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EFFICIENCY OF MONTHERAPY WITH PROTEFLAZID IN THE TREATMENT OF PATIENTS WITH CHRONIC EBV INFECTION IN THE STAGE OF REACTIVATION

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Chronic influence of xenobiotics on man, increase of the pathogens resistance degree, inefficiency of traditional antimicrobial and antiviral stimulatory factors, inadequate reaction of the immune system to pathogen intervention, increase of "epidemiological synergy of viruses" - are only a small part of the so-called "global environmental problems of humanity" that result in genetic defects and the formation of pathological processes in various organs and systems of the human body. The already known viruses are characterized by mutation of its genes, synthesis of immunotoxins, lesions of other organs, tropism to the cells of the nervous and immune systems, progression of diseases that are resistant to conventional therapy [1].

In their practice, doctors of many specialties work with diseases caused by herpes virus, that relate to opportunistic infectious agents. The main feature of herpes virus infections is the tendency to chronic forms. Patients with these infections are treated by physicians of different specialties, hence the difference in methodological approach, diagnosis and treatment of such patients, that significantly affects the records, epidemiology and other qualitative and quantitative indicators of disease [2].Herpes virus belongs to the slow human virus infections with the following features: 1) sufficiently long incubation period; 2) slow progressive course; 3) multiform organs and tissues injury; 4) the formation of severe complications and death. Long (even lifetime) immunity is formed against the background of the normal functioning of the immune system as a result of infection with herpesvirus. Multiple infection of immunocompetent person by new herpes virus strains, generally doesn't cause pathological changes. This is normal epidemiological phenomenon that enriches the spectrum of antiherpetic immunity.

In recent years, a growing number of patients with chronic recurrent herpes infections observed. Labial and genital herpes, herpes zoster, acquired and congenital cytomegalovirus infection are the most common in clinical practice. Regarding infection caused by the Epstein-Barr virus (EBV), the awareness of physicians about form of infection, peculiarities and treatment is not sufficient. Epstein-Barr virus (EBV) is representative of the γ-herpes virus that is capable to persist in the body for life, causes the development of infectious mononucleosis at the primary infection, and it is associated with a number of hematological (especially lymphoproliferative) and autoimmune diseases (vasculitis, ulcerative colitis etc.).

In addition, EBV may be a cause of chronic fatigue syndrome. This virus causes chronic, manifest, and erased atypical forms of the disease (chronic EBV- infection), affects the central and peripheral nervous systems. Today EBV is associated with different clinical syndromes of damage of lymphoid, muscle and joints, digestive systems, circulatory system, skin, the development of congenital immunodeficiency, in particular, the known immunodeficiency associated with EBV – Duncan syndrome. EBV infection often develops as opportunistic infections against the decrease in activity of the immune system, with the formation of acquired immune deficiency - D84.8, during the treatment with corticosteroids, cytotoxic and monoclonal drugs [3-5].

Therefore, a hard study of the characteristics of clinical course of this disease is important for doctors of different specialties - infectiologists, hematologists, oncologists, rheumatologists, immunologists, neurologists and others. Today, there are two main approaches to the treatment of viral infections: the use of antiviral drugs and immunotherapy. Principles of treatment of EBV infection are developed much less than treatment, for instance, the treatment of herpes infection caused by the herpes simplex of 1 and 2 types. There are no effective antiviral drugs for EBV infection not only in Ukraine but also worldwide. Acyclovir can be used, but in very high doses (up to 5 g per day),or ganciclovir (Cymevene), foscarnet, which have a large number of side effects and are expensive to treat the infection, especially of the nervous system. On the basis of the abovementioned data, the development of new drugs with antiviral and immunoregulatory activity for the treatment of EBV infection is extremely important today. The combination of antiviral and regulatory actions on the immune response in these conditions is a promising trend in drug therapy of virus infections. Proteflazid is just exactly this type of drug.

