, no IgA generation, immunoglobulin synthesis’s class shift (from M to G), CIC increase; on the part of innate resistance factors – increase in CD16 cells, oxygen-dependent neutrophilic metabolism depression. Progression of IFN-status disorders was noted – steady reduction in the amount of CD119 cells and stimulated production of IFN γ. As in the acute disease period, spontaneous generation and serum content of IFN γ and IFN α were increased.

Inosine pranobex prescription to patients with acute bronchitis led to positive dynamics of cellular and humoral immune response parameters and of innate resistance factors. A restoration of amount of T lymphocytes, T helpers, CD8 cells was noted. There was a tendency to normalization of the number of CD20 cells and CIC content; IgA generation stimulation and class shift of immunoglobulin synthesis from M to G were observed. Further increase in the number of CD16 lymphocytes and a tendency towards restoration of oxygen-dependent neutrophilic metabolism intensity were registered. The drug affected IFN-status parameters: there was a tendency towards restoring the number of CD119-positive cells and normalization of IFN γ and IFN α generation stimulation coefficient.

Thus, the conducted study results indicate that ARI clinical form and course are determined by a complex relationship in the system “parasite-host”. Apart from pathogenic properties of causative agents, an important role is played by the imperfection of structure functional components of child’s body defense mechanisms – insufficient maturity of barrier mechanisms, of innate resistance factors, cellular and humoral immune response [1-3]. Moreover, unfavorable influence is caused by exogenous and endogenous risk factors, which led to malfunction of respiratory tract’s barrier mechanisms and child’s body functional systems in whole and forming of secondary immunodeficiency state [6, 7].

Patients develop not only activation signs, but also immune system disorders as a result of immaturity of child’s body protective systems, risk factors, background immunodeficiency state and immunosuppressive activity of causative agents. The examined patients revealed disorders of immunocompetent cells’ activation, proliferation and differentiation processes – reduction in CD3-, CD4- and CD8 lymphocyte content and cells with early activation marker (CD25) expressing apoptosis readiness receptor (CD95), increase in the number of late activation lymphocytes (HLA-DR), reduction in CD20 lymphocytes, IgA and IgG production, increase in CIC and CD16 cells, neutrophilic metabolic activity inhibition, IFN-status state disorder (increase in IFN γ and IFN α production, reduction in CD119 receptor expression).

Affection of target cells by infectious agents at immunosuppression results in formation of an inflammation nidus in respiratory tract’s mucous tunic; this clinically manifests with the symptomatology of general infectious and catarrhal syndromes [3, 6]. Patients with acute nasopharyngitis have low frequency of risk groups and moderate immune status alterations. Clinical symptomatology includes low-grade fever and moderately expressed intoxication symptoms with intense catarrhal phenomena – pronounced rhinorrhea, dry cough, oropharyngeal mucous tunic’s hyperemia.

High rate of anamnestic risk factors, more profound disorders of adaptive cellular and humoral immune response, immunocompetent cells’ activation parameters, innate resistance factors (IFN and CD16 lymphocyte systems) was revealed in patients with acute bronchitis. The intensity of inflammatory reaction in respiratory tract’s mucous tunic is more significant, which is why clinical symptomatology of acute bronchitis is characterized by febrile fever, pronounced intoxication symptoms, productive cough, pulmonary rales and frequent development of complications.

ARI treatment optimization is the introduction of Isoprinosine into therapy program; this leads to a pronounced positive dynamics of clinical-immunological parameters in 94.4% of patients due to the drug’s complex antiviral, immunocorrecting and cytoprotective activity [8-12]. Early positive dynamics of clinical symptoms – general infectious and catarrhal syndromes – is noted regardless of ARI form. The drug has a rather wide range of immunomodulatory activity. Immunocorrecting action of inosine pranobex is the modulation of cellular immune response – normalization of CD3-, CD4- and increase in CD8 lymphocytes. Antibody response stimulation (increase in IgA, synthesis shift from IgM to IgG) is noted in the setting of CIC elimination improvement. There is an increase in natural killer cells, restoration of neutrophilic metabolic activity on the part of innate resistance factors. The drug also influences IFN-status restoring IFN γ and IFN α production and improving their reception.

