Content of Proinflammatory Cytokine in Patients with Clinical Remission of Chronic Herpes Infection during Immunocorrection

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The concentrations of cytokines (interleukin-1β, interleukin-6, and interferon-γ) in blood plasma from patients with remission of chronic herpes infection were measured during immunocorrective therapy. Our results indicate that immunocorrection is pathogenetically substantiated and immunologically effective. It was manifested in reduction of inflammation and activation of antiviral protection

Key Words: *herpes infection; cytokines; immunocorrection*

Prevention of recurrent chronic herpes infection (CHI) is an urgent problem [1,2,10-12,15]. Herpes virus has low immunogenic activity and cannot induce a sufficient immune response, which would contribute to virus elimination from the organism [7,8]. Stimulation of the macrophage system with a complex of low-immunogenicity antigen and adjuvant compound is followed by induction of a specific immune response [5]. Therefore, the use of immunomodulating drugs in combination therapy and immunorehabilitation for CHI is pathogenetically substantiated [2,5,6,8,10]. Immunotropic preparations of *Echinacea* can serve as immunomodulators [13,14].

Here we studied the dynamics of antiinflammatory cytokine production in patients with clinical remission of CHI before and after immunocorrective therapy (ICT).

MATERIALS AND METHODS

The patients with CHI (n=52, 17-52 years old) were admitted to the Dermatology Department of the Berdyansk municipal hospital. They were examined during remission of the disease. Acute and chronic inflammations were not diagnosed in patients over 1 month before the trial.

A plant preparation containing extracts from *Echinacea purpurea* (60%) and *Echinacea pallida* (40%, GMI phytomicrospheres) was used for ICT. Treatment was performed as follows: on day 1 the patients received 1 capsule in the morning and 1 capsule in the evening and on days 2-5 they received 1 capsule per day [3]. The control group included 14 patients with CHI receiving no ICT. Informed consent for participation in the trial was obtained from all patients. This trial was approved by Ethics Committee.

The patients were examined before that start of ICT and on days 7, 14, and 21 after a 5-day course of therapy.

The concentration of cytokines interleukin-1β (IL-1β), IL-6, and interferon-γ (IFN-γ) in blood serum was measured using commercial kits (Proteinovyi kontur).

Normal values of the test parameters were estimated at the Laboratory of Reproductive Immunology (Scientific Center of Clinical and Experimental Medicine) [4].

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The results were analyzed by methods of nonparametric statistics. The differences were significant at a probability level of 95%.

RESULTS

Antigenic stimulation (*e.g.*, virus exposure) causes a biphasic immune response [9]. Phase 1 of the immune response (monocyte-macrophage phase) is determined by activation of cytokines with antiinflammatory and activation-differentiation functions. Variations in the concentration of IL-1β (major proinflammatory cytokine) play the major role in this process.

During the first examination, IL-1β concentration in patients of the main and control groups was above normal ($p<0.01$). IL-1β concentration in patients of the main group decreased on day 7 after ICT ($p<0.05$). IL-1β concentration tended to increase on days 14 and 21 after ICT, but did not exceed the pre-treatment level. These changes reflect reduction of inflammation and maintenance of organism's resistance over 3 weeks after ICT. No changes in IL-1β concentration were revealed in patients of the control group. Moreover, variations in IL-1β concentration in control group patients were statistically insignificant in all periods of study (Fig. 1).

IL-6 concentration increases during inflammatory diseases of different genesis (particularly in chronic inflammation). IL-6 concentration in patients of the main and control groups was above normal ($p<0.05$). IL-6 concentration in patients of the main group decreased on day 7 after ICT ($p<0.05$). However, IL-6 concentration in these patients increased on day 14 and practically did not differ from the pre-treatment level. IL-6 concentration on day 21 was higher than on day 14 ($p<0.05$).

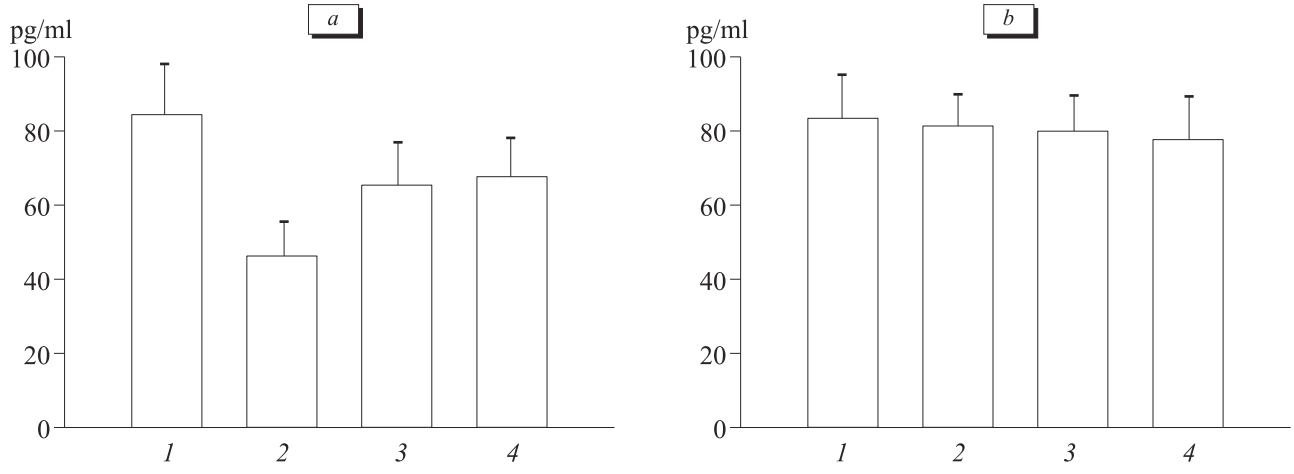

Fig. 1. IL-1β concentration in blood plasma from patients with clinical remission of CHI. Here and in Figs. 2 and 3: main group (*a*) and control group (*b*). Before ICT (*1*) and days 7 (*2*), 14 (*3*), and 21 after ICT (*4*).

