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- THE REGIONAL IMMUNISATION CALENDAR AS A STEP IN THE IMPROVEMENT OF PREVENTION
- TT VIRUS INFECTION
- TREATMENT OF CHRONIC EBV HEPATITIS
- EFFICACY OF THE ADMINSTRATION OF BACTERIAL LYSATES FOR ARD

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Immune Modulation Therapy for Chlamydial Infection in Children

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The article shows the feasibility of treating chronic chlamydial infection in children with the immune-modulating drugs Influcid and Immunal. A clinical immunological survey of patients serves as the basis for illustrating the results of this therapy. The application of combination therapy, including immune modulation therapy, based on the stages of the disease and various manifestations of somatic pathology in the presence of the infection, resulted in improvement: Manifestations of immune deficiency and the number of recurrences were reduced, making it possible to recommend the administration of these drugs in treating patients with chlamydial infection.

Keywords: Chlamydial infection in children, Influcid, Immunal, therapeutic and preventive efficacy

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Chlamydial infection (CI) remains a considerable problem for pediatric practice. This is due to its high level of contagion and high incidence, as well as to the torpid course of this infection. Today CI is in strong second place after pneumococcal bacteria among the causative agents of pneumonia, which not infrequently tends to become chronic (74%) and to have a severe course with a lethal outcome (12.9%) [Refs. 1, 2]. The long symptom-free course, non-specificity of clinical manifestations and the complexity of the interpretation of laboratory findings make the clinical diagnosis of chlamydiosis difficult [Refs. 3-6]. CI most often develops in the presence of reduced immunological reactivity, and itself contributes to immunosuppression. This situation constitutes a factor responsible for the disease's long persistence and chronic course and the addition of intercurrent diseases, in particular, ARD (acute respiratory disease) [Refs.7, 8], making it necessary to administer immunotrophic drugs in combination therapy for CI [Refs. 9, 10].

The purpose of our study was to evaluate the efficacy of immune modulation therapy with Influcid and Immunal for optimising the treatment of chlamydial infection in children and for preventing intercurrent diseases.

The Study's Materials and Methods

A study was made of 184 patients with chlamydial infection, aged from 6 months to 18 years, who had been monitored at the Center for Persistent Infections and Parasite Invasions of Municipal Teaching Hospital 5 in Samara from the years 2004 through 2009. The majority of the children (60.3%) were from 4 to 14 years of age.

Clinical methods were employed to verify the diagnosis: two-time (one month apart) testing by immune-enzyme analysis for serological (blood) markers (reagent kits from ZAO Vektor-Best and NPO Mediko-Biologicheskiy Soyuz [Russia], and R-ELISA from Medac Diagnostica (Germany) were used in our study); and chlamydia and herpes virus (including cytomegalovirus) DNA was detected in the blood by a polymerase chain reaction (PCR) using Litekh (Moscow) domestic test systems.

We used the following diagnostic criteria to determine the stage of the disease [Ref. 1]:

– With the presence of IgM and IgA titers > 1:50, the stage was rated as acute.

– Reactivation of the process was diagnosed with an IgA titer value > 1:50 and high IgG titer values (to 1:51,200).

– The chronic stage was characterised by the presence of IgA (to 1:200) in combination with elevated IgG titers (to 1:1600).

The immunological analyses included the determination of level-1 immunogram indices, interleukin-4, and interferon-γ (at the Samara immunological laboratories).

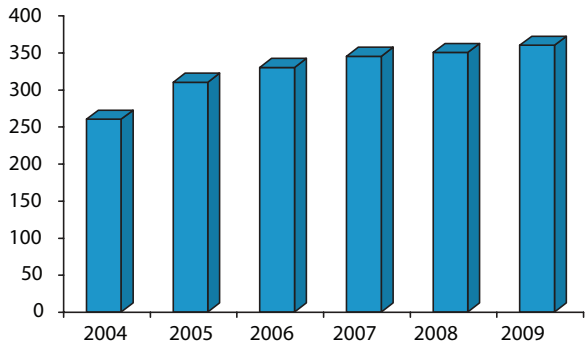

Figure 1. Number of children with chlamydial infection according to records for children at the Center for Persistent Infections and Parasite Invasions of Municipal Teaching Hospital 5 in Samara

Immunological analyses were performed twice (before treatment and after treatment, six months apart).

