

CLINICAL PHARMACOLOGY

UDC: 618.11-002:615.254

DOI: 10.18413/2500-235X-2016-2-4-55-67

Abramova S.N.¹,
Lazareva G.A.²**PHARMACOTHERAPY EXACERBATIONS OF CHRONIC
INFLAMMATORY CONDITIONS OF FEMALE GENITAL SPHERE
USING TO GEPON AND LONGIDAZA**

- 1) post graduate student of the Department of obstetrics and gynecology of Kursk State Medical University 3, K. Marksa St., Kursk, 305041, Russia. e-mail: 23011984008@mail.ru
- 2) Doctor of Medical Sciences, Professor of the Department of obstetrics and gynecology of Kursk State Medical University, 3, K.Marksa St., Kursk, 305040, Russia. e-mail: g_lazareva@yandex.ru

Abstract. Researches of the last years showed that changes of local immunity at inflammatory diseases of appendages at women, to be exact a condition of a secondary immunodeficiency at the local level, arising against the main pathological process, are a consequence of an immune inflammation, violation of structure and function of cellular membranes because of lipid peroxidation. Research objective was establishment of changes of the metabolic status at an aggravation chronic salpingoophoritis and detection of efficiency of use in «Gepon's» complex pharmacotherapy and «Longidaza's» various medicinal forms. For this purpose under continuous supervision was the 70th women aged from 20 till 35 years with the established diagnosis chronic salpingoophoritis in an aggravation stage. All patients were divided into four groups according to age, minimum satellite, severity of illness and providing treatment. The first experimental group was included 18 patients with chronic adnexitis in the exacerbation phase, where the standard therapy. The second group was included patients (17 women), which put on «Longidaza» in the form of suppositories (1 suppository 3000 per recti 1 times a day for 5 days). In the third group (18 patients), patients received, in addition to a standard treatment regimen «Gepon» (10 mg per 1 times a day for 5 days). The fourth group was included patients (17 women), which put on «Longidaza» injections (1 suppository 3000 intramuscularly 1 time per day for 5 days). As a result of a research efficiency of use of immunocorrective preparations («Gepon» and «Longidaza») at patients chronic salpingoofority in an aggravation stage in correction of metabolic frustration is established. «Longidaza's» use in the form of candles has corrective and normalizing impact on the broken indicators of the metabolic status at patients chronic salpingoophoritis at local level whereas purpose of an injection form of this preparation normalizes parameters of the oxidatic status at system level. Results of a research allow to draw a conclusion that application in complex pharmacotherapy of patients with chronic salpingoophoritis longidaza and gepon in comparison with standard treatment makes more expressed impact on clinical picture of disease and laboratory indicators at system and local levels, thus maximum efficiency possesses a preparation of longidaza in the form of injections.

Keywords: chronic salpingoophoritis, immune status, metabolic disturbances, gepon, longidaza

Introduction. In modern terms of chronic inflammatory conditions, of the uterine appendages, are the actual problem of obstetrics and gynecology due to unexpressed clinical aspects. Extent of exposure, frequent relapses, leading to the development of adhesive processes, in the small pelvis, a breach of immunological reactivity and other changes [1, 2, 3, 4]. The systemic protection mechanisms, are diseases in cases of long-stretching and recurrent diseases of the uterine appendages against which it is most likely a violation of the

pelvic organs with the development of the power of local tissue hypoxia [5, 6, 7]. There is a study about production, of inflammatory mediators of different nature a relatively new subject of study pathogenetic mechanisms of inflammation in the uterine appendages of women antioxidant protection, from which expression depends on changes in the level body, systems and organism as a whole [8, 9].

Recent researches have shown, changes in local immunity the state of the secondary immunodeficiency at the local level that occurs on a

background of the primary pathological process, are the result of immune inflammation, disruption of the structure and function of cell membranes due to lipid peroxidation [10].

The use of anti-inflammatory medication therapy has an active effect on the bacterial flora, but not enough to impair immune and metabolic status, which is opened the prospect of doing research to find effective ways and means of pharmacological immunorehabilitation [11].

Accordingly, only the use of standard therapy, doesn't always lead to full recovery. So for the successful treatment of patients, with chronic inflammatory diseases, it must be integrated etiopathogenetic treatment, including an appropriate immune rehabilitation and prevention of adhesions [12].

As the results of previous researches using only immunomodulatory drugs in the correction of immune and oxidant disturbances that occur during exacerbation of chronic adnexitis is not enough, so in this respect it could be effective to use the drug with immunomodulating and enzymatic activity. Longidaza, being a derivative polyoxidonium in conjunction with hyaluronidase, and in a variety of pharmaceutical forms of its release [13, 14]. There are enough facts for appropriate effectiveness of the injection Longidaza, while suppository form of the drug has been understudied [15]. Also, it may be a promising application Gepon drug interferon inducer link immunity [16, 17].

On this basis, the development of pathogenetically substantiated pharmacotherapeutic strategy exacerbation of chronic adnexitis is one of the urgent problems of modern medicine.

Our objective: To identify the clinical and immunological effectiveness using complex processes, in the pharmacotherapy of acute exacerbations of chronic adnexitis Gepon and different dosage forms Longidaza.

Research objectives:

- To determine effects of Gepon on the immune status and lipid peroxidation in patients with chronic adnexitis in the exacerbation phase.

- To determine the effect of various dosage forms of pharmacotherapy, drug «Longidaza» on the immune status, and processes peroxidation, lipid in patients with chronic adnexitis in the exacerbation phase.

- To compare immunomodulatory and antioxidant effects «Gepon» and «Longidaza» in the form of suppositories or injectable solution in complex patients with acute exacerbation of chronic adnexitis.

