Evaluation of the Efficiency and Safety of Anaferon (Pediatric Formulation) in the Treatment of Chickenpox in Children

V.N. Timchenko, E. B. Pavlova, T. M. Chernova, S. L. Bannova, T. I. Savel'eva, S. A. Tarasov, M. V. Kachanova, and M. A. Siver'yanova

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 148, Suppl. 1, pp. 39-42, August, 2009
Original article submitted August 1, 2008

Addition of anaferon (pediatric formulation) to the therapy of chickenpox patients led to more rapid disappearance of the main symptoms and alleviated the course of the disease. The safety of the preparation is confirmed by the absence of undesirable events and stability of laboratory indexes against the background of therapy.

Key Words: *chickenpox; children; treatment; anaferon (pediatric formulation)*

Chickenpox (CP) is steel the most prevalent disease after acute respiratory and intestinal infections in children. Taking into account the existence of severe forms of the disease and specific complications, etiotropic therapy of CP is an important problem [5]. Preparations used for the treatment of viral disease (remantadine, acyclovir, *etc.*) have a narrow spectrum of action and are characterized by a number of toxic effects [2]. The search for new drugs for the treatment of CP is now in progress. It is known that the main role in antiviral defense is played by IFN system; the effect IFN is determined by inhibition of replication of RNA- and DNA-containing viruses [4]. Modern IFN preparations produce etiotropic and immunomodulatory effects and are characterized by a wide spectrum of antiviral activity, so they can be used in some viral infections, including herpetic one [1,3].

Here we evaluated the efficiency of anaferon (pediatric formulation), a preparation, containing affinity-purified antibodies to human IFN-γ (a mixture of homeopathic dilutions) and producing antiviral and immunomodulatory effect [6], as the therapeutic means in children with CP.

Department of Infection Diseases in Children, Department of Clinical Pharmacology, St. Petersburg State Pediatric Medical Academy, Children's Polyclinic No.71, St. Petersburg,

MATERIALS AND METHODS

The study was performed in January-May, 2007, in children's polyclinic No. 71, St. Petersburg. Sixty children aging 1-18 with CP diagnosed on the basis of typical clinical symptoms were observed. All children were included in the study on days 1-2 of the disease. They have fever ≥37.5°C, intoxication symptoms (headache, malaise, low appetite, *etc.*), skin rash (spot, papule, vesicle). The children receive no antibacterial, antiviral, immunomodulatory therapy. Examination of all patients included analysis of disease history, daily (for 10 days) examination with scoring of CP symptoms (by a 3-point scale), prescribed therapy, the presence of undesirable effects, and total assessment of disease severity. Laboratory tests were performed on days 1 and 10: total and biochemical blood tests (ALT, AST, bilirubin, urea, creatinine, and total protein) and routine urine test.

The children were randomly divided into 2 groups. Group 1 patients (n=30) received AP (Materia Medika Holding) in addition of complex therapy, group 2 patients (n=30) received placebo. The groups were similar by sex, age, height, body weight (Table 1) and clinical manifestations of CP (Tables 2, 3). AP and placebo were given for 7 days according to the following scheme: 1 tablet every 30 min during the

0007-4888/09/1482-0291

TABLE 1. Age, Height, and Body Weight of Patients Included into Clinical Study (*M*±*m*)

Parameter	AP	Placebo
Age, years	5.9±0.6	6.1±0.5
Height, cm	115.0±3.6	115.3±2.9
Body weight, kg	22.5±0.2	25.0±2.2

first 2 hours, then 3 tablets with equal time intervals during day 1 and 1 tablet 3 times a day starting from day 2. Skin rash elements were treated with 1% ethanol solution of brilliant green (symptomatic therapy). Antipyretic drugs (nurofen, ibuprofen, paracetamol, panadol) were given to 13 patients in group 1 (43.3%) and 12 patients in group 2 (40.0%). Five patients in both groups (16.7%) with severe skin rash received antihistamine preparations (tavegyl, loratadine). The efficiency of treatment was evaluated by the terms of body temperature normalization, appearance of last rash elements, disappearance of itch, and reduction of intoxication symptoms; the presence and severity of CP complications were taken into account. The presence and character of undesirable effects and their interrelationship with drug intake served as the criteria of treatment safety.