The data obtained were processed mathematically on a personal computer under Windows XP using Microsoft Office Excel 2007 and Statistica 6.0 software and employing multifactor system analysis.

Results and Discussion

An analysis of medical statistical data showed that the total number of children with chlamydial infection grew over the six-year period (2004-2009) (Fig. 1).

Chlamydial infection as a mono-infection (during the time period cited) was detected in 37% of the patients, and combined forms in 63% of the children (in combination with cytomegalovirus infection, in 17%; with an infection caused by the herpes simplex virus, in 33%; and with other infections (toxoplasmosis, giardiasis and helminth invasions), in 13%).

Primarily respiratory symptoms, long-duration coughing, frequent, recurring respiratory disorders of the bronchopulmonary system, and ENT pathology, lymphadenopathy, as well as complaints of weakness and asthenic syndrome, were the reasons for the children being sent to a doctor and being examined for chlamydial infection. The following were the primary clinical diagnoses: ARVI (acute respiratory viral infection), acute bronchitis, obstructive bronchitis, chronic tonsillitis, lymphadenitis, vegetative dystonia syndrome, dysbacteriosis, and atopic dermatitis.

Aconitum D3
Normalises body temperature; remedy for upper respiratory tract mucosal inflammation.

Gelsemium D3
Remedy for rhinitis; headache remedy.

Ipecacuanha D3
Acts as an expectorant.

Bryonia Dt
Remedy for a painful dry cough.

Eupatorium perfoliatum D1
Remedy for stiffness and aches in joints.

Phosphorus D5
Has an adaptogenic effect

Figure 2. Composition of the Drug Influcid

Antibacterial therapy was prescribed in the case of primary infection or its progression, and of reactivation of the infection. Macrolides (spiromycin, azithromycin, roxithromycin, clarithromycin, josamycin and macropen) were prescribed for 102 children.

Patients with chronic chlamydial infection regardless of exacerbation were prescribed immune modulation therapy.

Based on the fact that the secondary immunodeficiencies observed with chronic CI take place with pronounced interferon status disordering, our choice rested on interferon-inducing drugs – Influcid and Immunal. This choice was due to the high density of mixed forms of chlamydia, with an infection caused by the herpes simplex virus (33%), and a reduced interferon-γ level in the majority of the patients we monitored. Patients afflicted with ARD from 5 to 10 times a year were classified under the **group of frequently ill children**. Based on the fact that a heavy drug load on children with chronically occurring chlamydial infection, including when they have a cold too, results in even greater damage to the immune system, it is advisable to use agents of natural origin that do not produce an additional pharmacological load on the body [Refs. 11, 12].

The drug Influcid (produced by Deutsche Homöopathie-Union [German Homeopathy Union]) is an agent of natural origin possessing immune-modulation and antiviral activity. Influcid normalises the body's hormone/neurotransmitter balance, and, combined with normalisation of interferon status, prevents the development of ARVI [Ref. 13].

At *NII grippa* SZO *RAMN* [a Russian Academy of Medical Sciences influenza research institute] (St. Petersburg), Influcid's antiviral effect was proven in vitro for reference current human influenza strains A(H3N2), A(H1N1) and B; highly pathogenic bird influenza strain A; reference pandemic influenza strain A(H1N1); and a representative Russian pandemic flu strain isolated in September 2009 [Refs. 14-16]. Influcid substantially reduces the cytopathic effect of type 1 and type 2 herpes viruses in vitro [Ref. 16].

The results of Influcid's effect are provided by its unique composition (see Fig. 2, active ingredients). Its components exert an effect on the body's internal reserves. Influcid provides a great number of the effects of medicinal products [conventional drugs] and helps to avoid excessive drug administration.