- To compare the clinical and immunological effectiveness of methods, pharmacocorrection including immunotropic drugs in patients suffering from chronic adnexitis in the exacerbation phase.

- To identify correlations between clinical symptoms, and laboratory parameters for inclusion in a comprehensive standard pharmacotherapy, Gepon and Longidaza and an exacerbation of chronic adnexitis.

It was established clinical and immunological efficacy immunocorrective drugs («Gepon» and various forms of «Longidaza») in patients, with chronic adnexitis in the exacerbation phase. Using «Longidaza» in the form of suppository has a corrective and normalizing effect on the impaired performance immune status of patients with chronic adnexitis mostly at the local level, while the appointment of the injectable form of the drug normalizes immune parameters and oxidative status at the system level. The use of complex pharmacotherapy of patients with chronic adnexitis «Longidaza» and «Gepon» is compared with standard treatment and had more pronounced effect on the clinical symptoms disease and laboratory parameters on the system and local levels, with the maximum efficiency has drug injection «Longidaza».

There were effective complex methods for patients with chronic pharmacotherapy adnexitis in the exacerbation phase using «Gepon» or «Longidaza». Clinical and immunological efficacy of the applied sketch of pharmacotherapy of patients with chronic adnexitis is ascending in the following order: standard pharmacotherapy → standard therapy + «Gepon» standard therapy + «Longidaza» in the form of suppositories → standard therapy treatment + «Longidaza» in the form of injections.

There were significant interactions between indicators immunometabolic status on the system and local levels, and clinical symptoms that gives an indication of the effectiveness of the treatment, the dynamics of symptom exacerbation of chronic adnexitis and predicting disease outcome.

In clinical research it was used a team approach to the study of immunocorrective and antioxidant effects of immunomodulatory drugs in women of gynecological separation OBUZ «Regional Perinatal Center» in Kursk with chronic adnexitis in the exacerbation phase, in accordance with the recommendations of the World Health Organizations.

The learning of pharmacological corrective effects «Gepon» (LLC «Immapharma», Russia) and «Longidaza» («research and manufacturing association Petrovax Farm», Russia) on the immune, oxidative disorders and clinical symptoms in patients

with chronic adnexitis in the exacerbation phase was carried out using an enzyme multiplied immunoassay, laboratory methods for assessing oxidative indicators, activity of antioxidant systems and using widely certified methods of statistical data processing.

OWN RESEARCHES

Clinical impressions. There were 70 patients with chronic adnexitis in the exacerbation phase at the age of 20-35 years under constant surveillance on the basis of OBUZ «Regional Perinatal Center». Clinical exclusion was established on the basis of complaints, medical history, laboratory and physical examination [18, 19]. The control group consisted of 22 healthy volunteer donors of the same age. The inclusion criteria were:

- The age of 20-35 years;
- Medical history to 3 years;
- Certain disease is chronic adnexitis in the exacerbation phase;
- The severity of the state no more than moderate severity;
- Negative findings of STD;
- Tolerance of used drug ;
- A written consent to participate in doing research.

Exclusion criteria:

- Patients in serious and critical condition;
- Verified persons with specific STD;
- Persons with concomitant somatic pathology in the stage of incomplete remission and the exacerbation phase;
- Persons with an allergic reaction to the treatment;
- Patients who refuse to doing research.

In all cases, it was carried out direct microscopic

for the exclusion of gonococcus infection (swabs were prepared then they were stained with 1% aqueous methylene blue and Gram) and biological (inoculation of medium for detecting *Neisseria gonorrhoea*) research of vaginal-cervical lavage.

To detect trichomonas it was carried out native and painted watercolor solution of methylene blue drugs, inoculation of medium for the culture diagnosis of trichomoniasis.

Diagnosis of chlamydia, mycoplasma, ureaplasma, gardnerella infection was producing by examining scraps obtained PCR using commercial kits firm «DNA diagnosis» All patients were subjected to testing for lues and HIV, which staged the standard serological tests. All patients made direct microscopic and bacteriological content of the Exploration of the cervical canal and urethra, performed a colposcopy, ultrasound investigation.

Laboratory methods of blood tests were carried out by conventional methods. It were taken hemogram as a basis for the physiological norm, corresponding to the international system of units (SI) in clinical trials.

All patients were divided into four groups according to age, minimum satellite, severity of illness and providing treatment (Table 1).

The first experimental group was included 18 patients with chronic adnexitis in the exacerbation phase, where the standard therapy is held: cefazolin (1.0 intramuscularly 4 times a day number 20), gentamicin (80 mg intramuscularly 3 times a day number 21), nystatin (500 thousand units inside. 4 times a day № 28) trichopolom (0,5 orally 3 times daily № 15) indometacinum (100 mg once per rectum № 10) and clotrimazole topically (Table 1. per vagina singly evening № 10).

Table 1.

Distribution of patients according to the method of treatment.

| | № | Treatment mode | Number |
|--|---|--|--------|
| Patients with chronic adnexitis in the exacerbation phase | 1 | Standard medicinal treatment | 18 |
| | 2 | Standard medicinal treatment + «Longidaza» suppositories | 17 |
| | 3 | Standard medicinal treatment + «Gepon» | 18 |
| | 4 | Standard medicinal treatment + «Longidaza» injections | 17 |
| All | | 70 | |
| Donors | | | 22 |

The second group was included patients (17 women), which put on «Longidaza» in the form of suppositories (1 suppository 3000 per recti 1 times a day for 5 days).

In the third group (18 patients), patients received, in addition to a standard treatment regimen «Gepon» (10 mg per 1 times a day for 5 days).