Isoprinosine is well tolerated by patients. The drug’s high clinical efficacy, wide range of immunomodulatory activity, safety of use allow recommending introduction of inosine pranobex in ARI treatment complex in children of 3 years of age and older regardless of disease form and character of immune status disorders.

**Conclusions**

1. ARI clinical form and course in children depend on causative agent’s pathogenic properties, patient’s premorbid background condition and intensity of immune status alterations.
2. It is necessary to include inosine pranobex into the complex of therapeutic measures in order to increase ARI treatment, as it is conductive of reduction in disease symptoms’ duration, positive dynamics of immunological parameters and well tolerated.
3. Inosine pranobex is indicated to ARI patients of 3 years of age and older regardless of disease form and character of immune status disorders.

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**Table 1.** Immune status parameters in children with acute respiratory infections with account of disease form

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameters** | **Acute nasopharyngitis** | **Acute bronchitis** | **Healthy children** |
| CD3, % | 65.8±1.30.1 | 62.3±1.20 | 69.5±1.2 |
| CD3, 109/l | 2.06±0.051 | 1.79±0.090 | 2.1±0.07 |
| CD4, % | 37.2±1.30 | 37.9±1.10 | 41.5±1.3 |
| CD4, 109/l | 1.16±0.031 | 1.01±0.050 | 1.21±0.07 |
| CD8,% | 26.9±1.31 | 21.8±0.90 | 26.5±1.1 |
| CD8, 109/l | 0.84±0.041 | 0.62±0.050 | 0.73±0.05 |
| CD4/CD8 | 1.43±0.051 | 1.71±0.050 | 1.52±0.05 |
| CD25,% | 0.82±0.140 | 0.88±0.150 | 2.12±0.12 |
| CD25, 109/l | 0.02±0.0060 | 0.02±0.0050 | 0.06±0.01 |
| HLA-DR, % | 12.6±1.10.1 | 16.5±1.60 | 8.3±0.2 |
| HLA-DR, 109/l | 0.39±0.020.1 | 0.47±0.030 | 0.31±0.02 |
| CD95, % | 2.4±0.80 | 2.1±0.20 | 4.1±0.3 |
| CD95, 109/l | 0.07±0.010 | 0.06±0.010 | 0.12±0.02 |
| CD20, % | 9.7±0.90 | 12.1±0.90 | 21.4±1.4 |
| CD20, 109/l | 0.34±0.030 | 0.33±0.040 | 0.64±0.03 |
| IgA, g/l | 0.92±0.11 | 0.98±0.06 | 0.92±0.03 |
| IgM, g/l | 1.15±0.090 | 1.12±0.050 | 0.86±0.05 |
| IgG, g/l | 9.3±0.3 | 9.8±0.2 | 9.3±0.4 |
| CIC, standard units | 95.3±7.90 | 91.3±4.60 | 48.2±4.4 |
| CD16, % | 15.8±0.80.1 | 13.1±0.60 | 7.3±1.4 |
| CD16, 109/l | 0.49±0.030.1 | 0.37±0.040 | 0.21±0.03 |
| NBT sp., standard units | 65.1±5.30 | 67.6±3.70 | 99.9±5.3 |
| NBT st. c. | 1.52±0.07 | 1.50±0.06 | 1.62±0.04 |
| CD119, % | 18.1±1.20.1 | 13.3±1.30 | 38.1±1.4 |
| CD119, 109/l | 0.56±0.040.1 | 0.38±0.030 | 1.15±0.12 |
| Serum IFN γ, pg/ml | 16.8±2.00.1 | 9.8±1.60 | 1.8±0.4 |
| Sp. IFN γ, pg/ml | 18.8±1.50.1 | 12.1±1.10 | 3.8±0.4 |
| IFN γ st. c. | 31.3±1.10.1 | 21.2±1.50 | 66.1±1.6 |
| Serum IFN α, pg/ml | 18.1±1.20.1 | 12.1±1.50 | 1.1±0.3 |
| Sp. IFN α, pg/ml | 7.6±0.60.1 | 4.6±0.50 | 2.2±0.3 |
| IFN α st. c. | 1.43±0.210 | 1.33±0.220 | 3.12±0.43 |

*Note*. 0 – significance of differences in parameters in comparison with healthy children; 1 – significance of differences in parameters between patients with acute nasopharyngitis and patients with bronchitis.