Proteflazid (by Ecopharm (Ukraine) manufacturer) is a liquid alcohol extract which is obtained from wild cereal plants Deschampsia caespitosa L. and Calamagrostis epigeios L. The main active ingredient of Proteflazid is flavonoids. One drop of extract contains 2 mg of active substance - active flavonoids. Antiviral activity of Proteflazid is based on the fact that the drug inhibits enzyme thymidine kinase and DNA polymerase in virus infected cells that inhibits or completely blocks replication of viral proteins and, consequently, prevents viral replication. The peculiarity of the drug is its effect on the immune response: increased cytotoxic activity of natural killer cells, promotion of the synthesis of endogenous interferon (α-IFN), and activation of phagocytic system. In addition, it has apoptosis modulating effect on the cells. Proteflazid enhances detoxification function of the liver and kidneys. The drug is available in vials and is used internally and externally, is absorbed in the stomach and intestines, distributed mainly in virus-infected cells, and only a small part of the drug is decomposed during the initial passage through liver. [6-8,10,11]

Inclusion of Proteflazid in the scheme of treatment of viral infections is based on data on its impact on the systemic and local immunity in viral and bacterial-viral diseases, as well as on its antiviral effect. This drug meets the existing requirements regarding cancerigenic and teratogenic safety and refers to 4^{th} criteria of toxicity (low toxic substances) [10, 11].This medicinal agent is easy to use, well tolerated, inexpensive, compare to other antiviral drugs. Its effectiveness in the treatment of herpes infection in children [9], recurrent genital herpes [12, 13, 17]viral hepatitis is proved [14, 15]. In the literature we met a few reports of its effectiveness in chronic EBV infection, and its results are conflicting [16,18].

The aim of study was to examine the effectiveness of Proteflazid impact on the clinical course, immunological and virological markers in patients with chronic EBV infection in the stage of reactivation.

Materials and methods.

25 patients (12 men, 13 women aged 19-44 years) who were diagnosed with chronic EBV infection in the stage of reactivation basing on medical history, clinical outcomes, instrumental, immunological and laboratory testing, were under our monitoring. To evaluate the clinical manifestations of disease we carried out a comprehensive assessment of symptoms and syndromes specific to the reactivation of chronic EBV-infection such as: fever, lymphadenopathy, sore and scratchy throat, redness of the mucous throat, myalgia, arthralgia, insomnia, mood swings, skin rashes and so on. The degree of each of these symptoms were rating from 0 (no or normal) to 3 (significant manifestations).

Specific molecular genetic studies to identify EBV DNA were conducted in all patients. Patients whose DNA of virus was not detected in at least one of the biological matrix (blood, saliva, mucous membrane scraping of posterior pharyngeal wall) were not taking part in study. The presence of reactivation of EBV infection in patients was confirmed by the discovery of high levels of specific IgG antibodies to nuclear ENBA-EBV and capsid VCA-EBV antigens.

The assessment of immune system of the patients was conducted by the following methods: the determination of the absolute number of all components of leukogram in venous blood, the number of main populations and subpopulations of lymphocytes using monoclonal antibodies («Becton Dicksnson»,USA), absorbance of neutrophils and monocytes relatively E.Coli-FITC (phagocytic index) using «Opregen» (Germany)reagents on FACSCalibur flow cytofluorometer (USA), the level of transforming growth factor - b (TGF-b) in serum by immunoenzyme method (FACSCAN, Austria) with test systems (UBS, USA).

All study were carried out before and after the drug administrations in patients (before the prescription of Proteflazid and 2 months after the prolonged treatment course). Proteflazid was administrated by patients according to the following prolonged scheme: the first two days - 5 drops, 3 times a day; 3-4th day - 8 drops, 3 times a day; 5thand for the next two months - 10 drops, 3 times a day. The drug was recommended for administration after meal. In the case of lesions on the skin and mucous membrane, the applications of Proteflazid solutions (on the basis of 1 part of drug and 7 parts of saline) were used 3 times a day, for 2 weeks. Throughout the study period, patients have not taken immunotropic and other antiviral drugs.

Statistical analysis.