The fourth group was included patients (17

women), which put on «Longidaza» injections (1 suppository 3000 intramuscularly 1 time per day for 5 days).

All drugs were administered according to the guidelines outlined in the guide «Medicines», «Doctor-register own funds of Russia» (2010) and instructions on the use of drugs.

Laboratory research. Content FNO α , IL-18,

INF α , IL-10, C3 and C4 components of the complement system, factor H was determined in the blood plasma and cervical-vaginal lavage with the help of ProCon reagent kit (LLC «Protein contour», St. Petersburg) by enzyme immunoferment analysis.

Intensity of lipid peroxidation was evaluated on the content in the blood and cervical-vaginal lavage malonic dial [20]. The measured activity of catalase [21], SOD, the concentration of ceruloplasmin-governmental stable metabolites of nitric oxide [22], α_1 -antitrypsin, α_2 -macroglobulin and total antioxidant activity of blood serum [23].

Erythrocytes were prepared from 5 ml heparinized blood by the method of E. Beutler with minor modification. Whole blood is asserted twice in 10 mM Na-phosphate buffer (pH 7.4) containing 0.9% sodium chloride and 3% dextran T-500, for 30 minutes at 37 ° C. Thereafter, the blood was centrifuged, the supernatant was removed by aspiration. Packed red blood cells were further purified to the chromatographic column through HBs-cellulose.

We determined the total sorption capacity of red blood cells and the sorption capacity of glycocalyx.

On the functional state of erythrocytes as judged by the accumulation of malonic dial and activity of superoxide dismutase.

Statistical analysis of the results. Statistical processing of results of research was carried out using non-parametric methods, factor analysis, cluster analysis, and Spearman's rank correlation coefficient. Differences were considered statistically

significant with $p < 0,05$.

For immunological parameters were calculated ratio diagnostic value, determined by the formula of immune disorders system by selecting from all the studied parameters of the top three most distinguished level of standards expected level of immune disorders, ranking algorithm largest extent disorders conducted.

Correlation analysis between indices immunometabolic and clinical data, calculated the amount of degrees of correction for each treatment regimen.

RESULTS OF RESEARCH

Immune and metabolic disorders in patients with chronic adnexitis in the exacerbation phase before and after standard treatment. The studied parameters of patients with chronic adnexitis in the exacerbation phase in the surveyed group to the treatment of each other do not differ. Patients with chronic adnexitis in the exacerbation phase plasma at admission to hospital revealed increasing concentrations FNO α , IL-18, INF α , C3 and C4 components of the complement system and reduced levels of IL-10 over 4 pain and factor H (Table 2).

Using the standard treatment in patients with chronic adnexitis in the exacerbation phase allowed to reduce, but not to the level of standards, the concentration of IL-18, C3 and C4 of the complement system and the Component to increase the concentration of factor H (Table 2).

Table 2.

Cytokines and complement concentration of system components in patients with chronic adnexitis in the exacerbation phase plasma on a background of standard treatment.

| Exponents | Units | 1 | 2 | 3 |
|----------------|-------|------------------|---|-----------------------------------|
| | | Healthy | Patients with chronic adnexitis in the exacerbation phase | |
| | | | Before treatment | After treatment |
| FNO α | pg/ml | 1,77 \pm 0,08 | 5,8 \pm 0,15 ^{*1} | 5,48 \pm 0,25 ^{*1} |
| IL-18 | pg/ml | 40,45 \pm 2,35 | 195,8 \pm 8,8 ^{*1} | 150,1 \pm 10,35 ^{*1,2} |
| IL-10 | pg/ml | 18,5 \pm 0,42 | 3,5 \pm 0,2 ^{*1} | 3,89 \pm 0,24 ^{*1} |
| INF α | pg/ml | 11,5 \pm 1,21 | 28,6 \pm 3,4 ^{*1} | 26,2 \pm 2,19 ^{*1} |
| C ₃ | pg/ml | 106,4 \pm 6,9 | 228,2 \pm 7,6 ^{*1} | 152,48 \pm 7,17 ^{*1,2} |
| C ₄ | mg/dl | 13,6 \pm 1,31 | 47,7 \pm 1,6 ^{*1} | 40,01 \pm 1,24 ^{*1,2} |
| Factor H | ng/ml | 41,3 \pm 3,3 | 23,7 \pm 2,9 ^{*1} | 34,8 \pm 3,17 ^{*1,2} |

Note. Hereafter the asterisk marked significant differences of average arithmetical ($p < 0,05$); figures close to the star are in relation to that of a group of these differences.

In the cervical-vaginal lavage in women with chronic adnexitis in the exacerbation phase revealed raising FNO α , IL-18, INF α , system components plementa someone, but the decline in the level of secretory IgA, factor H and IL-10 (Table 3). Against

the background of standard treatment in patients with chronic adnexitis in the exacerbation phase in the vaginal-cervical lavage is reduced, but not to the level of standards, the concentration of IL-18, INF α and increased levels of IL-10 (Table 3).

Table 3.