CIC – circulating immune complexes, NBT – nitro blue tetrazolium recovery test, St. c. – stimulation coefficient.

**Table 2.** Duration of acute respiratory infections’ symptoms in children with account of therapy scheme (in days)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Symptoms** | **Acute nasopharyngitis** | | **Acute bronchitis** | |
|  | **Standard therapy** | **Standard therapy + inosine pranobex** | **Standard therapy** | **Standard therapy + inosine pranobex** |
| Fever | 3.6±0.3 | 1.8±0.2\* | 4.3±0.3 | 2.5±0.2\* |
| Intoxication | 4.6±0.2 | 2.8±0.2\* | 5.2±0.3 | 3.5±0.2\* |
| Rhinitis | 9.8±0.2 | 6.7±0.3\* | 8.9±0.4 | 7.2±0.2\* |
| Catarrhal symptoms | 10.8±0.3 | 7.6±0.4\* | 10.2±0.4 | 7.6±0.3\* |
| Cough | 10.3±0.2 | 6.7±0.3\* | 11.6±0.4 | 7.9±0.4\* |
| Rough respiration | 11.3±0.3 | 8.6±0.2\* | 12.6±0.3 | 9.6±0.4\* |
| Pulmonary rales | - | - | 8.2±0.4 | 6.2±0.3\* |

*Note*. \* - significance of differences in parameters.

**Table 3.** Immune status parameters in children with acute nasopharyngitis with account of therapy scheme

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Parameters** | **Standard therapy** | | **Standard therapy + inosine pranobex** | | **Healthy children** |
| **Height** | **Recovery** | **Height** | **Recovery** |
| CD3, % | 65.8±1.30 | 66.1±1.20.2 | 66.1±1.20.1 | 69.8±1.3 | 69.5±1.2 |
| CD3, 109/l | 2.06±0.051 | 1.91±0.050.2 | 1.98±0.05 | 2.13±0.06 | 2.1±0.07 |
| CD4, % | 37.2±1.30 | 36.3±1.30.2 | 37.0±1.20.1 | 39.9±1.1 | 41.5±1.3 |
| CD4, 109/l | 1.16±0.031 | 1.04±0.050.2 | 1.11±0.05 | 1.19±0.04 | 1.21±0.07 |
| CD8,% | 26.9±1.3 | 27.6±1.3 | 26.6±1.21 | 30.6±1.30 | 26.5±1.1 |
| CD8, 109/l | 0.84±0.04 | 0.79±0.052 | 0.81±0.041 | 0.92±0.040 | 0.73±0.05 |
| CD4/CD8 | 1.43±0.05 | 1.32±0.050 | 1.43±0.12 | 1.33±0.12 | 1.52±0.05 |
| CD25,% | 0.82±0.140 | 1.15±0.160.2 | 0.86±0.120 | 0.77±0.110 | 2.12±0.12 |