An electronic database was created based on the obtained results using Microsoft Excel 2000 programs. The statistical processing was carried out using the Statistica for Windows 5,0 software package. The checking of correctness of sampling results distribution was carried out using Shapiro-Wilk test. The Student's t-test was used in case of distribution accuracy comparing two groups. The comparative analysis was carried out by Mann–Whitney U test in the absence of the normal distribution of samples. Assessment of the dynamics of indicators in the middle of the group was conducted using a paired t-test in case of normal distribution of test samples; Wilcoxon signed-rank test was used in the absence of normal distribution. The value of $P < 0.05$ were considered as probable.

Results and discussion.

All patients were in outpatient treatment at the Western-Ukrainian Center for Clinical Immunology and Allergology in 2007-2008. Almost half of patients (52%) were under the age of 30 years, and in most cases they were men (62%). The duration of illness ranged from 1 -29 months and in average was 8.3 months. Patients were directed to consultation of medical immunologists, family doctors, internists, neurologists or went to a doctor by themselves.

An objective examination of the patients (body temperature determination, examination of the skin, mucous membranes, conjunctiva, palpation and evaluation of lymph nodes, spleen, liver), evaluation of subjective complaints (pain in joints and muscles, the heart, throat irritation and sore throat, irritability, sleep disruption, general weakness, fatigue), the general clinical examination of patients with assessments of other organs and systems using palpation, auscultation, instrumental methods and so on, were conducted throughout the study. The changes of the lungs and heart in all patients were not found during clinical examination; enlargement of the liver and spleen are not recorded.

The obtained data about complaints of patients and objective evaluation of the results of clinical markers in patients before and after treatment are shown in Table 1.

Before the treatment, all patients complained about sore and throat irritation, general weakness, increased fatigue; hyperemia of the mucosal in throat was registered in these patients on examination as it is shown in Table 1.Enlarged lymph nodes were palpated in 22 (88%) of patients - submandibular (13 patients) and cervical (9 patients).Lymph nodes were slightly painful, moving, and have 1,5-3,0 cm in diameter. Long-lasting subfebrility was registered in 20 (80%) of patients. In addition, 18 (72%) of patients complained about myalgia, 4 (16%) - about arthralgia; 7 (28%) – about frequent mood swings and irritability, intolerance towards others, conflict situation at home and at work. Skin changes were registered in 6 (24%) patients during examination, five of them suffered from no significant maculopapular eruptions on the face and hands, and one patient complained about micropustular eruptions localized on the skin of the anterior chest wall.

Table 1

Dynamics of the main complaints of patients and clinical manifestations of the disease during treatment

Complaints, clinical symptoms	**Before treatment**		**After treatment**	
	Number of patients	**%**	**Number of patients**	**%**
fever	20	80	2	8
lymphadenopathy	22	88	2	8
sore throat and throat irritation	25	100	2	8
hyperemia of the mucosal in throat	25	100	2	8
mood swings and irritability	7	28	2	8
myalgia	18	72	-	-
arthralgia	4	16	-	-
sleep disruption	8	32	1	4
cutaneous eruption	6	24	-	-
general weakness	25	100	4	16

In addition, two patients were diagnosed with uveitis and conjunctivitis. Repeated clinical assessment of patients was carried out on 7-10 days after prolonged (2 months) course with Proteflazid. Results of the analysis showed that the overall condition of 20 (80%) of patients improved significantly, fever, myalgia and arthralgia, sore throat and throat irritation disappeared, size of lymph nodes returned to normal, the palpation were painless, mood improved, sleep became normal, weakness and a feeling of fatigue decreased significantly or disappeared. Patients with cutaneous eruption were administrated the applications of diluted Proteflazid (against its enteral acceptance), which contributed to the rapid regression of cutaneous manifestations. Three (12%) patients maintained weakness, sleep disruptions and fatigue, the severity of which is determined by 1 point of a scale (with 3-grade assessment). Two (8%) patients, against the above mentioned symptoms retained lymphadenopathy, cervical lymph nodes, low-grade fever that does not exceed 37,2°C, slight hyperemia of the mucosal in throat.

