Modern infections. - 2005. –No. 3-4. – p. 121-124.

PROTEFLAZID IN TREATMENT OF SUBJECTS WITH INFECTIOUS MONONUCLEOSIS CAUSED BY EPSTEIN-BARR VIRUS

A.I. Hlei

National Medical University named after O.O. Bogomolets, Kyiv

Department of Infectious Diseases

Keywords: EBV infection, infectious mononucleosis, treatment, Proteflazid

Despite the emergence of new antiviral drugs, the issue of prevention and treatment of herpesvirus infections, including those infections, caused by the Epstein-Barr virus (EBV) remains relevant. Clinical efficacy of majority of them is disputable, treatment schemes are incomplete.

Proteflazid is one of such drugs, which has antiviral and immunomodulatory action, and, at the same time, it does not have mutagenic and teratogenic effects. It meets the existing requirements of cancerogenic safety, and when receiving per os, it refers to 4 grade of toxicity (materials of low danger) [7,8]. The drug is easy to use, well tolerated, not expensive compared to other antiviral agents. Its effectiveness was shown in the treatment of herpes infection in children [3], recurrent genital herpes [4.10], viral hepatitis [5,8]. We met few reports in the literature about its efficacy in EBV infection, the results of which are contradictory [9].

The aim of our study was to evaluate the effectiveness of treatment of subjects with acute infectious mononucleosis and exacerbation of chronic EBV infection due to infectious mononucleosis, with addition of Proteflazid in comprehensive basic treatment.

In 2003-2004, 27 subjects with acute EBV infectious mononucleosis with typical moderate disease, without concomitant chronic disease were treated by Proteflazid. The control group consisted of 20 subjects with acute infectious mononucleosis, EBV, they received conventional therapy (antibacterial and antihistamines). The diagnosis was confirmed by detection of EBV DNA in the subjects` blood by semiquantitative polymerase chain reaction (PCR) and specific serological studies (detection of anti EBV IgM with negative anti EBV IgG to early antigen in subject`s blood) by enzyme immunoassay (ELISA).

Glucocorticosteroid drugs were not used in both groups of subjects. All subjects were aged from 15 to 22 years. The average age of subjects was 17.4 years. The average hospital stay in the two groups was around 10.

Subjects, who received Proteflazid (10 drops three times a day before meals) in comparison with control group, had clear positive trend in a more rapid reduction in size of lymph nodes and spleen, hemogram improvement (reducing the number of white blood cells, loss or reduction in the number of atypical mononuclear cells) and biochemical parameters (normalization or reduction of transaminase activity). For example, on 10^{th} day of receiving this drug (on the average -18 days of illness) normalization of transaminases was noted in 78% of subjects of the main group and 45% in the control group; disappearance of virocytes - 85% and 60% respectively ($P \leq 0,05$).

Table 1

Dynamics of some indicators, demonstrating efficiency of Proteflazid in treatment of acute infectious EBV-mononucleosis compared with basic treatment

Groups of subjects	Persistence of pathologic indicators at the moment of discharge		
	Virocytosis	Hyperenzymemia	Splenitis
Basic group, n=27	4 (14,8%)	6 (22%)	10 (37%)
Control group, n=20	8 (40%)	11 (55%)	11 (55%)

There is no sense to compare such factors as the duration of fever and tonsillitis, since they were absent in almost all subjects at the time of confirmation of diagnosis (4-5 day of stay in the hospital) and Proteflazid administration. The length of viremia is indicative in this case. Without antiviral therapy in subjects with EBV-infectious mononucleosis, it lasts up to 1 year in some cases - more than [1.2]. Thus, during dynamic examination of subjects for the presence of viral DNA in 2 months, viremia was noted only in 48% of subjects who received Proteflazid, and in 95% of subjects, who received basic therapy ($P \leq 0{,}001$).

Here is an example of an extract from medical report:

Subject G., age 15 entered infectious department on 07.12.2003 in 13th day of illness, the first day of rash, febrile fever, symptoms of angina, generalized lymphadenopathy and abundant macula-papular rash. He was treated by district doctor, who diagnosed angina at him, he received Amoxil.

Hemogram at admission: leukocytes 10.9 x 10^9 /l, stab - 4%, segmented - 18%, eosinophils - 1% basophils - 2%, lymphocytes - 51%, monocytes - 11%, virocytes - 11%, plasmocytes - 2%; alanine aminotransferase activity (ALT) in the biochemical analysis of blood was 300 u/l. Ultrasound (US) investigation showed hepatosplenomegaly (anteroposterior size of the right hepatic lobe - 15.2 cm, the left lobe - 10.5 cm, S max of spleen – 148 cm^2, V of spleen - 1300 cm^3), the presence of lymph nodes (up to 2 cm in diameter) at the liver gate. PCR method revealed EBV DNA (IC - 253) in subject`s blood, and anti EBV IgM (VCA) was revealed by ELISA method.

Subject canceled treatment by Amoxil, Rovamicin and Diazolin were prescribed to him in average medium therapeutic doses, as well as Proteflazid.

At 5 day of stay in the hospital, body temperature was normalized, lymph nodes and spleen size were decreased (S max - 99 cm2), rash was vanished almost completely, phenomenon of tonsillitis was disappeared; hemogram indicators were normalized, ALT activity was decreased (120 u/l).

He was discharged from hospital on 18.12.03 in satisfactory state, and continued to take Proteflazid for 2 months. He felt good, no side effects of the drug were noted.

He was re-examined on 20.02.04. Pathological changes in the hemogram and biochemical were absent, size of lymph nodes and spleen were normalized. His liver was slightly increased in size (anteroposterior size of the right destiny - 14.2 cm), availability of lymph nodes at liver gate and spleen was not found. Result of examination of the subject's blood for EBV DNA in PCR was negative.