The concentration of cytokines and complement components in patients current with chronic adnexitis in the exacerbation phase in the vaginal-cervical lavage against standard treatment (M ± m).

| Exponents | Units | 1 | 2 | | 3 |
|----------------|-------|-----------|---|----------------------------|---|
| | | healthy | Patients with chronic adnexitis in the exacerbation phase | | |
| | | | Before treatment | After treatment | |
| FNO α | pg/ml | 1,19±0,08 | 6,1±0,2 ^{*1} | 6,65±0,46 ^{*1} | |
| IL-18 | pg/ml | 2,58±0,13 | 14,3±0,9 ^{*1} | 10,91±0,89 ^{*1,2} | |
| IL-10 | pg/ml | 5,12±0,77 | 1,8±0,14 ^{*1} | 3,94±0,57 ^{*1,2} | |
| INF α | pg/ml | 8,37±0,59 | 14,5±1,1 ^{*1} | 10,8±1,2 ^{*1,2} | |
| C ₃ | mg/dl | 24,3±2,9 | 40,6±1,7 ^{*1} | 41,55±2,08 ^{*1} | |
| C ₄ | mg/dl | 1,13±0,07 | 2,5±0,02 ^{*1} | 2,42±0,11 ^{*1} | |
| Factor H | ng/ml | 29,8±2,14 | 17,3±1,1 ^{*1} | 18,0±1,21 ^{*1} | |
| sIgA | mg/dl | 37,6±1,24 | 31,8±0,1 ^{*1} | 31,96±1,09 ^{*1} | |

In the blood plasma of patients with identified chronic adnexitis in the exacerbation phase raising MDA, α 1-AT, α 2-MG, stable metabolite of nitric oxide in reducing CRP during General antioxadantive activity serum, SOD and catalase activity, the concentration of ceruloplasmin (Table 4).

On the background of the standard treatment for this category of patient current plasma malonic dial concentration decreases, CRP, proteolytic ferments, but increased the activity of catalase, SOD, General antioxadantive activity, but not to the level healthy donors (Table 4).

Table 4.

Indicators of metabolic status of patients with chronic adnexitis in the exacerbation phase in the blood on the background of standard treatment (M ± m).

| Exponents | Units | 1 | 2 | | 3 |
|---------------------------------|-------------|------------|---|----------------------------|---|
| | | healthy | patients with chronic adnexitis in the exacerbation phase | | |
| | | | Before treatment | After treatment | |
| Malonic dial | umol/l | 1,98±0,15 | 4,1±0,08 ^{*1} | 3,8±0,05 ^{*1,2} | |
| General antioxadantive activity | % | 50,1±0,99 | 39,3±0,7 ^{*1} | 43,2±0,56 ^{*1,2} | |
| SOD | U/ml | 12,8±0,99 | 4,2±0,2 ^{*1} | 5,93±0,34 ^{*1,2} | |
| Catalase | μ kat/L | 22,65±1,63 | 11,4±0,3 ^{*1} | 12,86±0,28 ^{*1,2} | |
| ceruloplasmin | mg/dl | 33,2±2,05 | 24,5±1,9 ^{*1} | 22,0±1,19 ^{*1} | |
| CM _{NO} | umol/l | 3,68±0,21 | 4,0±0,1 ^{*1} | 2,82±0,09 ^{*1,2} | |
| α 1-AT | mg/dl | 80,6±4,3 | 134,3±3,7 ^{*1} | 90,88±2,3 ^{*1,2} | |
| α 2-MG | mg/dl | 89,57±2,09 | 140,4±6,1 ^{*1} | 113,0±3,48 ^{*1,2} | |
| CRP | mg/dl | 1,35±0,33 | 2,1±0,04 ^{*1} | 1,73±0,08 ^{*1,2} | |

In the cervical-vaginal lavage women with chronic adnexitis in the exacerbation phase revealed increased concentration of malonic dial, stable metabolites of azote oxide, α 1-AT, α 2-MG and

reducing General antioxadantive activity, the activity of SOD, catalase, the concentration of ceruloplasmin (Table 5).

Table 5.

Indicators of metabolic status of patients with chronic adnexitis in the exacerbation phase in the vaginal-cervical lavage on a background of standard treatment (M ± m).

| Exponents | Units | 1 | 2 | | 3 |
|---------------------------------|-------------|------------|---|---------------------------|---|
| | | healthy | patients with chronic adnexitis in the exacerbation phase | | |
| | | | Before treatment | After treatment | |
| Malonic dial | umol/l | 0,87±0,03 | 2,1±0,05 ^{*1} | 1,98±0,08 ^{*1} | |
| General antioxadantive activity | % | 15,6±1,12 | 4,8±0,27 ^{*1} | 7,46±0,45 ^{*1,2} | |
| SOD | U/ml | 2,07±0,08 | 0,5±0,05 ^{*1} | 0,62±0,09 ^{*1} | |
| Catalase | μ kat/L | 3,16±0,09 | 1,5±0,18 ^{*1} | 1,14±0,34 ^{*1} | |
| ceruloplasmin | mg/dl | 2,48±0,04 | 0,7±0,06 ^{*1} | 0,97±0,04 ^{*1,2} | |
| CM _{NO} | umol/l | 0,51±0,03 | 0,6±0,05 ^{*1} | 0,46±0,04 ^{*2} | |
| α 1-AT | mg/dl | 13,7±0,71 | 40,0±2,06 ^{*1} | 15,7±0,98 ^{*2} | |
| α 2-MG | mg/dl | 18,09±1,13 | 25,8±2,09 ^{*1} | 21,6±3,35 ^{*1} | |

Using a standard treatment regimen in patients with chronic adnexitis in the exacerbation phase possible to normalize the level of α_1 -AT, but to correct burdened obstetric history, concentration of ceruloplasmin, without affecting the rest of the indicators changed in the metabolic status (Table 5).

We have further studied the sorption properties of red blood cells and the concentration within them of malonic dial and SOD activity. Thus, in patients with chronic adnexitis in the exacerbation phase in erythrocyte malonic dial concentration increased and reduced on-SOD activity (Figure 1).

