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CONTENT

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VETERINARY SCIENCES

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CLINICAL AND LABORATORY CHARACTERISTICS OF INFECTIOUS MONONUCLEOSIS CAUSED BY EPSTEIN – BARR, EFFECTIVENESS OF TREATMENT METHODS

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Abstract
The efficacy of combined use of Valacyclovir and Nuclex in complex therapy of patients with infectious mononucleosis caused by Epstein – Barr virus (EBV) was studied. The use of such therapy was found to promotes regression of clinical symptoms, contribute to normalization of indices of clinical blood tests and lead to a decrease of the number of EVB's DNA copies in the blood serum or complete elimination of virus.

Keywords: infectious mononucleosis. Epstein-Barr virus, clinical picture. diagnosis, therapy

Epstein-Barr virus is one of the most common human viruses in the world. Actuality of study of infectious mononucleosis is conditioned by high infected of population by the Epstein–Barr virus (EBV), specific virus affinity to the immunocompetent cells, lifelong virus persistence in an organism and often latent process. The EBV is representative of oncogenic DNA viruses, diameter of capsid is 120-150 nm, surrounded by tunica |1, 2|. There are groups of immunogenic proteins.

Infectious mononucleosis is caused by a lymphotropic virus, which capable of replicating in B-lymphocytes. It has a moderate cytopathogenic effect to cells. Due to the possibility of embedding viral DNA into the human cell genome, a long-term persistence of the virus in the body arises. The virus can persist for a long time in the host cells as a latent infection. The active proliferation of the virus in organs, which containing lymphoid tissue, leads to changes in all parts of the immune system. Immune disorders in this disease can be cause of long-term disease probably |1, 4|. Such selective damage to blood cells is caused the possibility of lymphoproliferative diseases with active replication of the virus. EBV is known to be an etiological factor in diseases such as nasopharyngeal carcinoma, Burkitt's lymphoma, T-cells lymphoma and Hodgkin's disease. In addition, infectious mononucleosis is an AIDS-related disease.

Infectious mononucleosis is a clinical entity characterized by sore throat, cervical lymph node enlargement, fatigue, and fever most often seen in adolescents and young adults and lasting several weeks [3]. The virus enters lymphogenously the regional lymph nodes, contributing to their hyperplasia. In the future virusemia develops with the spread of the pathogen in the body, which leads to a reaction from the lymphoid tissue. The development of an infectious-allergic reaction and the formation of an immune response corresponds to the healing period. This stagnation is observed in acute infection. Natural killers, or NK-cells and T-lymphocytes CD4+, CD8+ control the proliferation of B-lymphocytes infected with EBV. In acute infection, cytotoxic lymphocytes are directed to proteins that are formed during virus replication, resulting in lysis of the affected lymphocytes is developing [4, 5]. The acute phase of the disease is observed after the first contact of the patient with a virus characterized by the development of infectious mononucleosis. Children and young people under 35 years old get more illnesses.

The key to success in the treatment of patients is timely diagnosis, proper and strictly individual approach to aetiotropic and pathogenetic treatment, timely hospitalization of patients with severe forms of infectious mononucleosis. Today there is controversy regarding the specific treatment of infectious mononucleosis caused by EBV, which would give the opportunity to eliminate the persistent virus from the human body. Treatment in most cases remains pathogenetic and symptomatic with application of detoxification, desensitizing, anti-inflammatory medications, corticosteroids, and so forth [5]. As aetiotropic treatment using some antivirals (acyclovir, valacyclovir), which in most cases, EBV is stable. These medications lead to improve the condition, temporary reduction of virus isolation from saliva, however there is no significant difference between the viral load of the blood in patients, that receive antiviral therapy compared with those who don't receive it; there may be relapses of the disease [6]. In the literature, there are data on the possibility of increasing the efficiency of etiotropic therapy by applying combat two drugs with different mechanism of antiviral effect. It is known that medications of ribonucleic acids are widely used in clinical practice as antiviral agents. Proven their efficacy in the treatment of acute respiratory viral infections and HCV-infection [7]. One of the most effective preparations of this series is nuclex, which also has anti-inflammatory and immunomodulatory activity. Nuclex has a stabilizing effect of membrane, stimulates cell metabolism, enhances the synthesis of endogenous nucleic acids, specific proteins and enzymes, increases the mitotic activity of bone marrow cells. The aim of this work was to study the efficiency of complex therapy in patients with infectious mononucleosis caused by EBV.

Materials and methods of research. Research on the work topic was conducted at the Department of Infectious Diseases of Kharkiv National Medical University. A total of 45 patients with infectious mononucleosis (26 men and 19 women) who were hospitalized at the Regional Clinical Hospital in 2018-2019 years were surveyed. The vast majority of patients with infectious mononucleosis were young people aged from 18 to 25, of whom 59,7 % were students.

