IMMUNE STATUS OF PATIENTS INFECTED WITH CHLAMYDIAE AND ITS CORRECTION BY MEANS OF LAFEROBION DRUG

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Results of the study performed indicate the presence of secondary immunodeficiency in patients infected with Chlamydiosis. Use of Laferobion drug in these patients restores both cellular and humoral immunity, contributing to elimination of chlamydia from the body and complete recovery of patients in 96.2% of cases.

Key words: urogenital chlamydiosis, treatment, immune status, Laferobion.

In the analyzing the scientific publications data, the growth of inflammatory pelvic organs diseases (pelvic inflammatory disorders, PID) was detected. According to different authors, the frequency of this pathology makes 60.0-65.0% among outpatients and 30.0% among those hospitalized [1, 2].

Lately, experts pay more attention to chlamydial infection, since the frequency of the disease among women under the age of 30 has grown to 57.0% [4].

Urogenital Chlamydiosis pathogen is Chlamydia trachomatis, namely serovars D, E, F, G, H. I. Y, K. [3]

Chlamydia are bacteria with a structure peculiar for prokaryotes having the form of small Gram-negative cocci. They are obligate intracellular parasites with a unique development cycle, having two forms of existence - elementary and reticular bodies [4].

Elementary body is a highly infectious pathogen form, adapted to the extracellular existence, and reticular body is an intracellular form of the parasite’s existence, providing reproduction of the microorganism. In the initial stage of infection, the elementary body turns into the reticular one, thus, the number of ribosomes and polyribosomes in it grows, the typical bacterial nucleoid is clearly revealed, growth of its size and shape is observed and binary fission forms appear. All these processes are taking place inside the vacuole of the host cell, where reticular bodies are accumulated [3, 4].

Chlamydial infection is known [5] to cause mobilization of cellular and humoral immune response, increased production of interferon against Chlamydia growth. However, under current conditions, immune reactivity decrease is observed [6], thus preconditioning the suppression of the mechanisms for host cells defense against Chlamydia that causes the development of adverse immune reactions leading to host tissues damage and to Chlamydiosis progression. As a result of the above processes, favorable conditions are formed for the disease chronization, leading in its turn to the increased risk of infertility development. In addition, the existing immune failure may cause lack of the standard etiotropic therapy’s efficiency in the chlamydial infection treatment.

That is why to increase the standard therapy efficiency, a variety of drugs having the immunomodulatory effect is often included into the treatment regimen. In this situation, interferon preparations and drugs that stimulate its production are the most widely applied. The latter mostly effect healthy and intact cells. Under the conditions of the immune system’s cells depression, that is typical of any chronic infection in general, and Chlamydiosis in particular, the use of interferon inducers leads to additional stimulation of immune cells, but it does not allow to achieve adequate immunomodulatory action.

Objective of the reseach: to study the immune homeostasis in patients infected with Chlamydiosis, and assessment of its correction efficiency when Laferobion drug is used (manufacturer PAT "Biopharma").
MATERIALS AND METHODS

The total of 53 female patients were examined at the age of 20 to 39 with PID of Chlamydial etiology.

In 32 (60.4%) women, infertility and a generative function impairment was observed, which they applied with to the clinic.

Chronic salpingitis was diagnosed in 38 (71.7%) patients, endocervicitis - in 25 (47.2%) patients, urethritis - in 16 (30.2%) patients.

All the patients were subject to the complete physical examination, using laboratory, immunologic, ultrasonic (US), colposcopic, oncocyto logical, microbiological and molecular biological research methods.

In addition, to determine the systemic immunity features, 15 healthy women were examined.

The material for the systemic immunity study was peripheral blood. To assess the state of cellular immunity, the following parameters were determined: the total number of T-lymphocytes (CD3 +), their immunoregulatory subpopulations – T-helpers / inducers (CD4 +) and T-suppressors / killers (CD8 +), the number of B-lymphocytes (CD22 +), NK-cells (CD16 +), immunoregulatory index (CD4 + / CD8 +) was calculated. Studies were performed by means of the indirect immunofluorescence reaction, using murine monoclonal antibodies (mMCA ISO) [7]. Humoral immune system was evaluated by the the concentration of circulating immune complexes (CIC) according to Diogen et al., and immunoglobulins (Ig) of A, M, G classes by the radial immunodiffusion method according to Mancini et al.[7].

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Chlamydiae monoculture
Mycoplasma + ureaplasma + chlamydiae
Mycoplasma + ureaplasma Association
Ureaplasma + chlamydiae Association

Dyspareunia
Uterine cervix edema and hyperemia
Muco-purulent vaginal discharge
Dysuria
Uterine adnexa tenderness
Lower abdominal dull pain
External genitalia discomfort

Figure 1. Microflora pattern at urogenital Chlamydiosis (%)

Figure 2. Clinical symptoms of Chlamydial infection development in the examined patients
b) 10⁹/L

Figure 3. Cell immunity indices in the examined women patients

Figure 4. Humoral immunity indices in the examined women patients
Phagocytic activity of neutrophilic granulocytes was studied by determining the phagocytic index (PI) and the phagocytic number (PN) [7]. Systemic immunity indices were studied before and after treatment.

The indication for Laferobion prescription was the index of T lymphocytes sensitivity determined for the given drug.

Patients with chlamydial infection of the urogenital tract received a pathogenic immune correction course with Laferobion drug (manufacturer: PAT "Biopharma") simultaneously with the common causal (etiotropic) therapy.

Laferobion was administered rectally by 3 million IU 2 twice a day with a 12-hour break for 10 days. Re-treatment was carried out in 5 days after the first course was over. Such an
immunocorrection regimen with the use of Laferobion drug in the background of the etiotropic treatment allows influence on 7 cycles of Chlamydiae development.