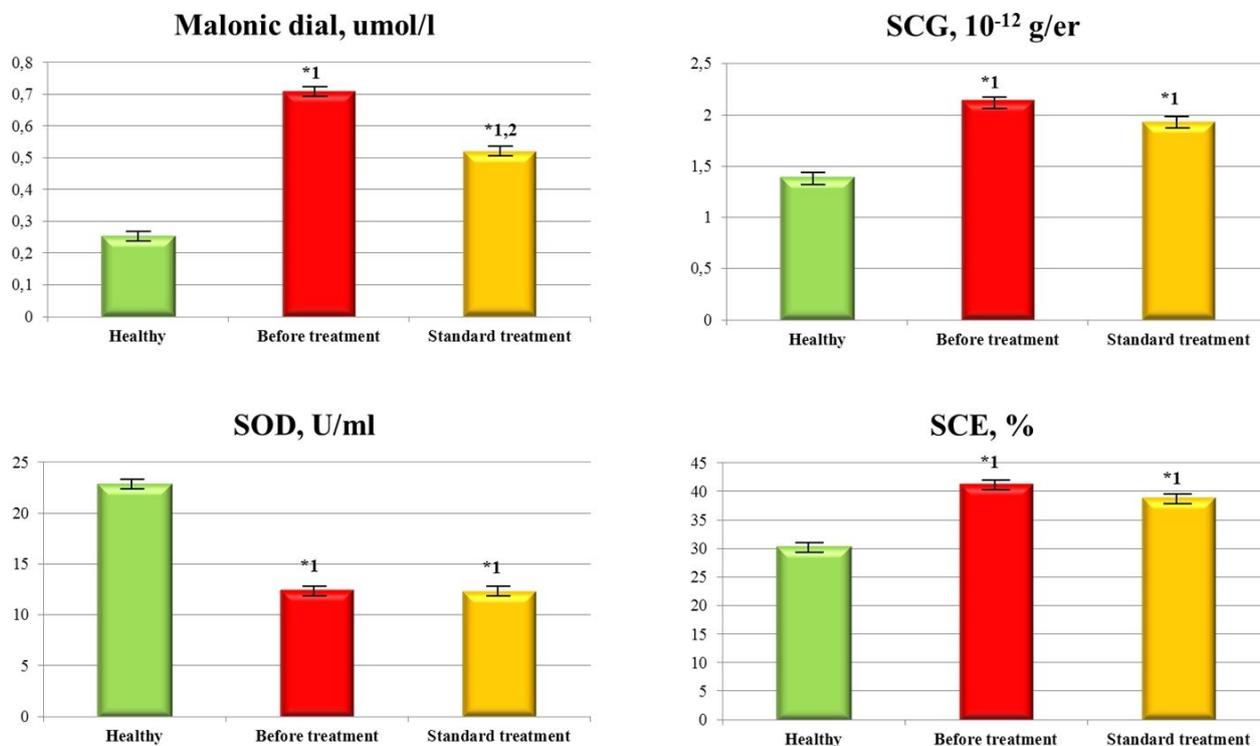


Figure 1. The state of immune and metabolic status in patients with chronic adnexitis in the exacerbation phase at the local level.

In addition, when you receive in this category of patients increased sorption properties of erythrocytes: sorption capacity of erythrocyte and sorptive capacity glycocalyx (Figure 1.). Against the background of standard treatment in patients with chronic adnexitis in the exacerbation phase concentration decreases in erythrocyte malonicdial, but not to the level of standards, while other indicators remain at the same

level changed (Figure 1).

Comparing the total number of different parameters of normal levels in patients with chronic adnexitis in the exacerbation phase found that if such indicators before treatment was 96.6%, after the standard pharmacotherapy such indicators was 94.2, which is not enough (table 6).

Table 6.

The effectiveness of standard treatment in patients with chronic adnexitis in the exacerbation phase (% Indicators).

| Indicators (% Of the total number of indicators) | Standard treatment |
|---|--------------------|
| Excellent level of standards before treatment | 96,6 |
| normalized | 2,4 |
| corrected | 23,3 |
| Not changing | 70,9 |
| Excellent level of standards after standard therapy | 94,2 |

Immune efficacy of «Gepon» and «Longidaza» in patients with chronic adnexitis in the exacerbation phase. Using «Longidaza» in the form of suppositories for patients with chronic adnexitis in the exacerbation phase in addition to a standard treatment regimen will normalize the blood

concentration of the C3 component of complement system, $\text{INF}\alpha$, reduce, but not to the level of standards, the level $\text{FNO}\alpha$, IL-18, C4 component of the complement system (Table 7).

At the local level in patients with chronic adnexitis in the exacerbation phase against

application «Longidaza» in the form of suppositories to normal levels of IL-18, INF α , C4 component of the complement system, of sIgA, corrected, but not to the level of standards, the concentration of FNO α , factor H (Table 8).

Appointment «Longidaza» in the form of suppositories patients with chronic adnexitis in the exacerbation phase additory to the standard treatment regimen helped normalize blood concentration of ceruloplasmin, CRP increase, but not to the level of standards, SOD activity, catalase, α_2 -MG (Table 7).

Women with chronic adnexitis in the exacerbation phase against application «Longidaza» in the form of suppositories in the vaginal-cervical lavage normalized level of malonic dial, SMNO proteolysilytic enzymes, corrected, but not to the level of standards activity catalase, SOD and the level of ceruloplasmin (Table 8).

Using «Gepon» in patients with chronic adnexitis in the exacerbation phase in addition to the standard treatment regimen helped correct the concentration in the blood FNO α , IL-18, INF α , but further increases the concentration of component B tem Complement: C3 and complement C4 component (Table 7).

At the local level in patients with chronic adnexitis in the exacerbation phase against application «Gepon» only corrected concentration of IL-18, and other indicators of immune status remain at the same level changed (Table 8).