| CD25, 109/l | 0.02±0.0060 | 0.03±0.0050.2 | 0.02±0.0050 | 0.02±0.0040 | 0.06±0.01 |
| HLA-DR, % | 12.6±1.10.1 | 15.6±1.10.2 | 12.9±1.10.1 | 10.5±1.3 | 8.3±0.2 |
| HLA-DR, 109/l | 0.39±0.020.1 | 0.45±0.020.2 | 0.40±0.020 | 0.32±0.05 | 0.31±0.02 |
| CD95, % | 2.4±0.80 | 2.7±0.50.2 | 1.5±0.80 | 1.6±0.20 | 4.1±0.3 |
| CD95, 109/l | 0.07±0.010 | 0.07±0.010.2 | 0.05±0.0040 | 0.05±0.0050 | 0.12±0.02 |
| CD20, % | 9.7±0.90 | 10.3±1.30.2 | 9.4±1.30.1 | 15.8±1.30 | 21.4±1.4 |
| CD20, 109/l | 0.34±0.030 | 0.35±0.040.2 | 0.28±0.050.1 | 0.47±0.040 | 0.64±0.03 |
| IgA, g/l | 0.92±0.11 | 0.84±0.052 | 0.91±0.111 | 1.25±0.080 | 0.92±0.03 |
| IgM, g/l | 1.15±0.090 | 1.22±0.100.2 | 1.14±0.050.1 | 0.95±0.03 | 0.86±0.05 |
| IgG, g/l | 9.3±0.3 | 9.5±0.52 | 9.2±0.31 | 10.5±0.30 | 9.3±0.4 |
| CIC, standard units | 95.3±7.90 | 86.1±6.80.2 | 93.3±8.10.1 | 50.6±6.1 | 48.2±4.4 |
| CD16, % | 15.8±0.80.1 | 13.3±0.50.2 | 15.2±1.10.1 | 17.5±1.10 | 7.3±1.4 |
| CD16, 109/l | 0.49±0.030.1 | 0.38±0.040.2 | 0.45±0.050 | 0.52±0.040 | 0.21±0.03 |
| NBT sp., standard units | 65.1±5.30 | 64.6±6.20.2 | 66.1±5.40.1 | 80.0±4.60 | 99.9±5.3 |
| NBT st. c. | 1.52±0.07 | 1.61±0.042 | 1.51±0.071 | 1.71±0.06 | 1.62±0.04 |
| CD119, % | 18.1±1.20 | 16.5±1.20.2 | 18.3±1.20.1 | 28.4±1.20 | 38.1±1.4 |
| CD119, 109/l | 0.56±0.040.1 | 0.47±0.030.2 | 0.53±0.050.1 | 0.84±0.060 | 1.15±0.12 |
| Serum IFN γ, pg/ml | 16.8±2.030.1 | 11.1±1.80.2 | 17.3±1.20 | 17.5±1.10 | 1.8±0.4 |
| IFN γ sp., pg/ml | 18.8±1.50.1 | 11.5±1.20.2 | 19.9±1.70 | 21.3±1.60 | 3.8±0.4 |
| IFN γ st. c. | 31.3±1.10.1 | 22.1±1.30.2 | 34.7±1.40.1 | 63.1±1.8 | 66.1±1.6 |
| Serum IFN α, pg/ml | 18.1±1.20.1 | 12.1±1.10.2 | 18.7±1.20 | 19.3±1.10 | 1.1±0.3 |
| IFN α sp., pg/ml | 7.6±0.60.1 | 5.8±0.70.2 | 8.0±0.70 | 8.3±0.50 | 2.2±0.3 |
| IFN α st. c. | 1.43±0.210 | 1.33±0.210.2 | 1.61±0.210.1 | 2.63±0.22 | 3.12±0.43 |