Simultaneously, a sexual partner was treated, recommendations on the diet, maintaining sexual activity were provided.

Laferobion application at urogenital Chlamydia is not accidental, since the above drug - recombinant interferon alfa-2b - has the ability to inhibit the intracellular generation of Chlamydiae due to the cellular synthesis of nucleic acids, which in cooperation with a number of enzymes and inhibitors destroy genetically foreign information. The given preparation, on the one hand stimulates phagocytosis, activity of natural killer cells, expression of antigens; on the other hand, it inhibits formation of antibodies, development of inflammation, delayed-type hypersensitivity, complement binding assay [6].

Clinical monitoring of the treatment efficiency was carried out for 6 months, the control bacteriological examination was performed after 14-21 days and after two menstrual cycles.

RESULTS AND DISCUSSION

The results of the performed studies suggest that Chlamydia mono-infection was observed in 54.7% of women patients. Among the microorganisms associations the most frequent were the following: ureaplasma + Chlamydiae in 20.8% of patients; mycoplasma + ureaplasma + Chlamydiae - in 5.7% of patients; mycoplasma + Chlamydiae - in 18.9% of patients (Figure 1).

Analysis of the data obtained during examination of the patient showed the presence of the classic symptoms of cervicitis, chronic salpingitis, urethritis: lower abdominal dull pain, uterine adnexa tenderness, external genitalia discomfort, uterine cervix edema and hyperemia, mucu-purulent vaginal discharge, dysuria, dyspareunia. The frequency of clinical manifestations in the examined patients is shown in Fig. 2.

In the analysis of the examined patients' cellular immunity evaluation results (Fig. 3) the immune homeostasis impairment was observed, that was determined by T-lymphopenia (1.9-fold decrease of CD3 +), reduction in the number of T-cells with helper action (2.2-fold decrease of CD4 +), reduction of subpopulations with suppressor action (1.6-fold decrease of CD8 +), thus having resulted in 1.3-fold reduction of immuno-regulatory index (Tx / Tc) (p <0.05). The number of B-lymphocytes was also observed (1.3-fold decrease of CD22 +) (p <0.05). As it is evident, B-system's immunity function is reduced due to impairment of the cooperation interaction of T-helper cells and B-lymphocytes subpopulations, which are manifested in hypopimunoglobulinemia: reduction of IgG by 2 times, IgA by 3.9 times, IgM by 2.1 times (p <0.05) (Figure 4.). PI and the PN were lower than in healthy women, respectively, 1.6 and 2.3-fold (p <0.05). Circulating immune complexes (CIC) number thus remained within the normal range (p> 0.05).

The findings of the immunological study in patients with chlamydia infection indicate the presence of immune system suppression in this category of patients, and that was the reason for Laferobion prescription.

As of today, it is found [6] that the efficiency of this class drugs’ immunomodulatory effects depends on each patient’s lymphocytes sensitivity to this immunomodulator. Therefore, one of the Laferobion prescription criteria we considered to be the level of lymphocytes sensitivity to the given drug of the women examined. The mean sensitivity of lymphocytes to the drug amounted to 49.6 ± 3.1%. It should be noted that among the women surveyed there were no patients with a complete lack of lymphocytes sensitivity to Laferobion. On separation of the patients according to the level of sensitivity, it was found that even at low levels of lymphocytes sensitivity to Laferobion, immunomodulatory effect of the drug was manifested.

Clinical monitoring showed that already during the first week of treatment in 24 (45.3%) women clinical manifestations of the urinary tract inflammatory diseases were reduced: 10 (18.9%) patients noted the pain syndrome decrease, 5 (9.4%) - the absence of burning...
sensation and discomfort when urinating; 12 (22.6%) - reduction of the vaginal discharge amount.

After treatment Laferobionom (Fig. 5, 6) of the surveyed patients had a change of almost all indicators immunogram (p <0.05) and bringing them into line with the parameters in healthy women (p> 0.05), which contributed to the normalization of the immunoregulatory index.

When using Laferobiona a marked effect on the dynamics of the FF and the FI, which was manifested not only in increasing the percentage of neutrophilic granulocytes, blood cells, which absorb antigenic latex particles, but also increase their digestive capacity, i.e. completion of all stages of phagocytosis.

Clinical and laboratory examination after the completion of treatment showed a positive effect in 51 (96.2%) patients, improvement - in 2 (3.8%) patients.

It should be noted that the application of Laferobion revealed no cases of adverse effects and drug intolerance.

Thus, the inclusion of Laferobion into the range of therapeutic measures at urogenital chlamydiosis permitted to rationalize treatment and achieve a positive result.

**CONCLUSIONS**

Patients infected with Chlamydiae acquire a secondary immunodeficiency, that requires the inclusion of immunomodulatory drugs into the treatment regimen to enhance the efficiency of standard causal treatment. Use of Laferobion drug in these patients leads to the restoration of both cellular and humoral immunity, contributing to elimination of Chlamydiae from the body and to the complete recovery of patients in 96.2% of cases, thus making it possible to prevent infertility at infectious diseases of urogenital organs in women and the complications development during pregnancy.

The immune status of patients infected with Chlamydiae and its correction with Laferobion drug

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The results of the study indicate the presence of secondary immunodeficiency in patients infected with Chlamydiae. Laferobion drug used in these patients leads to the restoration of both cellular and humoral immunity, contributing to the elimination of Chlamydiae from the body and to the onset of complete recovery of patients in 96.2% of cases.

**Key words:** urogenital Chlamydiosis, treatment, immune status, Laferobion.

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