In statistical analysis the following parameters were compared: the mean value of the parameter for the group of patients for parametric variables and percent of patients attaining specified value of the index for nonparametric variables. The significance of differences between the groups was evaluated using Student's *t* test for independent variables. The significance of the decrease in relative risk was evaluated using χ^2 test for uniformity of proportions.

RESULTS

Body temperature in children treated with AP returned to normal after 1.50±0.09 days *vs.* 4.10±0.18 days in children receiving placebo. Symptoms of intoxication in group 1 patients persisted for less then 2 days (malaise for 1.70±0.12 days, sleep rhythm disturbances for 1.60±0.16 days, low appetite for 1.80±0.15 days, irritability/capriciousness for 1.80±0.17 days), while in group 2 these symptoms were more long-lasting (3.50±0.14, 3.30±0.11, 3.30±0.17, and 4.70±0.20 days, respectively); all differences were significant. New rash elements were detected during 1.90±0.16 days in group 1 patients and during 5.50±0.17 days in group 2 patients. All stages of CP rash element development (spot-papule, papule, vesicle without central umbilicate impression, and vesicle with impression) were shorter in group 1 compared to those in group 2: 1.80±0.18 2.00±0.17, 3.00±0.14, and 2.90±0.13 days *vs.* 3.90±020, 3.80±0.17, 60.1±0.14, and 5.80±0.16 days, respectively. Skin itch accompanying CP rash persisted for 1.70±0.19 days in group 1 patients and was more long-lasting in group 2 patients (4.10±0.27 days). Crusts and pigmentation elements, terminal stages of CP rash, were detected during days 2-4 in both groups. On the whole, the majority of children

TABLE 2. Initial Clinical Characteristics of Patient with CP

Parameter		Group 1		Group 2	
		abs.	%	abs.	%
Status					
	medium severity	9	30.0	9	30.0
	satisfactory	21	70.0	21	30.0
	body temperature	37.7	37.5		
Intoxication symptoms					
	headache	19	63.3	18	60.0
	dizziness	5	16.7	8	26.7
	malaise	29	96.7	29	96.7
	disturbances of sleep rhythm	10	33.3	13	43.3
	irritability/capriciousness	16	53.3	16	53.3
	low appetite	23	76.7	25	83.3
	vomiting	1	3.3	2	6.6
	itch	27	90	24	80.0

TABLE 3. Amount and Localization of Rash Elements in CP Patients

Parameter		Group 1		Group 2	
		abs.	%	abs.	%
Amount of rash elements	<200	29	96.7	30	100.0
	200-300	1	3.3	—	—
Localization of rash elements	body temperature	37.7	37.5		
	scalp	19	63.3	18	60.0
	face	24	80.0	17	56.7
	trunk	28	93.3	22	73.3
	upper extremities	22	73.3	18	60.0
	lower extremities	21	70.0	18	60.0
	oral cavity	3	10.0	1	3.3
	genitals	1	3.3	2	6.6
	conjuctive	1	3.3	2	6.6
	itch	27	90	24	80.0

TABLE 4. Laboratory Parameters of Total and Biochemical Blood Tests of CP Patients ($M \pm m$)

