New Approaches to the Therapy of Erythema Multiforme Induced by Herpes Virus

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ABSTRACT

This report presents description of the clinical characteristics of 61 patients with diagnosis herpesinduced erythema multiforme and the results of the complex therapy with use of antiviral preparations, immunomodulator gosalidone, interferon inductor and hyposensibilizing therapy.

The results of the observations showed that after the complex treatment the frequency of recurrences decreased, on the average, two-times, recurrence duration shortened, on the average to 2-4 days, and remission longevity increased, on the average, 1,8-2 times. The use of the developed in Uzbekistan native inductor of interferon gozalidone in the complex therapy herpesinduced erythema multiforme showed marked clinical effect, that allowed increase duration of the clinical remission and shortened longevity of the recurrences. Our observations indicated about perspectives in relation to use of gozalidon in the therapy and prevention of the recurrences in the patients with herpesinduced erythema multiforme.

Keywords: Herpes Simplex Virus, herpes-induced erythema multiforme, therapy, interferon inductor, gosalidone.

How to Cite

Ismailova Guli Amindjanovna & Tagarov Asan. (2023). New approaches to the therapy of erythema multiforme induced by herpes virus. *Eurasian Medical Research Periodical.*

Introduction. Multiforme exudative erythema (MEE) is a common polyetiological disease of the skin and mucous membranes, with an acute, often relapsing course. The disease is found predominantly in young and middle-aged persons, it also occurs in children older than 5 years [1,2,11]. The etiological factors of MEE are varied. However, the causes of MEE development remain unknown in most cases. There is a trigger factor that "turns on" the mechanism of the hypersensitivity immune reaction in patients with MEE. These factors are divided into two groups: first are allergens, most often of a medicinal, food nature, causing a toxic-allergic type of dermatosis, and second are infections - viruses, bacteria, protozoa, which cause the infectious-allergic form of MEE. In this regard, the idiopathic or

infectious-allergic form of MEE is distinguished, which is evidenced by a chronic relapsing course, the seasonal factor of rashes, the presence of a prodromal period, and symptomatic, or toxic-allergic, which is most often associated with taking medications [5,14,15]. Herpes simplex virus (HSV) is one of the most common causes of manifestation of idiopathic MEE [6,11,13,17,18]. Possibly the virus plays the role of a trigger factor in the development of MEE, and the interaction of the virus with peripheral blood mononuclear cells and endothelial cells of skin vessels may be considered as a potential model for the pathogenesis of herpes-induced MEE. In addition, the positive dynamics of the clinical manifestations of MEE as a result of treatment of patients with antiviral drugs confirms the relationship of this disease with HSV [2,7,13].

To date, the ambiguity of the pathogenesis of MEE, the increase in its recurrence, the lack of effectiveness of the available methods of treatment and prevention, dictate the need to study the characteristics of various clinical forms of this disease and the factors that affect the clinical manifestations and outcome of the disease. Management of herpes induced MEE is carried out according to the therapy regimens for the infectious-allergic form of MEE and it includes the use of etiological drugs (synthetic nucleosides) and symptomatic treatment. It is worth noting, that the treatment of the disease should include both stopping the exacerbation of the infection and suppressive therapy aimed at preventing virus replication [2,9,12].

According to various sources, the approach to the treatment of herpes induced erythema multiforme is mainly in the episodic or continuous use of synthetic nucleosides. The main method of preventing erythema multiforme caused by HSV is the continuous use of acyclovir [8,11,15].

M.A. Samgin and A.A. Haldin, in 2002 [7,9] used a two-stage scheme for the treatment of the disease. The first stage was to stop exacerbations of MEE, the second - to prevent the recurrence of herpes simplex, which is the trigger mechanism for this type of exudative multiforme erythema. Famvir or Valtrex was used for management of exacerbation. At the second stage, preventing relapses, an interferon inducer, ridostin (ds-RNA lysate of the killer yeast Candida cerevisiae), was used. Observation of patients after the end of the proposed two-stage course of therapy (in terms of 1 to 1.5 years) showed that the vast majority of patients did not experience both manifestations of herpes simplex and exacerbation of MEE, and as a result herpes relapses proceeded in a much milder form. The effectiveness of this type of therapy speaks in favor of the possibility of using immune-targeted drugs in MEE [3,4,10,12,16].

In this regard, it seems relevant to search for new methods of immunocorrection in herpes-induced MEE, including the evaluation of the effectiveness of the domestic interferon inducer «Gozalidone».

Purpose of the study. To evaluate the results of complex therapy of patients with herpes-induced MEE with the use of antiviral drugs, an immunomodulator - an interferon inducer (gozalidone) and hyposensitizing therapy.