The plant-based biogenic stimulator Immunal (produced by the Lek D.D. company, Slovenia) exerts an immune-modulating and anti-inflammatory effect and stimulates bone-marrow blood production. It activates cellular immunity primarily, stimulates the phagocytic

activity of macrophages and granulocyte chemotaxis, aids cytokine release, enhances interleukin-1 production by macrophages, accelerates the transformation of b-lymphocytes into plasma cells, and strengthens antibody formation and T-helper activity. It increases the body's nonspecific resistance, including to causative agents of herpes.

Immunal's active ingredient is the sap of the herb Echinacea purpurea, which also provides its immune-stimulating effect.

We studied the therapeutic and preventive efficacy of Influcid and Immunal in 60 (33% of the total number monitored) children from 7 to 14 years of age with chronic mixed chlamydial infection combined with the herpes simplex virus. The first group comprised 20 children who had been given Influcid in a dose of 1 tablet twice daily (children from 7 to 12 years old) or thrice daily (patients from 13 to 14 years old); the second group comprised 20 children who had been given Immunal in a dose of from 10 to 20 drops thrice daily (depending on their age). The control (3rd) group comprised 20 children with CI from 7 to 14 years of age with no preventive therapy.

The patients received two therapeutic-and-preventive courses of treatment one month in duration, one year apart. The drugs were prescribed immediately following an antibacterial course of treatment with macrolides. The children were monitored for 24 months.

The results of treatment were evaluated in the children of the various groups 3 months following the preventive course of treatment, for the number of cases of ARD; 6 months later, for immunological indices; and 12 and 24 months later, for the number of recurrences of chlamydial infection and the incidence of ARD.

Three months following completion of the preventive course of treatment, 6% of the children of the first group fell ill again, 28% in the second group, and in the third group the percentage of those who fell ill practically did not change. During the monitoring period, the children in the first and second groups were not given antibacterial drugs after the first course of etiotropic therapy, whereas in the third group exacerbation of CI and the addition of ARD took place in eight children.

The level of class IgG antibodies against chlamydia trended toward a reduction in the first 2 to 4 months in 60% of the patients who had been given Influcid, and in 45% who had been given Immunal. In the control group, the level of antibodies against chlamydia remained the diagnostic levels in the majority of the patients (90%). In the first year of treatment, recurrences of CI were observed in 15% of the patients who had been given Influcid, and in 20% of those who had been given Immunal. There were no recurrences noted following the second course of treatment. In the children of the control group, who had not been given preventive treatment, the recurrences repeated themselves: in 40% in the first year of monitoring and in 35% of cases in the second.

Table 1. Effect of different kinds of preventive treatment on incidence of ARD in children with mixed chlamydial infection

Incidence of ARD Per Year in Children of Various Groups			
Monitoring Period	Influcid (n = 20)	Immunal (n = 20)	Control (n = 20)
Prior to treatment	6.4 ± 0.3	5.9 ± 0.8	6.1 ± 0.7
After treatment	3.3 ± 0.8*	4.1 ± 0.2*	5.9 ± 0.5

* $p < 0.05$ – Significant differences in the groups prior to and after treatment

In analysing the effect of the immune-modulating drugs Influcid and Immunal on the incidence of ARD over a period of 24 months, it was noted that Influcid reduced the incidence to a greater degree with statistical significance ($p < 0.05$) (Table 1).

A similar trend in children in the three groups was also noted when analysing immunograms prior to and after treatment (but after six months in the control group) (Table 2).

One can see from Table 2 that the prescription of immune drugs contributed to a reduction in dysglobulinemia (an increase in total IgA with a reduction in the levels of total IgM and IgG), and to a reduction in the CIC level, which can be explained by a reduction in the causative agent's immunosuppressive activity. The increase in phagocytic protection was explained by an increase in phagocytic digestion activity. The increase in the production of interferon-γ testified to the interferon-inducing activity of the drugs administered. This effect was pronounced to a greater degree with Influcid.

Conclusion

The results of the study proved the therapeutic and preventive efficacy of the administration of the drugs Influcid and Immunal to children with chronic mixed chlamydial infection (combined with the herpes simplex virus). When the patients had been provided immune modulation therapy, manifestations of immune deficiency were reduced, the number of recurrences of chlamydial infection was significantly reduced, and the incidence of ARD was reduced; this makes it expedient to administer these drugs to children with chronic mixed chlamydial infection, including at a time when there is a rise in the incidence of ARD.