The etiology was decoded according to a laboratory algorithm that included the detection of IgG antibodies to early antigen EBV (EAG), IgM antibodies to capsid antigen EBV (VCA), IgG antibodies to capsid antigen EBV (VCAE), IgG antibodies to nuclear antigen EBV (EBNA) by enzyme-linked immunosorbent assay (ELISA) on EUROIMMUN Analyzer I using the EUROIMMUN test system (Germany). In all patients before and after treatment (day 21 from the start of therapy), viral load in serum was quantified by real-time by quantitative polymerase chain reaction (PCR) analysis on amplifier analyzer «Tertzik» with fluorescence detector «Gin» (DNA Technology, Russia). To exclude viral hepatitis and HIV-infection, all patients were screened for the appropriate markers: anti-HAV IgM, HBsA, anti-HCV IgG, and HIV antibodies, which were determined by ELISA on a Cobas analyzer using a Roche Diagnostics test system (Switzerland) after signing a patient agreement.

Depending on the therapy, examined patients were divided into two groups, which are related by age, sex, total duration of the disease. Group I included 16 patients who were prescribed traditional pathogenetic therapy (reosorbylact, saline, sorbents, desensitizing and anti-inflammatory non-steroidal medications) and valaciclovir 500 mg twice daily for 14 days. Patients of group II (15 patients) received in addition to pathogenetic therapy, valaciclovir 500 mg 2 times a day for 14 days and nuclex 2 tablets (500 mg) 2 times a day for 21 days. Statistical analysis of the data was performed by methods of variational statistics using the Student's t-test.

Results and discussion. Patients complained of fever from subfebrile to high numbers (91 %), chills were observed in 11 % of patients, sweating in 18 %, muscle pain – in 20 %, aches and joint pain in 24 %. General weakness and malaise (77 %), headache (45 %), decreased appetite (37 %) were quite often seen. Manifestations of tonsillitis were determined in the majority of patients (59 %), the patients from the first days of the disease complained of a sore and scratchy throat. 25 % of patients was determined by nasal congestion. Visible changes on the tonsils were observed during an objective examination in 57 % of patients starting from 3-6-th day. In 74 % of patients had hyperemia and the "grain" posterior pharyngeal wall, in 10 % – moderate jaundice of the skin and sclera. Lymphadenopathy was generalized as one of the leading syndromes during the infectious mononucleosis. Most (85 %) increased back-, anterior cervicale nodes and maxillofacial lymph nodes. Ultrasound of the abdomen revealed enlarged liver and spleen in 100 % of patients. Moderate severity infectious mononucleosis diagnosis was set basing on clinical data, results of laboratory and instrumental examination methods according to generally accepted clinical practice criterias. Patients' general blood analysis was determined by moderate leukocytosis, normocytic with lymphocytosis, atypical mononuclear cells >10 %.

Observation and examination in dynamics showed that in patients of both groups, in most cases, the general condition was considerably improved: weakness and sickness disappeared, sleep and appetite were improved. jaundice was decreased, body temperature was normalized. syndrome of nasopharyngeal tonsillitis was less prolonged, as a common syndrome of systemic response too. Observation revealed a gradual decrease of size of lymph nodes. size of liver and spleen. The comparative analysis determined that the disappearance of the aforementioned clinical symptoms occurred earlier for patients who received valacyclovir + nuclex than for patients of I group. During therapy there was almost complete elimination of clinical symptoms of the disease in patients who received valacyclovir + nuclex.

In the treatment of patients both I and II groups, the number of lymphocytes was decreased, but the degree of decline was most significant in patients of group II (39,5 % compared to initial level). In the treatment with the use of pathogenetic therapy and valacyclovir number of atypical mononuclear cells tended to decrease, and with the additional appointment nuclex this process occurred most rapidly – a decrease of 59,5 %, whereas in the comparison group — at 43,57 %. Thus, an additional purpose of nuclex in complex therapy with valacyclovir for patients with average severity infectious mononucleosis diagnosis accelerates the normalization of the haemogram.

At the beginning of therapy, the groups were correlated in terms of viral load. Evaluation of viral load indicates that patients in group I showed only a tendency to its decrease, while patients in group II experienced a decrease in viral load by an average of 100 times, i. e. by 2 log ($P < 0,05$). Obtained results indicate a much higher efficeincy of complex therapy with valacyclovir and nuclex, which may be due to the antiviral activity of the nuclex drug.

Conclusion.

Thus, evaluation of the effectiveness of the use of valacyclovir and nuclex in the complex therapy of patients with infectious mononucleosis caused by Epstein-Barr virus. indicates a more significant regression of clinical symptoms. significantly more pronounced positive impact on the indicators of clinical blood analysis and the number of copies of EBV DNA in blood serum than in the comparison group. Obtained results allowed to substantiate the use of complex therapy of valacyclovir and nuclex in patients with infectious mononucleosis caused by EBV.

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