Appointment «Gepon» patients with chronic adnexitis in the exacerbation phase, in addition to the standard treatment regimen has allowed to correct blood SOD and catalase, the concentration of ceruloplasmin (Table 7).

Women with chronic adnexitis in the exacerbation phase against application «Gepona» in the vaginal-cervical lavage normalized level α_1 -AT, corrects the activity of catalase (Table 8).

Using «Longidaza» in the form of injections in patients with chronic adnexitis in the exacerbation phase additionally to the standard treatment regimen helped normalize blood concentration FNO α , C3 and C4 component of the complement system, INF α , the fact that H, corrected, but not to the level of standards, IL level -18 and IL-10 (Table 7).

At the local level in patients with chronic adnexitis in the exacerbation phase against application «Longidaza» in the form of injections corrected FNO α level and IL-18 (Table 8).

Appointment «Longidaza» in the form of injections patients with additional chronic adnexitis in the exacerbation phase to the standard treatment regimen helped normalize blood concentration of ceruloplasmin, α_1 -AT, CRP increase, but not to the level of standards of asset are SOD and catalase, the concentration of α_2 -MG (Table 7). Women with chronic adnexitis in the exacerbation phase against application «Longidaza» in the form of injections in the vaginal-cervical lavage normalized level of malonic dial, General antioxadantive activity, SMNO and α_2 -MG, corrected, but not to the level of standards, catalase activity and the level of α_1 -AT (Table 8). The use of «Gepon» corrects inside the erythrocytes malonic dial level and sorption capacity of erythrocyte, «Longidaza» in the form of suppositories further sorptive capacity glycocalyx, while the use of «Longidaza» in the form of injections normalize sorption properties of red blood cells (Figure 2).

Table 7.

Immune and metabolic status at the system level in patients with chronic adnexitis in the exacerbation phase the therapy (M ± m).

| Exponents | Units | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|------------------|-------------|------------|---|-----------------------------|---------------------------------|-----------------------------|--|----------------------------|
| | | healthy | patients with chronic adnexitis in the exacerbation phase | | | | | |
| | | | Standard treatment + «Longidaza» suppositories | | Standard treatment + «Gepon» | | Standard treatment + «Longidaza» injections | |
| | | | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment |
| FNO α | pg/ml | 1,77±0,08 | 6,0±0,15 ^{*1} | 2,51±0,06 ^{*1,2} | 5,9±0,15 ^{*1} | 3,59±0,15 ^{*1,4} | 5,8±0,15 ^{*1} | 1,79±0,07 ^{*6} |
| IL-18 | pg/ml | 40,45±2,35 | 198,4±9,8 ^{*1} | 137,73±4,33 ^{*1,2} | 190,7±8,7 ^{*1} | 70,17±2,58 ^{*1,4} | 191,7±10,2 ^{*1} | 53,1±2,4 ^{*1,6} |
| IL-10 | pg/ml | 18,5±0,42 | 3,7±0,2 ^{*1} | 3,35±0,15 ^{*1} | 3,6±0,3 ^{*1} | 3,64±0,11 ^{*1} | 3,3±0,2 ^{*1} | 9,8±1,09 ^{*1,6} |
| INF α | pg/ml | 11,5±1,21 | 27,5±2,5 ^{*1} | 12,5±1,96 ^{*2} | 28,8±3,1 ^{*1} | 20,4±2,3 ^{*1,4} | 29,9±3,1 ^{*1} | 12,03±2,14 ^{*6} |
| C ₃ | mg/dl | 106,4±6,9 | 246,1±12,1 ^{*1} | 112,9±3,2 ^{*2} | 212,8±9,6 ^{*1} | 175,64±4,04 ^{*1,4} | 230,8±10,5 ^{*1} | 115,47±2,18 ^{*6} |
| C ₄ | mg/dl | 13,6±1,31 | 49,1±1,8 ^{*1} | 25,92±0,88 ^{*1,2} | 43,5±1,7 ^{*1} | 56,06±1,7 ^{*1,4} | 50,6±1,3 ^{*1} | 14,83±1,45 ^{*6} |
| Factor H | ng/ml | 41,3±3,3 | 25,1±1,8 ^{*1} | 32,8±4,7 ^{*1,2} | 24,2±1,4 ^{*1} | 30,2±2,51 ^{*1,4} | 23,2±1,9 ^{*1} | 43,5±4,0 ^{*6} |
| MDA | umol/l | 1,98±0,15 | 1,98±0,15 | 4,3±0,09 ^{*1} | 4,0±0,07 ^{*1} | 3,62±0,16 ^{*1,4} | 4,4±0,09 ^{*1} | 2,43±0,07 ^{*1,6} |
| OAA | % | 50,1±0,99 | 50,1±0,99 | 39,5±0,8 ^{*1} | 38,8±0,8 ^{*1} | 42,59±0,66 ^{*1,4} | 40,1±0,8 ^{*1} | 44,45±0,69 ^{*1,6} |
| SOD | U./ml | 12,8±0,99 | 12,8±0,99 | 4,5±0,3 ^{*1} | 4,1±0,3 ^{*1} | 9,06±0,89 ^{*1,4} | 4,1±0,3 ^{*1} | 8,13±0,24 ^{*1,6} |
| Catalase | μ kat/L | 22,65±1,63 | 22,65±1,63 | 11,1±0,4 ^{*1} | 10,9±0,3 ^{*1} | 14,23±0,17 ^{*1,4} | 11,3±0,3 ^{*1} | 18,46±0,19 ^{*1,6} |
| ceruloplasmin | mg/dl | 33,2±2,05 | 33,2±2,05 | 24,8±1,8 ^{*1} | 23,8±1,8 ^{*1} | 25,36±1,29 ^{*1} | 22,8±1,9 ^{*1} | 31,06±3,5 ^{*6} |
| CM _{NO} | umol/l | 3,68±0,21 | 3,68±0,21 | 4,2±0,7 ^{*1} | 4,1±0,2 ^{*1} | 2,6±0,16 ^{*1,4} | 4,2±0,2 ^{*1} | 2,82±0,11 ^{*1,6} |
| α_1 -AT | mg/dl | 80,6±4,3 | 80,6±4,3 | 141,2±3,8 ^{*1} | 131,8±3,8 ^{*1} | 91,2±2,5 ^{*1,4} | 131,4±3,6 ^{*1} | 81,3±1,87 ^{*6} |
| α_2 -MG | mg/dl | 89,57±2,09 | 89,57±2,09 | 141,8±6,2 ^{*1} | 135,9±6,1 ^{*1} | 136,8±3,66 ^{*1} | 134,6±6,2 ^{*1} | 96,4±2,56 ^{*1,6} |
| CRB | mg/dl | 1,35±0,33 | 1,35±0,33 | 2,2±0,05 ^{*1} | 2,3±0,08 ^{*1} | 1,91±0,09 ^{*1} | 2,0±0,04 ^{*1} | 1,52±0,03 ^{*6} |