In addition, 4 subjects were treated with Proteflazid, they were under clinical observation due to aggravation of chronic EBV infection, accompanied by viremia, increase in the size of lymph nodes and spleen, hematologic changes (EBV-acute mononucleosis in medical history). Availability of

EBV in serum was confirmed by detection of viral DNA in PCR, acuteness of process was testified by appropriate serological profile (anti EBV (EBNA) IgG +).

After 2 months of therapy with Proteflazid, all the subjects had no viremia together with significant improvement of general state (reduction in the size of lymph nodes and spleen, improvement of hemogram). This drug is well tolerated by subjects, adverse events were not found.

Subject M., 20 years old was staying in the 2-nd department of Central Municipal clinical hospital from 19/05 till 27.05.2003 with acute infectious EBV mononucleosis, without any related chronic diseases. The diagnosis was confirmed by detection of EBV DNA in the subject's blood (IC - 238) and anti EBV IgM in high titers.

Subject had “classic” onset of disease, he had generalized lymphadenopathy, with prevalence of cervical lymphadenitis, nasal congestion and tonsillitis. Fever was subfebrile and short (18-22.05). He was under outpatient treatment, district doctors made diagnosis “angina”. He was treated by Erythromycin and antihistamines.

At admission to the hospital, his hemogram showed moderate leukocytosis with lymphomonocytosis (50%) and virocytosis (34%); in the biochemical analysis of blood - moderate increase of transaminase activity with normal bilirubin and ultrasound hepatosplenic syndrome were detected during US investigation of the organs of abdominal cavity organs (OAC), at that enlargement of the spleen (S max = 162 cm2 , V = 1200 cm 3) was prevailed on the enlargement of the liver (anteroposterior size of the right part - 15.6 cm, left part - 10.2 cm).

The treatment was prolonged (up to 22.05) treatment, prescribed by district doctor. Corticosteroid and antiviral therapy were not performed. Discharged person has satisfactory state of health with a slightly expressed events of lymphadenopathy and hepatosplenic syndrome. Fever and tonsillitis were regressed, hemogram figures were normalized.

He was under medical observation for 6 months. That time he felt good and there were no pathological changes of hemogram and ultrasound investigation of OCA. In December, the subject's condition got worse: low-grade fever appeared, all groups of lymph nodes were moderately increased. Ultrasound investigation helped to reveal moderate increase of spleen size (S max = 88 cm^2). High level (IC - 204) of EBV in blood was determined by PCR method. Aggravation of chronic infectious EBV-mononucleosis was diagnosed at subject; Proteflazid was prescribed for him (10 drops three times a day) for a period of two months. During the first week of treatment, body temperature was normalized, lymph nodes were decreased in size, spleen size were normalized. During repeated studies (in 2 and 6 months) of EBV DNA investigations, the result was negative.

FINDINGS

1. Proteflazid at a dose of 10 drops three times per day is effective for the treatment of acute and chronic EBV infection as monotherapy. Its usage leads to positive dynamics of pathological process compared to the basic treatment.

2. Side effects were not found. Application of Proteflazid stabilized a diet, which is important because of liver injury.

3. Viremia in 2 months after recovery from acute EBV-mononucleosis on background of Proteflazid intake remained in significantly fewer number of subjects compared to subjects, who received basic treatment.

References:

1. Filipovich A.H., Gross T., Juonochi H. Immune-mediated hematologic and oncologic disorders, including Epstein-Barr virus infection. // In. Stiehm E.R. Immunologic Disorders in Infants and Children. 4th Ed. - W.B. - 1996. - P. 871-888.

2. Pipp M.L., Means N.D., Sixbey J.W. et al. Acute Epstein-Barr virus infection complicated by severe thrombocytopenia // Clin. Infect. Dis. - 1997. - P. 1237-1239.

3. Brezhneva Yu.V. Efficiency of Proteflazid application in complex treatment of diseases caused by herpes simplex in children. // Immunology and allergology. - 2002. – No. 3. - P.60.

4. Garmash L.L. et al. Proteflazid in treatment of genital herpes // Immunology and

allergology - 2002. – No. 3. - P. 64-65.

5. Korchynskyi M.Ch. Properties of Proteflazid in the treatment of subjects with chronic hepatitis C // Chemotherapy and immunotherapy of infectious diseases. Materials of scientific and practical conference and plenum of Association of infectious disease specialists of Ukraine.- Ternopil. - 2005. - p. 50-53.

6. Proteflazid. Informational materials on the properties and methods of application // SMC “Ecopharm”.- Kyiv. - 2002. – p. 68.

7. Proteflazid. Information and methodical materials for practitioners. // SMC “Ecopharm”.- Kyiv. - 2004. – p. 40.

8. Savelyev V.G., Bondareva V.V. Efficacy of Proteflazid in subjects with viral hepatitis // Chemotherapy and immunotherapy of infectious diseases. Materials of scientific and practical conference and plenum of Association of infectious disease specialists of Ukraine. - Ternopil. - 2005. - p. - 85-86.

9. Shuliak V.I., Filyurina A.N., Anikins O.V. Clinical and laboratory performances of efficiency of standard and immune modeling treatment in subjects with infectious mononucleosis // Chemotherapy and immunotherapy of infectious diseases. Materials of scientific and practical conference and plenum of Association of infectious disease specialists of Ukraine. - Ternopil. - 2005. - p. – 105-106.

10. Fedotov V.P. et al. Application of Proteflazid in treatment of subjects with recurrent genital herpes // Dermatology, cosmetic medicine, sexopathology. - 2002. – No, 3-4. - p. 204-206.