*Note*. 0 – significance of differences in parameters in comparison with healthy children; 1 – significance of differences in parameters between periods of disease height and recovery; 2 – significance of differences in parameters in patients receiving standard therapy and its combination with isoprinosine.

CIC – circulating immune complexes, NBT – nitro blue tetrazolium recovery test, st. c. – stimulation coefficient.

**Table 4.** Immune status parameters in children with acute bronchitis with account of therapy scheme

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Parameters** | **Standard therapy** | | **Standard therapy + inosine pranobex** | | **Healthy children** |
| **Height** | **Recovery** | **Height** | **Recovery** |
| CD3, % | 62.31±1.20 | 60.2±1.60.2 | 62.2±1.20.1 | 66.7±1.3 | 69.5±1.2 |
| CD3, 109/l | 1.79±0.090.1 | 1.54±0.060.2 | 1.67±0.040.1 | 2.02±0.05 | 2.1±0.07 |
| CD4, % | 37.9±1.10 | 37.7±1.20.2 | 37.2±1.00.1 | 40.1±1.1 | 41.5±1.3 |
| CD4, 109/l | 1.01±0.050 | 0.96±0.060.2 | 1.02±0.050.1 | 1.20±0.04 | 1.21±0.07 |
| CD8,% | 21.8±0.90 | 19.6±1.20.2 | 20.7±0.90.1 | 25.8±1.1 | 26.5±1.1 |
| CD8, 109/l | 0.62±0.050.1 | 0.51±0.040.2 | 0.56±0.040.1 | 0.77±0.05 | 0.73±0.05 |
| CD4/CD8 | 1.71±0.050.1 | 1.90±0.050.2 | 1.81±0.120 | 1.62±0.11 | 1.52±0.05 |
| CD25,% | 0.88±0.150 | 0.77±0.140 | 0.84±0.120 | 0.68±0.060 | 2.12±0.12 |
| CD25, 109/l | 0.02±0.0050 | 0.03±0.0050 | 0.02±0.0040 | 0.02±0.0050 | 0.06±0.01 |
| HLA-DR, % | 16.5±1.60 | 15.6±0.30.2 | 16.9±1.60.1 | 12.2±1.40 | 8.3±0.2 |
| HLA-DR, 109/l | 0.47±0.030 | 0.41±0.020 | 0.45±0.050 | 0.36±0.05 | 0.31±0.02 |
| CD95, % | 2.1±0.20.1 | 3.0±0.30 | 2.1±0.20 | 2.5±0.30 | 4.1±0.3 |
| CD95, 109/l | 0.06±0.010 | 0.07±0.010 | 0.06±0.010 | 0.07±0.010 | 0.12±0.02 |
| CD20, % | 12.1±0.90 | 12.6±1.10 | 12.5±1.10.1 | 15.2±1.30 | 21.4±1.4 |
| CD20, 109/l | 0.33±0.040 | 0.32±0.030.2 | 0.33±0.050.1 | 0.45±0.040 | 0.64±0.03 |
| IgA, g/l | 0.98±0.06 | 0.94±0.042 | 0.97±0.051 | 1.14±0.050 | 0.92±0.03 |
| IgM, g/l | 1.12±0.050 | 1.21±0.050.2 | 1.17±0.050.1 | 0.95±0.05 | 0.86±0.05 |
| IgG, g/l | 9.8±0.2 | 9.8±0.2 | 9.6±0.21 | 10.6±0.20 | 9.3±0.4 |
| CIC, standard units | 91.3±4.60 | 84.1±4.40.2 | 93.4±4.50.1 | 74.8±4.10 | 48.2±4.4 |
| CD16, % | 13.1±0.60 | 12.6±0.90.2 | 12.6±1.20.1 | 15.6±1.10 | 7.3±1.4 |
| CD16, 109/l | 0.37±0.040 | 0.32±0.030.2 | 0.34±0.050.1 | 0.46±0.040 | 0.21±0.03 |
| NBT sp., standard units | 67.6±3.70 | 72.6±3.90 | 68.1±4.30.1 | 88.7±5.10 | 99.9±5.3 |
| NBT st. c. | 1.50±0.06 | 1.51±0.052 | 1.51±0.081 | 1.72±0.06 | 1.62±0.04 |
| CD119, % | 13.3±1.30 | 11.7±1.30.2 | 12.8±1.30.1 | 26.1±1.30 | 38.1±1.4 |
| CD119, 109/l | 0.38±0.030.1 | 0.29±0.040.2 | 0.34±0.060.1 | 0.78±0.050 | 1.15±0.12 |
| Serum IFN γ, pg/ml | 9.8±1.60.1 | 5.1±1.10 | 10.4±1.30.1 | 6.5±1.10 | 1.8±0.4 |
| IFN γ sp., pg/ml | 12.1±1.10.1 | 5.8±0.80.2 | 12.5±1.40.1 | 8.3±1.40 | 3.8±0.4 |
| IFN γ st. c. | 21.2±1.50.1 | 13.1±1.50.2 | 23.3±1.70.1 | 44.3±1.80 | 66.1±1.6 |
| Serum IFN α, pg/ml | 12.1±1.50.1 | 8.8±1.30 | 12.5±1.90.1 | 9.9±1.40 | 1.1±0.3 |
| IFN α sp., pg/ml | 4.6±0.50.1 | 2.1±0.52 | 5.0±0.60 | 5.9±0.50 | 2.2±0.3 |
| IFN α st. c. | 1.33±0.220 | 1.22±0.130.2 | 1.54±0.420 | 1.77±0.260 | 3.12±0.43 |

*Note*. 0 – significance of differences in parameters in comparison with healthy children; 1 – significance of differences in parameters between periods of disease height and recovery; 2 – significance of differences in parameters in patients receiving standard therapy and its combination with isoprinosine.

CIC – circulating immune complexes, NBT – nitro blue tetrazolium recovery test, st. c. – stimulation coefficient.