Thus, based on the evaluation of the objective (on the part of doctor), subjective (on the part of patient) data and clinical examination it is fair to say that the use of Proteflazid contributes to a significant improvement of general condition of the patient, promotes regression of the disease and have a positive effect on the mood of the patient, normalizing sleep and adequacy of behavior. Side effects of abovementioned drug administration were not found. Clinical efficacy with positive effect has been established in 80% of patients under observation.

Reactivation of chronic EBV-infection was verified by determining the DNA EBV of patients before treatment: in blood - in seven (28%) patients, in saliva and blood - in eight (32%) patients, in mucous membrane scraping of posterior pharyngeal wall - in ten (40%) patients; in general, DNA-positive patients with EBV were examined.

Molecular genetic studies by PCR method to detect DNA virus in the blood, saliva and mucous membrane scraping of posterior pharyngeal wall were carried out to determine the antiviral properties of Proteflazid in all patients after 2 months of prolonged treatment. The analysis of the obtained results showed that DNA virus was registered in only two (8%) patients (Fig. 1).

The analysis of population and subpopulation of blood lymphocytes in patients, who participated in the study, was carried out. The determination in absolute and relative numbers of different types of lymphocytes (CD3 +, CD4 +, CD4/CD25+, CD8+, CD16+56+,CD19+) was made during treatment with monoclonal antibodies. The results of the study of cell lymphocytes listed in Table 2. It is known that reducing the number and functional activity of immune cells can be acquired through the action of various harmful factors, including virus persistence. The major symptoms of acquired immunodeficiency (D84.8), which often accompanies EBV infection, is the reducing of anti-infectious and antiviral immunity, of systemic character.

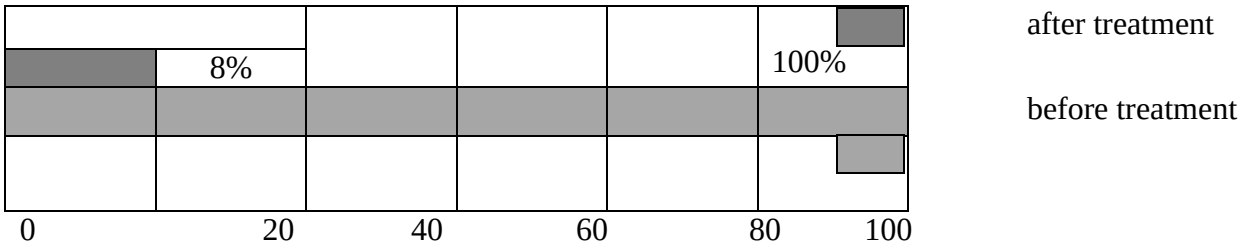

Fig. 1.The frequency of EBV DNA determination in patients with chronic EBV infection reactivation stage before and after treatment with Proteflazid.

Due to the fact that the studied drug is a stimulant of lymphocytic cellular level of antiviral protection of the body, it was important to study its impact, actually, on the indicators of the immune system of patients before and after treatment. The studies of the dynamics of lymphocytic indicators of immune system are presented as relative as well as absolute numbers and that gives an opportunity to examine the impact of Proteflazid on them. Therefore, we conducted a study of numbers of the main populations and subpopulations of lymphocytes in the patients before and after treatment. Before treatment patients had probable($P < 0.05$) decrease in the absolute number of lymphocytes, mainly due to the downward trend of decrease in the absolute number of T-lymphocytes (CD3+) and T-helper cells. Number of cytotoxic T-lymphocytes (CD8 +) in patients before treatment was significantly lower than absolute numbers ($P < 0.05$)in healthy persons, confirming the reduction of high specific lymphocytic cellular antiviral care in patients. Number of CD16*+56* -lymphocytes in 14 (56%) patients was higher than in healthy individuals, and in 11 (44%) patients - were in the normal range and the average was 14,70±1,47%/0,33±0,06g/l, that significantly differed from similar markers in healthy individuals as an absolute ($P < 0.001$) and relative terms ($P < 0.05$).