Table 2. Results of a study of key immunity indices in the process of treating children with ARD in the presence of chronic mixed chlamydial infection

Index	Group 1 (Influcid)		Group 2 (Immunal)		Control Group	
	Prior to Treatment	After Treatment	Prior to Treatment	After Treatment	First Examination	6 Months Later
IgA, g/L	1.11 ± 0.07	2.03 ± 0.05*	1.13 ± 0.08	1.8 ± 0.07*	1.12 ± 0.09	1.29 ± 0.07
IgG, g/L	12.15 ± 2.6	9.94 ± 2.3*	13.15 ± 2.8	10.79 ± 2.1*	11.1 ± 2.7	10.9 ± 2.3
IgM, g/L	2.2 ± 0.42	1.5 ± 0.4*	2.15 ± 0.37	1.8 ± 0.31*	2.3 ± 0.44	2.1 ± 0.39
Fibronectin	600.07 ± 63.9	515.11 ± 63.8*	589.37 ± 59.3	538.7 ± 49.8*	580.5 ± 65.6	540.4 ± 59.8
CIC, spec. units	72.11 ± 1.5	51.58 ± 1.3*	72.53 ± 1.8	56.75 ± 1.2*	72.11 ± 1.5	69.1 ± 1.2
CD3+, cells x 10^9/L	3.12 ± 0.2	3.57 ± 0.1*	2.99 ± 0.2	3.38 ± 0.2*	2.95 ± 0.2	3.1 ± 0.18
CD4+, %	35 ± 2.1	39 ± 2.14*	35.4 ± 1.9	38 ± 2.12*	35.6 ± 2.33	37.5 ± 2.76
CD8+, %	22 ± 1.57	20 ± 1.62*	21.9 ± 1.79	21 ± 1.85	20.3 ± 1.45	21.5 ± 1.77
CD20+, %	18 ± 0.85	16 ± 0.78*	18 ± 1.13	16.8 ± 1.1*	18.5 ± 0.93	17.9 ± 0.75
HLA-DR, cells x 10^9/L	0.55 ± 0.01	0.49 ± 0.01*	0.54 ± 0.02	0.51 ± 0.01*	0.56 ± 0.02	0.52 ± 0.01
CD16+, cells x 10^9/L	0.76 ± 0.02	0.81 ± 0.01*	0.75 ± 0.02	0.79 ± 0.01*	0.77 ± 0.02	0.79 ± 0.01
CD4+/CD8+	1.1 ± 0.01	1.8 ± 0.01*	1.1 ± 0.01	1.6 ± 0.01*	1.1 ± 0.01	1.4 ± 0.01
Phagocytosis, %	58 ± 4.8	63 ± 4.2*	59 ± 5.6	61 ± 5.1	57 ± 5.2	59 ± 4.9
Interleukin-4, pg/mL	25.14 ± 3.28	29.16 ± 3.1*	27.52 ± 3.41	28.1 ± 3.9	26.38 ± 3.34	27.1 ± 3.12
Interferon-γ, pg/mL	639.55 ± 12.9	700.61 ± 13.3*	638.23 ± 21.8	701.18 ± 22.4*	639.52 ± 16.9	645.53 ± 17.6
Complement, for 50% chemolysis, %	29 ± 3.8	31 ± 3.1	31.5 ± 4.9	29.6 ± 4.1	27 ± 4.4	27.8 ± 4.0
Phagocytic protection factor, spec. units	34.96 ± 3.6	48.61 ± 2.9*	36.64 ± 3.4	45.8 ± 3.* 2	32.78 ± 3.5	33.6 ± 3.1
Specific immune potential (lymphocyte-monocyte), spec. units	52.32 ± 2.1	60.02 ± 2.0*	54.37 ± 2.4	58.7 ± 2.0*	51.65 ± 2.2	53.6 ± 2.0

* $p < 0.001$ – Significance of differences prior to and after treatment

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