Table 8.

Immune and metabolic status at the local level in patients with chronic adnexitis in the exacerbation phase the therapy (M ± m).

| | Units | 1 | 2 | 3 | 4 | 5 | 6 | 7 | |
|------------------|--------|------------|---|---------------------------|------------------------------|---------------------------|---|----------------------------|--|
| | | healthy | patients with chronic adnexitis in the exacerbation phase | | | | | | |
| | | | Standard treatment + «Longidaza» suppositories | | Standard treatment + «Gepon» | | Standard treatment + «Longidaza» injections | | |
| | | | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment | |
| FNO α | pg/ml | 1,19±0,08 | 6,5±0,3 ^{*1} | 2,52±0,39 ^{*1,2} | 6,3±0,2 ^{*1} | 6,19±0,26 ^{*1} | 5,9±0,3 ^{*1} | 4,75±0,36 ^{*1,6} | |
| IL-18 | pg/ml | 2,58±0,13 | 12,8±0,8 ^{*1} | 2,69±0,33 ^{*2} | 14,5±0,9 ^{*1} | 6,2±0,7 ^{*1,4} | 15,6±0,7 ^{*1} | 6,95±0,49 ^{*1,6} | |
| IL-10 | pg/ml | 5,12±0,77 | 1,9±0,1 ^{*1} | 3,39±0,22 ^{*1,2} | 1,7±0,1 ^{*1} | 3,42±0,06 ^{*1,4} | 1,7±0,15 ^{*1} | 3,04±0,22 ^{*1,6} | |
| ИИФ α | pg/ml | 8,37±0,59 | 12,9±1,2 ^{*1} | 9,07±1,05 ^{*2} | 14,9±0,9 ^{*1} | 11,3±2,4 ^{*1,4} | 15,3±1,0 ^{*1} | 10,12±1,05 ^{*1,6} | |
| C ₃ | mg/dl | 24,3±2,9 | 36,6±1,9 ^{*1} | 40,68±3,76 ^{*1} | 46,7±1,6 ^{*1} | 40,67±2,2 ^{*1} | 40,2±1,1 ^{*1} | 40,31±4,05 ^{*1} | |
| C ₄ | mg/dl | 1,13±0,07 | 2,2±0,03 ^{*1} | 1,45±0,32 ^{*2} | 2,6±0,02 ^{*1} | 2,51±0,47 ^{*1} | 2,9±0,02 ^{*1} | 2,27±0,09 ^{*1} | |
| Factor H | ng/ml | 29,8±2,14 | 16,1±1,0 ^{*1} | 23,8±1,27 ^{*1,2} | 17,8±1,1 ^{*1} | 16,9±2,05 ^{*1} | 18,1±1,2 ^{*1} | 18,4±2,3 ^{*1} | |
| sIgA | mg/dl | 37,6±1,24 | 30,2±0,4 ^{*1} | 38,76±3,02 ^{*2} | 37,9±0,1 ^{*1} | 31,64±2,2 ^{*1} | 33,8±0,3 ^{*1} | 30,5±1,78 ^{*1} | |
| MDA | umol/l | 0,87±0,03 | 2,3±0,06 ^{*1} | 0,91±0,03 ^{*2} | 2,2±0,06 ^{*1} | 2,05±0,05 ^{*1} | 2,0±0,06 ^{*1} | 1,38±0,04 ^{*6} | |
| OAA | % | 15,6±1,12 | 4,4±0,3 ^{*1} | 13,3±0,49 ^{*1,2} | 4,9±0,25 ^{*1} | 7,82±0,54 ^{*1,4} | 4,6±0,3 ^{*1} | 14,76±0,56 ^{*6} | |
| SOD | U./ml | 2,07±0,08 | 0,6±0,05 ^{*1} | 1,73±0,07 ^{*1,2} | 0,4±0,04 ^{*1} | 0,72±0,02 ^{*1,4} | 0,6±0,06 ^{*1} | 0,63±0,03 ^{*1,6} | |
| Catalase | μkat/L | 3,16±0,09 | 1,4±0,1 ^{*1} | 2,86±0,12 ^{*1,2} | 1,6±0,15 ^{*1} | 2,05±0,11 ^{*1,4} | 1,4±0,09 ^{*1} | 2,01±0,13 ^{*1,6} | |
| ceruloplasmin | mg/dl | 2,48±0,04 | 0,8±0,07 ^{*1} | 2,1±0,04 ^{*1,2} | 0,6±0,07 ^{*1} | 0,94±0,02 ^{*1,4} | 0,8±0,07 ^{*1} | 0,9±0,04 ^{*1,6} | |
| CM _{NO} | umol/l | 0,51±0,03 | 0,6±0,08 ^{*1} | 0,45±0,04 ^{*2} | 0,7±0,06 ^{*1} | 0,44±0,05 ^{*4} | 0,6±0,06 ^{*1} | 0,47±0,03 ^{*6} | |
| α_1 -AT | mg/dl | 13,7±0,71 | 38,6±2,2 ^{*1} | 12,97±0,63 ^{*2} | 40,2±2,05 ^{*1} | 13,37±0,56 ^{*4} | 42,1±2,1 ^{*1} | 19,53±7,36 ^{*1,6} | |
| α_2 -MG | mg/dl | 18,09±1,13 | 26,2±2,2 ^{*1} | 17,72±1,36 ^{*2} | 24,1±2,1 ^{*1} | 24,9±2,07 ^{*1} | 27,1±2,1 ^{*1} | 18,4±0,46 ^{*6} | |