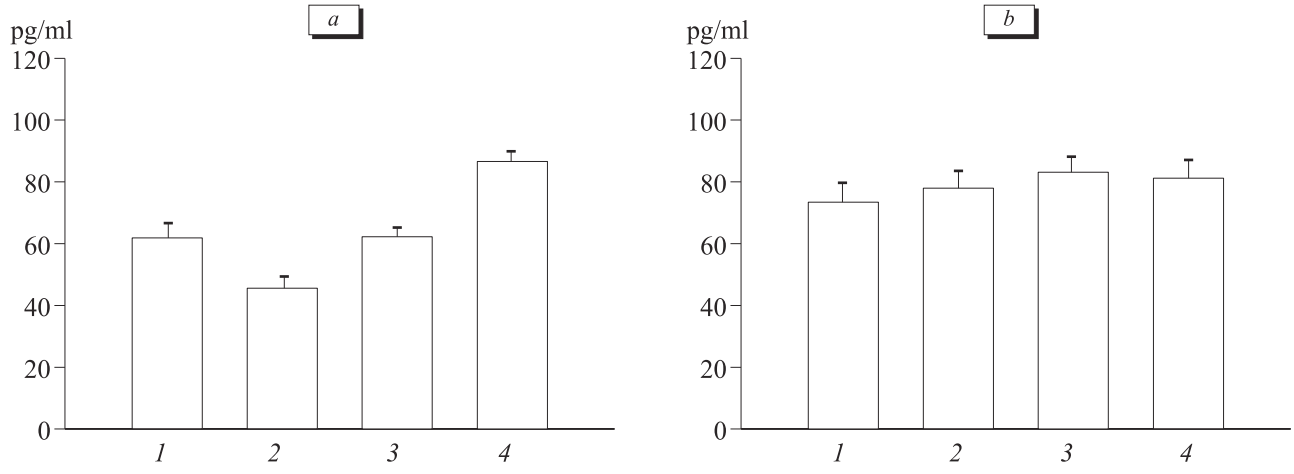

Fig. 2. IL-6 concentration in blood plasma from patients with clinical remission of CHI.

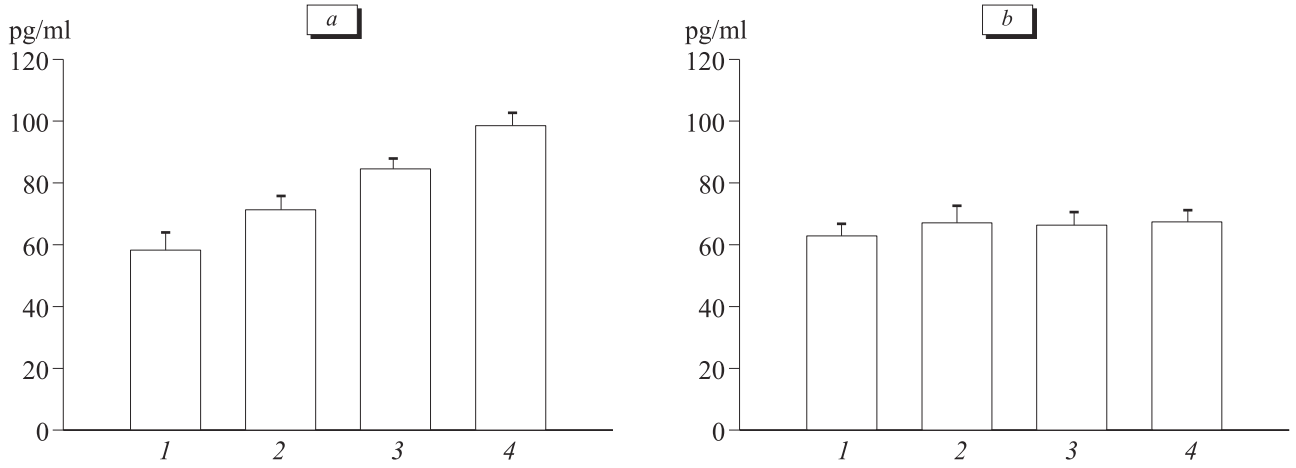

Fig. 3. IFN-γ concentration in blood plasma from patients with clinical remission of CHI.

Taking into account the dual role of IL-6, the increase in cytokine concentration reflects its involvement in the specific immune response (activation of antibody synthesis). In controls, variations in IL-6 concentration were statistically insignificant (Fig. 2).

The basal level of IFN-γ in patients of the main and control groups was above normal ($p<0.05$).

IFN-γ concentration in blood plasma from patients of the main group increased on day 7 after ICT ($p<0.05$). IFN-γ concentration progressively increased on days 14 and 21 and exceeded that observed before and 7 days after therapy ($p<0.01$ and $p<0.05$, respectively).

Hence, IFN-γ concentration progressively increased over 3 weeks after ICT. These changes were not revealed in control group patients (Fig. 3).

Clinical examination of patients showed that ICT is followed by lengthening of the remission period and decrease in the incidence of CHI relapses (by 2 times).

Our results indicate that the concentrations of IL-1β and IL-6 in blood plasma from patients of the main group significantly decrease after ICT. These changes reflect reduction of inflammation during remission of CHI.

ICT is accompanied by an increase in production of IFN-γ, which plays a key role in activation of antiviral protection.

We conclude that this scheme of ICT is pathogenetically substantiated and immunologically effective in CHI patients.

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