

**EXPERIENCE OF APPLICATION OF PROTEFLAZID  
IN TREATMENT OF INFECTIOUS MONONUCLEOSIS IN CHILDREN**

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**The article is devoted to the treatment of infectious mononucleosis in children. On the basis of dynamic clinical and laboratory studies (using specific methods to confirm etiologic role of Epstein-Barr virus), children with infectious mononucleosis were treated with domestic product “Proteflazid”, its clinical efficiency is described in this article.**

**Keywords:** infectious mononucleosis, children, Epstein-Barr virus, treatment, “Proteflazid”.

Infectious mononucleosis as a disease is known since 1885, when it was described as “ideopathic inflammation of the cervical gland” by Filatov M.F. Polisymptomity of this nosology and difficulties of differential diagnosis are clearly illustrated by the large number of titles (over 60), which were given to this disease in different years. Nowadays it has common name “infectious mononucleosis”. Epstein-Barr virus (EBV) of the herpesvirus family is pathogen of this disease.

Epstein-Barr virus infection is quite common among adults and children, the level of infection of adult population of Ukraine is about 100%, and more than 50% [5, 7] among children. Primary infection often occurs in childhood and runs either in the form of mononucleosis, or has low or absence of symptoms. Possible dangerous complications (myocarditis, neuropathy, thrombocytopeny) and generalization of process in immune compromised children on background of acute process, dangerous disease consequences, such as lymphoproliferative disease (lymphoma, leukoplakia, lymphogranulomatosis) and autoimmune conditions (SLE, rheumatoid arthritis) [1, 6, 7] encourage the scientists to search new methods of treatment of infectious mononucleosis. However, known antiherpetic drugs, atypical nucleotides, are almost not effective in this disease. We were attracted by new modern drug “Proteflazid”, which has antiviral effect and low toxicity, which is very important for children [2, 3, 5].

**Objective:** to evaluate clinical efficacy and tolerability of Proteflazid at infectious mononucleosis in children.

**Materials and methods.**

Under our supervision there were 38 children who suffered from infectious mononucleosis. Age children were 1 to 14 years. The boys were 20 girls - 18.

Comprehensive examination of children included general clinical methods (examination, palpation, percussion and auscultation) and additional non-specific laboratory examination methods (complete blood count with quantitation of atypical mononuclear cells, liver function tests, prothrombin level index, etc.). To confirm the etiologic role of Epstein-Barr virus with the help of enzyme-linked immunosorbent assay (ELISA), we determined the presence of anticapsid immunoglobulin M (IgM) in blood and polymerase chain reaction (PCR) - the presence of nucleotide sequences of DNA virus in buccal scrape. All children received comprehensive treatment against infectious mononucleosis according to “Treatment protocols of infectious diseases in children” [4]. 17 subjects from observation group additionally took domestic product “Proteflazid” (“Ecopharm”, Ukraine, registration number R.02.01 / 02777), which contains composition of flavonoid glycosides of cereals. This drug has virustatic properties (by inhibiting enzymes of virus specific enzymes – thymidine kinase and DNA polymerase), interferon inducing and antioxidant activity. Proteflazid was administered in the following doses:

children of 1-3 years - 2 drops (dr.) twice a day for one month;

children of 3-6 years - 2 drops three times a day - 1 week, 4 dr. three times a day - the 2nd and 3rd week treatment, 3 dr. three times a day - 4 week;

children of 7-14 - 3 dr. three times a day - 1 week, 5 dr. three times a day - the 2nd and 3rd week, 3 dr. three times a day - 4 week.

The effectiveness of treatment was assessed by dynamic results of clinical and laboratory examination. The safety and tolerability (good, satisfactory and unsatisfactory) were obligatory assessed in each clinical case; registration of side effects was conducted.

### Discussion of the results.

All the children in observation group suffered from increased body temperature on peak of disease. Majority of subjects had temperature up to 38°, which stayed unchanged (over 7 days) for a long period. Analysis of clinical examination of children (Table 1) showed that most children have signs of acute tonsillitis, lacunar or necrotic angina, many subjects had complicated nasal breathing due to "rear rhinitis", enlargement of liver and spleen and polylymphadenopathy.

Table 1 - Clinical manifestations of infectious mononucleosis in children of observation group.

Clinical symptom		Group of subjects, who	
		took Proteflazid	did not take Proteflazid
Increase of body temperature	37-38° C	3	3
	38° C and higher	14	18
Acute tonsillitis		15	19
Complicated nasal breathing		16	10
Hepatomegaly		15	15
Splenomegaly		14	14
Enlargement of lymphatic nodes	in 2 groups	7	7
	in 3 groups	5	4
	in 4 groups	4	7
Rash		1	3

Most of sick children had enlarged lymph nodes of cervical group. Enlargement of lymph nodes in 3 and more groups was noted in every second subject. Among the symptoms, which were met rarely met, we can note exanthema, which occurred only in 4 subjects and appeared on 3-7 day of disease on the background of antibiotic therapy.

These laboratory studies of blood of sick children are given in the Table No. 2.

Table No. 2 - Results of laboratory blood tests of children in observation group.

Observation group	Number of leukocytes (x10 <sup>9</sup> /ml)			Atypical mononuclear (%)			Increase	
	>9	9-11	<11	>10	<10	absence	ALT level	Thymol sampling
Subjects, who took Proteflazid	11	4	2	7	7	3	7	8
Subjects, who did not take Proteflazid	7	4	10	10	4	7	7	9

As you can see from the Table, almost half of children in both groups had leukocytosis and moderate cytolytic syndrome of liver. We found atypical mononuclear cells in peripheral blood of vast majority of children.

