Application of Ultralow Doses of Antibodies to Interferon-γ in Complex Therapy of Bacterial Infections and Prophylaxis of Bacterial Complications

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Comparative placebo-controlled clinical trials on the efficiency and safety of ultralow doses of antibodies to human IFN-γ (anaferon pediatric formulation and anaferon) and prophylaxis of bacterial complication showed that administration of these preparations in complex therapy of bacterial infection reduced the incidence of bacterial complications of viral infections and considerably decreased the duration of the main clinical symptoms of the disease.

Key Words: *anaferon; anaferon (pediatric formulation); bacterial infections; ultralow doses; antibodies to interferon-γ*

Acute respiratory diseases (ARI) rank first in the structure of acute infectious pathology. Despite considerable progress in the development of new and effective antimicrobial drugs, successful therapy of respiratory infections remains an actual problem [5], especially in pediatrics. This can be explained by high prevalence of these diseases and high incidence of serious bacterial complications in children. Another important aspect is growing resistance of pneumotropic bacteria to antibiotics caused by their wide and uncontrolled use in children.

MATERIALS AND METHODS

The efficiency and safety of ultralow doses (ULD) of antibodies to IFN-γ in the complex therapy and prophylaxis of bacterial infections were evaluated in controlled randomized clinical studies including 657 patients. Therapeutic efficiency of ULD of antibodies to IFN-γ was studied in 296 patients with pseudotuberculosis and pertussis [1,4] and 65 patients with ARI complicated by nosocomial pneumonia (pneumococcal etiology of the disease was verified in 22.1% patients). The capacity of ULD of antibodies to IFN-γ to prevent bacterial complications was evaluated in placebo-controlled studies involving patients with herpes-virus infections (296 children with chicken pox and infectious mononucleosis) [3,6].

The patients received anaferon or anaferon pediatric formulation containing ULD of antibodies to IFN-γ *per os* in the form of sublingual tablets (3-8 tablets per day). In evaluation of the therapeutic efficiency, the preparations were prescribed in the complex with antibacterial preparations and symptomatic therapy. Patients of the control group received standard therapy.

Apart from clinical efficiency of ULD of antibodies to IFN-γ, their immunomodulatory activity was assessed in 65 patients with ARI complicated by nosocomial pneumonia; to this end, the levels of serum and induced IFN-α and IFN-γ and the content of $CD4^+$, $CD8^+$, $CD16^+$ lymphocytes in the peripheral blood were measured.

RESULTS

Addition of ULD of antibodies to IFN-γ to the complex therapy of pseudotuberculosis and pertussis re-

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TABLE 1. Dynamics of Immunological Parameters in Patients with ARI Complicated by Nosocomial Pneumonia (*M*±*m*)

Parameter	Control group		Patients receiving ULD of antibodies to IFN-γ	
	initial	convalescence	initial	convalescence
Content of $CD4^+$ cells	494.1±23.3	788.7±18.6*	470.4±19.1	902.3±15.5*
Content of $CD8^+$ cells	661.3±14.5	601.3±19.7	671.5±12.2	466.7±14.8*
Content of $CD16^+$ cells	297.6±12.7	302.5±13.4	320.2±10.6	498.7±16.3*
Immunoregulatory index	0.74±0.06	1.31±0.02*	0.70±0.04	1.93±0.08*
Mitogen-stimulated production				
IFN-α, pg/ml	30.5±2.2	33.2±1.8	29.8±3.1	49.4±2.2*
IFN-γ, pg/ml	168.8±7.2	170.2±5.7	177.4±6.3	312.2±5.5*

Note. *$p<0.01$ compared to initial values.

duced the total duration of the disease compared to the control group ($p<0.05$), period of hepatomegaly and erythema nodosum (in case of pseudotuberculosis), duration of fever by 2.2 days, and the incidence of complications in the form of ARVI by 1.6 times (in case of pertussis).

Addition of ULD of antibodies to IFN-γ to complex therapy of ARI complicated by nosocomial pneumonia led to more rapid disappearance of the main clinical symptoms ($p<0.05$ compared to the control group): fever from 6.2±1.5 to 4.3±1.2 days; cough from 9.2±2.1 to 7.6±1.6 days, intoxication symptoms from 11.5±1.8 to 8.2±1.4 days. A positive dynamics was noted in auscultative picture of the lungs; the duration of detection of rales decreased by 2.4 times. X-ray-visualized focal infiltrative changes in the lung tissue also regressed more rapidly (20.6±2.7 *vs.* 14.2±2.2 days in the control). In patients receiving complex therapy (antibacterial preparations+ULD of antibodies to IFN-γ), the mean duration of antibiotic therapy was shorter by 2.1 days ($p<0.05$).

The use of ULD of antibodies to IFN-γ in the therapy of chickenpox and infectious mononucleosis in children showed that ULD of antibodies to IFN-γ reduced the percent of children requiring additional antibacterial therapy from 20 to 2.2% (chickenpox); in children with infectious mononucleosis receiving ULD of antibodies to IFN-γ no delayed bacterial complications were noted (over 2 weeks after 14-day therapy), while in the control group delayed complications developed in 23.2% patients.

No undesirable effects caused by administration of anaferon and anaferon (pediatric formulation) were recorded.

The main mechanism of the realization of antibacterial activity of ULD of antibodies to IFN-γ is induction of the synthesis of endogenous IFN, first of all, IFN-γ, a cytokine activating natural factors of antibacterial defense (phagocytic activity, antibody-production, T and B cell-mediated immune responses). The efficiency of ULD of antibodies to IFN-γ in prevention of bacterial infections is explained by the fact that the preparation enhances mitogen-stimulated production of IFN (Table 1), thus improving the capacity of the organism to develop soon and adequate immune response. Thus, the use of ULD of antibodies to IFN-γ for prophylactic and therapeutic purposes (as a component of complex therapy) is clinically and immunologicaly substantiated. The absence of undesirable effects caused by administration of the preparation suggests that it can be widely used in various groups of patients including young children. Clinical efficiency of the preparation against various infectious agents (viruses and bacteria) and its safety recommend ULD of antibodies to IFN-γ as a perspective preparation for the therapy of infectious diseases.

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