Material and methods. 61 patients diagnosed with herpes-induced MEE, including 27 (46.67%) men and 34 (53.33%) women aged 18 to 68 years. Most - 37 (60.6%) patients were young and middle-aged (from 18 to 44 years). The duration of the disease ranged from several months to 10 years or more, while in 15 (24.6%) patients it was up to 1 year; in 34 (55.7%) - 1-4 years; in 12 (19.7%) - more than 4 years. The duration of relapses ranged from 7 to 27 days. Patients sought medical attention on the 2nd-7th day of the recurrence of herpes induced MEE, more often in the cold months against the background of a deterioration in the general condition. All patients were examined for HSV 1, type 2 by enzyme immunoassay. Systemic diseases, drug intoxication, foci of local infection, other sexually transmitted infections, paraneoplastic processes were excluded. The complaints of the patients were weakness, malaise, fever, herpetic rashes on the skin with a moderate itching, painful rashes on the mucous

membranes of the mouth and genitals with a frequency of 3 to 10 times a year. In addition, at the beginning of the manifestation of the process, 10 patients also had a headache, 5 - gastrointestinal disorders, 8 - respiratory phenomena. From the anamnesis: 41 patients suffered from herpes simplex on the face, 20 patients – genital herpes. The patients most often noted psycho-emotional stress (22 people), hypothermia (15), menstruation (12), alcohol consumption (6) and 6 people found it difficult to answer among the factors that provoked MEE recurrences. At the same time, the development of the disease was preceded by herpetic manifestations on the face (lips, nose, chin) or genitals.

Results and discussion. It is known from the anamnesis that the recurrence of HSV has become more frequent in patients by 3 or more times over the last 1-4 years before the onset of MEE symptoms. Clinical manifestations typical for MEE in the form of edematous papules and spots from pale pink to bluish-red in color from 0.5 to 2-4 cm in diameter occurred after prodromal phenomena and the appearance of herpetic eruptions on the skin after 2-7 days. Lesions were represented by limited foci on the extremities or single disseminated or multiple grouped, rounded cocardiform elements. MEE rashes began acutely and appeared paroxysmal with an interval of several days, and were more often localized on the extensor surfaces of the extremities (dorsal surfaces of the hands and feet, forearms, lower legs, elbow, knee, ankle joints), less often on the face, neck and torso. Initially, MEE rashes appeared, as a rule, on the hands and (or) oral mucosa, then other areas of the skin were also affected, the genitals were affected in rare cases. Eruption elements on an erythematous background were represented by erosions covered with grayish films. Erosions were covered with thick brown hemorrhagic and purulent crusts on the red border of the lips. Regression of rashes in MEE happened on average within 2 weeks. It should be noted that MEE rashes were multiple and grouped in the initial period of the development of herpes simplex (especially type 1), while the development of MEE in the regression of herpes (or against the background of predominantly manifestations of HSV-1) was characterized by single, very limited elements.

We used acyclovir as an antiviral drug, and the drug gozalidone (a natural polyphenolic compound of cotton (synthesized at the Institute of Bioorganic Chemistry of the Academy of Sciences of the Republic of Uzbekistan, approved for clinical use as an interferon inductor in herpetic infections and urogenital chlamydia) for the formation of a full-fledged immune defense, as a complex treatment of patients with herpes-induced MEE. Gozalidone was used according to the scheme of 200 mg orally 3 times a day for 3 days with an interval of 3 days for 2-3 cycles, both in the acute period and in the remission phase [1,8]. The patients received basic therapy and were divided into 3 groups depending on the treatment regimen: with the use of acyclovir (21), monotherapy with gozalidone (18), combined administration of the mentioned drugs (22). The effectiveness criteria were indicators of the duration and frequency of relapses, the duration of the interrecurrent period. The following clinical features were identified in the group of patients with herpes-induced MEE who received acyclovir monotherapy (200 mg 5 times a day for 5-7 days): the duration of the relapse was 2-3 days, the duration of the interrecurrent period increased by 1.3 times. If the frequency of relapses before treatment was on average 4 times a year, after treatment it averaged 3 times a year. The duration of relapses was 4-6 days, and the duration of remission increased on average 1.6 times in patients who received gozalidone monotherapy. The frequency of relapses decreased by an average of 2 times and amounted to 1-2 times a year after complex treatment, while before treatment it averaged 3-4 times a year. The duration of relapses averaged 2-4 days, and the duration of remission increased by an average of 1.8-2 times.

Conclusions. Thus, the use of the domestic interferon inducer guanidine in the complex

therapy of herpes-induced MEE has a pronounced clinical effect, which made it possible to increase the duration of clinical remission and reduce the duration of relapses. Our observations indicate the prospects for the use of gozalidone in the treatment and prevention of relapses in patients with herpes-induced MEE.

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