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IMPROVING THE PRINCIPLES OF TREATMENT IN PATIENTS WITH ZOONOTIC LEISHMANIASIS WITH THE IMMUNOMODULATOR GEPON AND METHYLENE BLUE USING THE ALT-VOSTOK DEVICE

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Summary,

The object of the study was 102 patients with zoonotic leishmaniasis aged from 2 to 65 years. The diagnosis of zoonotic leishmaniasis was established by clinical and epidemiological data and confirmed by the results of parasitological studies.

We studied the duration of the clinical periods of zoonotic leishmaniasis against the background of complex therapy with methylene blue using the ALT-Vostok model-03 device in the control group of 51 patients and complex therapy with methylene blue using the ALT-Vostok model-03 device and the immunomodulator Gepon in the main group of 51 patients. The results of the study showed that in patients of the main group, on the background of treatment with the ALT-Vostok model-03 device using the immunomodulator Gepon, the duration of the main periods was significantly reduced than in the control group in whom only methylene blue was treated with the ALT-Vostok model-03 device.

Keywords: *leishmaniasis, methylene blue, ALT-Vostok model-03 device, immunomodulator Gepon*

概括,

该研究的对象是 102 名 2 至 65 岁的人畜共患利什曼病患者。人畜共患利什曼病的诊断是根据临床和流行病学数据确定的，并由寄生虫学研究结果证实。

我们在 51 名患者的对照组中，在使用 ALT-Vostok 03 型装置的亚甲蓝复合治疗和使用 ALT-Vostok 03 型装置的亚甲蓝复合治疗的背景下，研究了人畜共患利什曼病的临床期持续时间和免疫调节剂 Gepon 在 51 名患者的主要组中。研究结果表明，在主要组患者中，在使用免疫调节剂 Gepon 的 ALT-Vostok model-03 装置治疗的背景下，主要经期的持续时间比仅使用免疫调节剂的对照组显著缩短。亚甲蓝用 ALT-Vostok 03 型装置处理。

关键词：利什曼病，亚甲蓝，ALT-Vostok 03 型装置，免疫调节剂 Gepon

Cutaneous leishmaniasis remains relevant to this day. This has become one of the socio-problems of a number of countries. According to the World Health Organization (WHO), cutaneous leishmaniasis occurs in more than 80 countries around the world. According to the WHO, the number of patients per year is estimated from 600000 to 1000000 [1].

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The spread of cutaneous leishmaniasis is largely due to the ecological conditions of the local area located in a certain geographic region, as well as the interaction of the source with the pathogen, the carrier with the transmitted organism. This requires constant improvement of preventive and anti-epidemic measures in these areas [3].

An increased trophic immunomodulator Gepon was found in clinics in Moscow and Ukraine [4].

The effectiveness of complex treatment of postoperative wounds with local application in vitro studies evaluated the antiviral activity of Gepon on a culture of human cells infected with hepatitis C. The peptide protected human SW-13 cells from the cytopathogenic effect of the virus. The maximum antiviral effect of hepatitis was demonstrated at a concentration of 1 mg/ml of Gepon. The researchers used the antiviral agent interferon α -2a as a comparison drug. The latter turned out to be more effective as a protective agent for SW-13 cells [6].

Gepon is the ability to induce A- and B-interferons, to inhibit inflammatory cytokines-peptide information molecules of inflammatory immunity, acting on cells of the immune system. Due to this, Gepon has antiviral activity, the ability to activate local immunity and anti-inflammatory properties. The peptide enhances the production of antibodies, the concentration of CD-4 (a marker of T-helpers) and natural killer cells, improves the functionality of neutrophils and the viral load increases the body's resistance to infections caused by viruses, bacteria, fungi. Increases the synthesis of antibodies against any antigens of infectious etiology. In addition, the antiviral effect in human cells infected with the encephalomyocarditis virus, activity against hepatitis C, herpes types 1 and 2, rabies, sexually

transmitted infections, and can also be used for acute purulent postoperative infections [7]. There was a correlation between the increased production of interleukin-4 - IL-4 (increasing the production of IgE) by stimulated mononuclear leukocytes with an increase in the activity of phosphodiesterase associated with cAMP and, accordingly, with a decrease in its level [2, 5].

In vivo clinical trials on the effect of stimulating the humoral response against antigens increases CD-8 T cells, decreases blood levels of HIV-infected patients. Gepon peptide suppresses HSV-1, possesses antiviral. Gepon against rabies virus was carried out on outbred mice, which were injected with 0,01 - 0,1 mg of the drug intramuscularly. As a result, it was found that the drug protects 30-40% of mice from infection with the street rabies virus. In this case, the peptide has a dose-dependent effect protection from infection depends on the dose and the regimen of the drug. The most pronounced protection was observed when it was administered intramuscularly at a dosage of 0,1 mg [8].

The most effective methylene blue with local application of the ALT-Vostok model-03 apparatus with the use of the immunomodulator Gepon was revealed [9].

Purpose of the work:

Improvement of new methods of treatment based on clinical and immunological features of zoonotic leishmaniasis.

Objective of the work:

1. Patients of group 1 (control group). To determine the effectiveness of the use of topical 0,05% methylene blue in patients with zoonotic leishmaniasis using the ALT-Vostok model-03

apparatus in patients at early nodular, erosive and ulcerative stages.

2. Patients of group 2 (main group). To determine the effectiveness of the method of concomitant use of 0,05% methylene blue ALT Vostok model-03 and the immunomodulator Gepon in order to improve the method of treatment in the main group of patients with early nodular, erosive and ulcerative stages of zoonotic leishmaniasis.