Table 1

Population and subpopulations structure of lymphocytes in patients with chronic EBV infection in reactivation stage (M±m)

Markers		Healthy (n=20)	Such before treatment (n=25)	Sick after treatment (n=25)
Lymphocytes		2,13±0,62	1,50 + 0,29*	1,97 ±0,27
CD3+	%	65,91±1,41	69,4±3,62	72,41±4,66
	g/l	1 ,42±0,37	1,04±0,09	1 ,43±0,11^
CD4+	%	40,80±1,51	40,86±4,08	41,28 ±5,2 8
	g/l	0,58±0,08	0,44±0,05	0,58±0,07^
CD4+/25+	%	10,70±1,43	17,64±2,72*	9,70± 1 ,45^
	g/l	0,06±0,003	0,08±0,002*	0,05±0,003^
CD8+	%	25,40±3,28	23,82±1,12	26,0±1,87^
	g/l	0,50±0,19	0,23±0,06*	0,37±0,03*^
CD16+ + 56+	%	10,80±1,18	14,70±1,47*	10,57±1,54^
	g/l	0,22 + 0,04	0,33±0,05*	0,21*0,05^
CD19+	%	12,11 + 1,96	11,23±1,33	1 2,71 ±1,19
	g/l	0,27 + 0,04	0,18 + 0,03*	0,25±0,02

Increasing of NK cells against a background of active EBV replication probably indicates quantitative compensatory response of the immune system to enhancement of the formation of antiviral protection, but typically of the functional failure of these cells, primarily associated with the synthesis of interferon, which are known to have powerful antiviral activity. Such long-lasting situation in the body creates conditions for further persistent viral infection and development of immunoproliferative processes with the risk of lymphocytic leukemia.

Stable number of NK cells with the strengthening of their functional state is a physiological state for the body under conditions of viral infection [4]. Number of lymphocytes of suppressive regulatory subpopulation (CD4+/CD25+) in patients before treatment was significantly higher than in healthy individuals both in absolute (0,08 ± 0,00 g/l, P <0.002), and in relative (17,64±2.72%, P<0.01) values, which also indicates the presence of suppressive effects of these cells on cell antiviral defense of cellular component of immune system that can contributes to chronic process, development of various complications, primarily neurological and rheumatologic.

Thus, the initial indicators of the immune system in patients with chronic infection EBV in reactivation stage indicated for the acquired immunodeficiency (D84.8) for quantitative functional lymphocytic type that may be attendant diagnosis, for instance in patients with rheumatologic or neurological diseases.

Two months after the prolonged course of Proteflazid we observed an increase in the absolute number of lymphocytes without significant difference (P> 0.05).

During this period, the number of T-lymphocytes (CD3+) and T-helper cells (CD4+) had a clear tendency to normalization with the significant difference in absolute numbers after treatment (CD3+- lymphocytes: before treatment - 1,04±0,09g/l, after treatment -1,43±0,11g/l, P <0.01; CD4+ - lymphocytes: before treatment - 0,44±0.05g/l, after treatment - 0,58±0.07 g/l, P <0.05).The positive impact of Proteflazid regarding intensification of killing ability of lymphocytes is well illustrated by probable increase in the number of T-cytotoxic lymphocytes (CD8+ -lymphocytes: before treatment - 23,82+1,12% / 0,23 ± 0,06g/l, after treatment - 26.0 ± 1,87% / 0,37 ± 0,03 g/l, P <0.05).

Possible decline of relative and absolute numbers of NK-cells in patients after treatment (CD16+ +56+ -lymphocytes: before treatment - 14.70+1 47% / 0,33 ± 0,06 g/l, after treatment -

10,57±1,54% / 0,21±0.05 g/l, P <0.05) can indirectly indicate the stabilization of functional capacity of NK-cells regarding the synthesis of interferon (INF-α, β-INF).

Another proof of the positive impact of Proteflazid on cellular antiviral defense is a possible decline of absolute and relative number of subpopulation of suppressive regulatory cells (CD4+ / CD25+: before treatment - 17,64 ± 2,72% / 0,08 ± 0,002 g/l, after treatment - 9,70±1,45% / 0, 05±0,003 g/l, P <0.05).