Parameter		Group 1		Group 2	
		day 1	day 10	day 1	day 10
Hemoglobin, g/liter		123.8±2.8	127.2±1.9	125.7±4.2	130.8±2.3
Erythrocytes, 10^{12}/liter		4.2±0.1	4.4±0.1	4.5±0.1	4.6±0.1
Platelets, 10^9/liter		238.8±11.2	321.7±15.3	223.9±12.0	327.4±17.2
Leukocytes, 10^9/liter		6.7±0.5	7.7±0.4	6.3±0.4	7.5±0.5
Eosinophils, %		1.5±0.3	1.8±0.3	1.7±0.3	1.9±0.3
Neutrophils	trunk	28	93.3	22	73.3
	stab, %	2.0±0.6	1.0±0.2	1.4±0.2	0.9±0.1
	segmented, %	42.9±1.9	43.1±1.5	49.5±1.8	46.9±1.6
Lymphocytes, %		45.4±2.0	48.0±1.5	41.0±1.7	43.7±1.7
Monocytes, %		7.5±0.5	5.6±0.3	6.7±0.4	6.4±0.4
ESR, mm/h		11.7±1.0	9.5±0.9	11.2±1.1	9.5±0.9
AST, U/liter		33.9±6.4	24.6±2.2	29.1±2.2	26.6±3.6
Bilirubin, μmol/liter		8.1±0.4	8.2±0.5	8.7±0.6	8.6±0.5
Urea, μmol/liter		4.4±0.2	4.5±0.2	4.5±0.2	5.0±0.2
Creatinine, μmol/liter		57.3±2.7	53.3±2.3	55.9±2.7	54.8±2.2
Glucose, μmol/liter		5.0±0.1	4.8±0.1	5.1±0.2	4.8±0.1
Total protein, g/liter		68.5±1.1	68.9±1.1	69.7±1.3	70.3±1.0

(90 and 70% patients in AP and placebo groups, respectively) had mild form of the disease, while medium-severe form of CP was diagnosed in 10 and 30% patients, respectively. In none patients severe form of the disease was diagnosed (Fig. 1). No cases of aggravation of patient's status and complication development were noted.

No undesirable events were recorded against the background of therapy. Analysis of laboratory data in dynamics revealed no negative changes in total and

TABLE 5. Laboratory Parameters of Urine in CP Patients (*M*±*m*)

Parameter	Group 1		Group 2	
	day 1	day 10	day 1	day 10
Density, g/liter	1013.9±0.6	1016.3±0.9	1016±0.8	1016.3±0.26
Protein (trace amounts), g/liter	3	1	1	1
Glucose, g/liter	0.0±0.00	0.0±0.00	0.0±0.00	0.0±0.00
Ketone bodies, g/liter	0.0±0.00	0.0±0.00	0.0±0.00	0.0±0.00
Leukocytes, per visual field	2	0	3	2
Erythrocytes, per visual field	3	1	0	0
Cylinders, per visual field	0.0±0.00	0.0±0.00	0.0±0.00	0.0±0.00

biochemical blood tests and total urine test (Table 4, 5). The differences in the analyzed laboratory parameters in both AP and placebo groups were insignificant and were within the physiological range.

Thus, our clinical study showed that the use of AP accelerated disappearance of the main symptoms (fever, intoxication, rash, and itch) and alleviated the course of CP. The safety of preparation is confirmed by the absence of undesirable events, and stability of laboratory indexes against the background of therapy. These findings allow recommending AP for the treatment of CP in children.

REFERENCES

1. O. I. Afanas'eva, L. V. Osidak, E. G. Golovacheva, *et al., Detskie Infektsii*, No. 2, 48-53 (2003).
2. F. I. Ershov, *Antiviral Drugs. A Handbook* [in Russian], Moscow (1998).
3. L. A. Zhuravleva, K. I. Chuikova, O. I. Galactionova, *et al., Detskie Infektsii*, No. 3, 50-52 (2003).
4. S. A. Ketlinskii, *Manual for Physicians* [in Russian], St.Petersburg (1998), pp. 44-46.
5. L. D. Sluchenkova, *Chickenpox and Other Infections in Children* [in Russian], Moscow (2001).
6. O. I. Epshtein, M. B. Shtark, A. M. Dygai, *et al., Pharmacology of Ultralow Doses of Antibodies to Endogenous Regulators of Functions* [in Russian], Moscow (2005).