3. Determination of the reliability of the results obtained by statistical processing.

Material and methods:

102 patients with zoonotic leishmaniasis were examined. We studied 42 patients who presented at the nodal stage, 34 during the erosion period and 26 patients at the ulcer stage. Their average age ranged from 2 to 65 years. Of these, 26 are women and 76 are men.

Patient evaluation began with the collection of anamnesis and epidemiological data. To confirm the diagnosis, the main attention was paid to the patient's complaints on the onset and course of the disease, parasitological examination, as well as the formation of nodules, erosion and ulcers on the exposed parts of the body and the surrounding infiltration.

Changes in nodules, erosions and daily observation and dynamically. Urinalysis and blood analysis were checked for ulcers; the patient was assessed when indicated.

After the initiation of photodynamic therapy and immunostimulatory therapy, a total of three parasitological examinations were performed once a week to determine the survival time of leishmaniasis in order to study their etiologic effects. To assess the results of the

study, all patients were divided into two groups according to age, sex and severity of the disease.

51 patient of the control group and 51 patients of the main group were examined, respectively. For etiologic treatment, 51 patients (control group) at the age of nodular, erosive and ulceration were treated with 0,05% methylene blue using the ALT-Vostok model-03 apparatus. To determine the effectiveness of the method of concomitant use, 51 patients were treated with 0,05% methylene blue ALT-Vostok model-03 and the immunomodulator Gepon in order to improve the method of treatment in the main group of patients at the early nodular, erosive and ulcerative stages (main group).

Statistical method:

To determine the reliability of the results and data obtained in the course of the study, the average values of the indicators— M , the average error— m , the difference in reliability— P , the criteria methods proposed by Vorobiev A.A., Ashmarin I.P., were used (1962).

The R-reliability difference was obtained from the Steward table. In the surveyed region, in the questionnaires sent out in 2017-2020, the total number of patients who sought help doctors is 102, of which 42 are in the stage of nodules (the first 3 weeks after a mosquito bite); 34 in erosion stage; 26 ulcerated 94-10 weeks after mosquito bite). The patients undergoing treatment were between the ages of 2 and 65 years. In patients in the stages of nodular, erosive and ulceration, the diagnosis was confirmed by the parasitological examination method.

50% of the examined patients (51 patients of the control group) in the nodular, erosive and ulceration period of the disease applied 0,05 % methylene blue using the ALT Vostok model-03 apparatus once a day for 15-20 minutes for 12

days. In 50 % of patients (51 main groups) at the nodular, erosive and ulceration stages 0,05 % methylene blue was applied using the ALT Vostok model-03 apparatus, once a day for 15-20 minutes for 12 days with local application of the immunomodulator Gepon.

Table 1

The results of the use of methulene blue solution in patients with zoonotic leishmaniasis through the ALT-Vostok model-03 apparatus and the effectiveness of the immunomodulator Gepon

№	Clinical stages of leishmaniasis	Duration of periods (calculated days)		P
		Duration of clinical periods of patients (control group) who beat 0,05% methylene blue using the ALT-Vostok apparatus model-03	Duration of clinical periods of patients (main group) who beat 0,05 % methylene blue ALT-Vostokmodel-03 and immunomodulator Gepon	

		n=51, M±m	n = 51, M±m	
1	Nodular period	14,6±1,06	16,4±0,41	< 0,001
2	Erosive period	11,2±0,56	10,6±2,5	> 0,05
3	Ulceration period	21,6±0,9	14,1±1,20	< 0,001
4	Scarring period	17,6±0,97	12,6±0,51	< 0,001
5	Average duration of the disease	65,0±2,9	53,7±1,88	< 0,001

Note:

In all patients of the main and control groups, the number of nodes erosion and ulcers ranged from 1 to 6.

In 51 patients in the control group, methylene blue solution was injected once a day for 7 to 15 days using the ALT-Vostok apparatus model-03, 51 patients in the maun group were injected with metylene blue solution once a day for 7 to 15 days using the ALT-Vostok apparatus model-03 with local application of the immunomodulator Gepon. It should be noted that no side effects were observed in the treatment of the main and control groups of patients who were treated locally with the ALT-Vostok apparatus model-03 and the Gepon immunomodulator.

The duration was significantly correlated with the patients of the main and control groups for evaluating the therapeutic efficacy of the local administration method using the ALT-Vostok apparatus model-03, and Gepon was an

immunomodulator of the basic clinical symptoms. In particular, the duration of the nodular stage was $14,6 \pm 1,06$ days in the main group of patients and $16,4 \pm 0,41$ days in the control group ($p < 0,001$).

The duration of the erosion stage was $10,6 \pm 2,5$ days in the main group. Patients, while in patients of the control group it was $11,2 \pm 0,56$ days ($p > 0,005$).

The duration of the ulceration period was $14,1 \pm 1,20$ days in the main group of patients, while in the control group it was $21,6 \pm 0,9$ days ($p < 0,001$).

It was found that the duration of the scarring phase was $12,6 \pm 0,51$ in the main group of patients and $17,6 \pm 0,97$ days in the control group ($p < 0,001$).

The mean duration of the disease was approximately $65,0 \pm 2,9$ days in the main group patients, $53,7 \pm 1,88$ days in the control group ($P < 0,001$). The results show that the duration of all disease in the main group of patients achieved reliable results.

R-difference in statistical significance between the value of the main and control group of patients.

Conclusion:

According to the results, a positive effect with the local application of the methylene blue with the ALT-Vostok apparatus model-03 and the immunomodulator Gepon lengthened the nodal and erosive stages of zoonotic leishmaniasis, shortened the duration of the ulceration period, the general period of morbidity.

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