Thus, the Proteflazid administration in patients with chronic EBV infection in reactivation stage increases the weight of killing subpopulation of lymphocytes at the expense of T-cytotoxic lymphocytes, functional ability of NK cell regarding synthesis of interferons, reduces the suppressive activity of regulatory CD4+/CD25 + -lymphocytes activating the same acquired and congenital antiviral supervision. Along the growing influence of humoral suppressor mechanisms, accompanied by increasing levels of serum TGF-b in comparison with healthy (58,4+6,7ng/ml –in patients, 32.3+4, 7 ng/ml – in healthy persons; P <0.01) is registered in studied patients before treatment.

Table 3

Absorbing capacity of neutrophils and monocytes in patients before and after treatment with Proteflazid and in healthy persons (M±m)

Phagocytic indicator	Healthy persons (n=20	Patients before treatment (n=25)	Patients after treatment (n=25)
Phagocytic indicator of neutrophils %	93,30±6,89	80,20±7,51	89,48±5,39
g/l	2,81± 0,26	2,41±0,31	2,67±0,28
Phagocytic indicator of monocytes %	80,30±3,25	42,52±2,51*	75,48±5,39^
g/l	0,27±0,03	0,14±0,02*	0,20±0,03^

The reducing trend of the growth factor, but without the probability (40,5+6,8ng ml, P> 0.05) is observed in patients after two months of treatment. These changes in regular suppressor mechanisms of the immune response may indicate a strengthening of compensatory mechanisms of the immune system under Proteflazid administration that probably prevents the development of autoimmune and immunoproliferative processes in patients with prolonged chronic EBV-infection.

To determine the effect of Proteflazid on the activity of phagocytosis we investigated the absorption ability of monocytes and neutrophils (phagocytic index) in patients before and after treatment (Table 3). As seen from the presented data in Table 3, we observed a probable decline in the ability of monocytes to absorb antigensin relative (P <0.001) and absolute (P <0.05) numbers in patients before treatment (before treatment - 42,52 ± 2,51% / 0,14 ±0,02 g/l, after treatment - 75,48 ±5,39% / 0,20 ± 0,03 g/l, respectively). It is known that Proteflazid, increasing the synthesis of INF, enhances the phagocytic activity of these cells, contributes the transference of incomplete phagocytosis to complete, which in turn enhances antigen presentation process (virus - in our case) to T-cytotoxic lymphocytes that possess specific killing ability.

Thus, having a set of properties on the influence of both specific and innate antiviral factors of the immune system, and having immunomodulating properties, the Proteflazid have shown its effectiveness in EBV infection, which currently belongs to the herpes infection; the treatment of EBV infection with traditional antiviral drugs is still problematic.

CONCLUSIONS

1. Proteflazid has significant antiviral properties regarding Epstein-Barr virus, which is confirmed by specific molecular genetic studies aimed at identifying of DNA virus in patients' biomaterials.
2. Prolonged (two months) treatment course with Proteflazid at a dose of 10 drops three times daily is effective for the treatment of chronic EBV infections in the reactivation stage in the form of monotherapy. Its administration leads to more rapid clinical regression of pathological process.
3. Proteflazid administration in patients with EBV-infection promoted an increase in the number of lymphocytes, especially T-cytotoxic lymphocytes (CD8+), stabilized NK cells functional activity and reduced the suppressor activity of regulatory lymphocytesCD4+/+CD25, thus cellular non-specific and specific antiviral supervision reinforced.
4.Proteflazid increased the absorb capacity of blood mononuclear phagocytes, and therefore presenting ability of these cells to active killing ability of T cytotoxic lymphocytes with increased elimination of virus from body is also strengthened.
5.Proteflazid not cause adverse reactions and toxic manifestations of subjective, clinical and laboratory character and well tolerated by patients.