Specific additional tests to confirm the etiologic role of Epstein-Barr virus have been performed in 10 subjects, who took Proteflazid and 11 children, who did not take this drug. All the subjects had markers of Epstein-Barr virus infection, as reflected in the table No. 3.

Table 3 - Results of specific examination of children in observation groups to EBV

Observation group	IgM + PCR	IgM + PCR	IgM + PCR
Subjects, who took Proteflazid	3	5	2
Subjects, who did not take Proteflazid	3	6	2

Dynamic monitoring of subjects showed a difference in disease in children, who received Proteflazid in comparison with children, who did not receive this drug (Table 4, Fig. 1). So, despite the fact that the average length of stay in hospital was almost equal in both groups of subjects ( $11,05 \pm 4,6$  and  $11,3 \pm 4,7$  respectively), 6 children (35.3%), who received Proteflazid were discharged, being recovered, while the most favorable outcome from disease occurred only in four children (19.1%), who did not received such treatment.

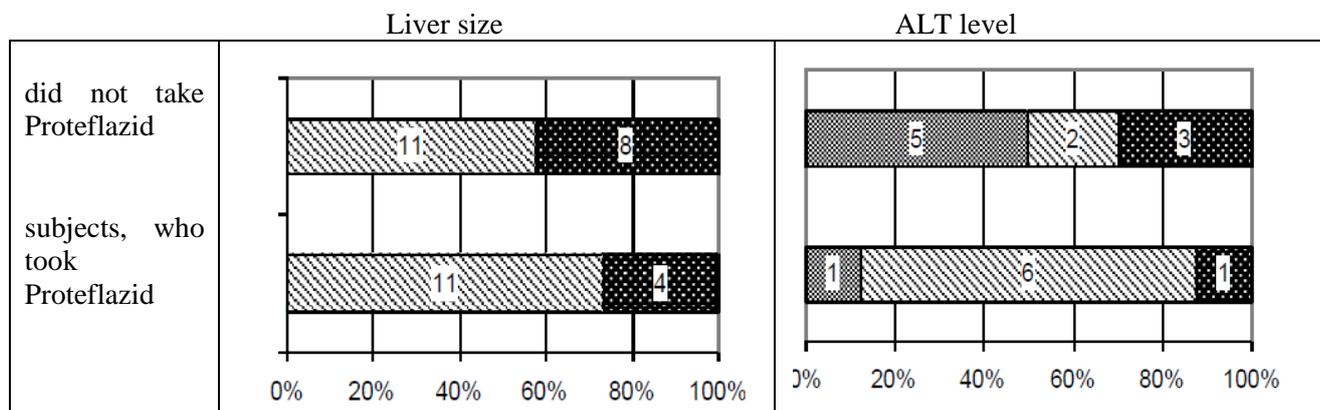
Table 4. – Dynamics of clinical indicators in children of observation group

Observation group		Normalization of temperature	Disappearance of angina	Reduction of lymph node size	Reduction of spleen size
Subjects, who	took Proteflazid	17	15	14	10
	did not take Proteflazid	21	19	10	8

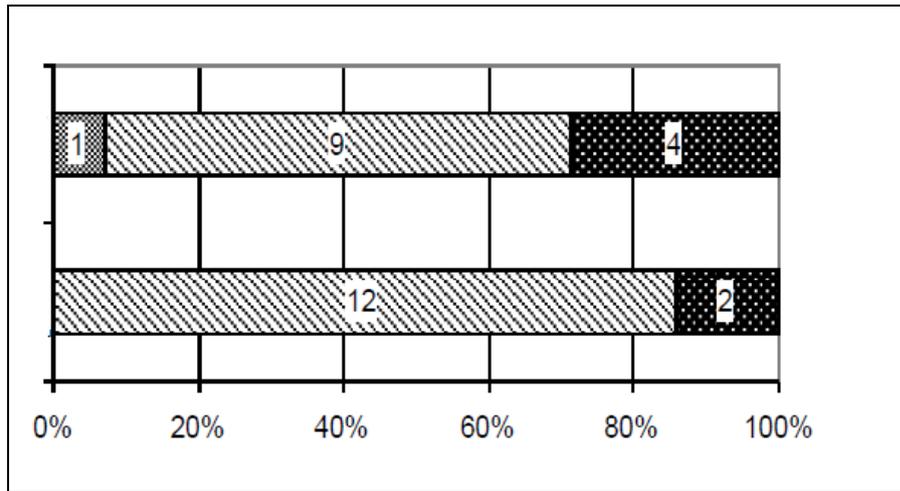
Dynamic increase of number of atypical mononuclear cells in blood was noted only in group of children, who did not receive Proteflazid at therapy (1 subject), and 4 (28.6%) children had no changes in this indicator. Almost half of subjects in this group did not have positive dynamics of liver size at the moment of discharge from hospital, 5 children even had increased ALT levels, and 3 children had retention of cytolytic syndrome. At that, 11 children (78.5%), who took Proteflazid, had gradual decrease in severity of hepatomegaly, and 6 (75% of children with cytolytic syndrome) had dynamic decrease of ALT level. For whole period of Proteflazid administration, no adverse event was registered. “Proteflazid” was well tolerable by all subjects.

**Findings:**

Obtained results testify efficacy of Proteflazid in comprehensive treatment of children with infectious mononucleosis, which shows positive dynamics of clinical symptoms and hemogram indicators. Faster termination of hepatocyte cytolysis was noted on background of Proteflazid intake, which is manifestation of sufficient severity of infectious mononucleosis course.



Number of atypical mononuclear cells



▣ increase   ▤ decrease   ▥ no changes

Figure 1. Dynamics of several clinic and laboratory indicators in children of observation groups on background of treatment.

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