REFERENCES

1. Shulzhenko A.E. A human and herpes // Physiology and pathology of immune system -2004.-№2-P.45-48
2.Dyudyun A.D., Polyon N.N., Polishko T.N. et al . Herpesvirus infections: modern aspects of diagnosis and treatment clinics // Clinical immunology. Allergology, Infectology.-2007.-№2 (07) .- P.55-58
3.Malashenkova I.K., Didkovskiy N.A., Sarsaniya Zh.Sh. et al. The clinical forms of chronic Epstein-Barr virus infection: questions of diagnosis and treatment // News of medicine and pharmacy. – 2007- №13 (219) .- Ar.20-21.
4.Hodak L.A., Knizhenko O.V., Zakharchenko N.M. Herpesvirus disease // International Medical journal.-2003.-№3.-P. 103-106.
5.Bondarev L.S., Zaplotnaya A.A. Herpesvirus infection - a modern view on the problem (first message) // Annals of acute and regenerative medicine. – 2006 -T.7, №2.-P.277-280.
6. Cytomegalovirus infection in immunocompetent adult patients: clinic, diagnosis and intensive care (guidance) .- Kyiv.-2005.-14p
7. The use of Proteflazid drug in the treatment of viral hepatitis (recommendation for infectiologists, gastroenterologists, therapeutics) - Kyiv.- 2004-14p.
8. Clinical use of the drug Proteflazid in the herpes virus infection (recommendations for infectiologists, dermatologists, neurologists) - Kyiv.-2004-20p.
9. Brezhneva Y.V. The effectiveness of Proteflazid in the complex treatment of diseases caused by the herpes simplex virus in children // Immunology and Allergology. - 2002. - № 3. - P. 60.
10. Proteflazid. Information materials on the properties and methods of application // SMC "Ecopharm". - Kyiv. - 2002. - 68 p.
11.Proteflazid. Information and educational materials for practitioners // SMC "Ecopharm". - Kyiv. - 2004. - 40 p.
12. Fedotov V.P. et al. Application of Proteflazid in the treatment of patients with recurrent genital herpes // Dermatology, cosmetology, sexual pathology. - 2002. - № 3-4. - P. 204-206.
13. Garmash L.L. et al. Proteflazid in the treatment of genital herpes // Immunology and Allergology. - 2002. - №3. - P. 64-65.
14. Savelyev V.G., Bondarev V.V. Proteflazid efficacy in patients with viral hepatitis // Chemotherapy and immunotherapy of infectious diseases. Proceedings of the conference and plenum of Association of infectiologists of Ukraine. - Ternopil. 2005. - C. - 85-86.

15. Korchynskyy M.Ch. Some possibilities of applicability of Proteflazid in the treatment of patients with chronic hepatitis C // Chemotherapy and immunotherapy infectious diseases. Proceedings of the conference and plenum of Association of infectiologists of Ukraine. Infectious diseases, Ternopil. - 2005. - P. 50-53.
16. Shulyak V.I., Filyurina O.M., Anikina O.V. Clinical and laboratory markers of standard and immunomodulating therapy in patients with infectious mononucleosis // Chemotherapy and immunotherapy of infectious diseases. Proceedings of the conference and plenum of Association of infectiologists of Ukraine. Infectious diseases, Ternopil. - 2005. - P. 105-106.

Abstract

EFFICIENCY OF MONTHERAPY WITH PROTEFLAZID IN TREATMENT OF PATIENTS WITH CHRONIC EBV-VIRAL INFECTION IN THE STAGE OF REACTIVATION

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The paper presents results of investigation of Ukrainian medicine Proteflazid for the treatment of patients with chronic Epstein-Barr viral infection in the stage of reactivation in the period of virus replicative activity (DNA+). Prolonged use of Proteflazid (about 2 months) leads to sooner regression of clinical signs of the disease and improvement of general condition of patients. It was proved that the medicine has significant antiviral properties, what was demonstrated by specific molecular-genetic study with the use of the method of polymerase chain reaction. Complex immunologic investigations let us make conclusions, that Proteflazid leads to increase of the number of T-cytotoxic lymphocytes (CD8+), stabilization of functional activity of NK-cells, decrease of activity of suppressive subpopulation of regulatoryCD4+/CD25+-lymphocytes, increase of engrossing and presenting properties of phagocytes. Complex of these factors increases cell specific and non-specific antiviral supervision.