Comparative clinical and laboratory efficiency «Gepon» and another forms «Longidaza» in patients with chronic adnexitis. Using «Gepon» normalizes 16.6% of the indicators, and the use of «Longidaza» in the form of suppositories - 28.6%, which reduced the number of

indicators other than the level of the norm to 77.6 and 65.6%. At the same time the using of «Longidaza» in the form of injections in patients with chronic adnexitis in the exacerbation phase allowed normalized larger number of indicators, making lower the number of modify to 58.8% (Table 9).

Table 9.

Efficiency of pharmacological diagram in patients with chronic adnexitis in the exacerbation phase (% indicators).

| exponents (% from the total exponents) | Standard therapy + «Gepon» | Standard therapy + «Longidaza» suppositories | Standart therapy + «Longidaza» injections |
|--|-------------------------------|--|---|
| Excellent on the level of the standard rate of pharmacotherapy | 94,2 | | |
| Normilized | 16,6 | 28,6 | 35,4 |
| Corrected | 25,6 | 36,4 | 35,2 |
| Unaltered | 52,0 | 29,2 | 23,6 |
| Excellent level of standards after additional pharmacological correction | 77,6 | 65,6 | 58,8 |

In determining its own corrective effects of treatment, regimens compared with standard conservative therapy found that the practically all indicators of immune status of all these diagram

effectiveness standard, as the average degree of correction in almost all performance parameters are proved positive.

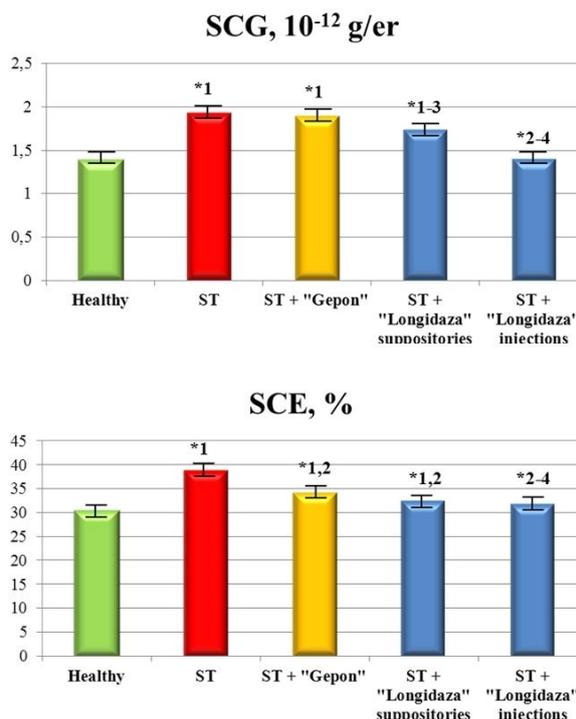
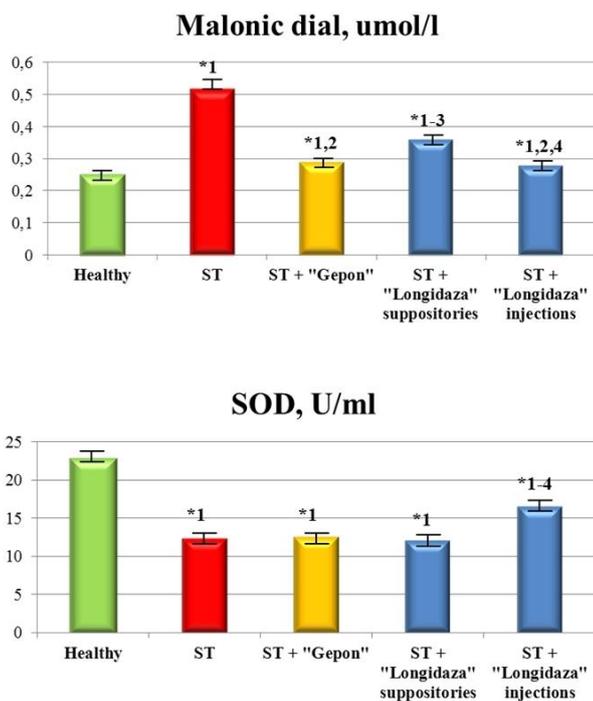


Figure 2. Condition of the metabolic status of erythrocytes in patients with chronic adnexitis in the exacerbation phase on a background of therapies

The maximum number of points set for the diagram, including «Longidaza» in the form of injections - 1097 points. Positive dynamics of Immune status coincided with the clinical effect of different treatments.

For example, 36.8% of patients after standard treatment with chronic adnexitis in the exacerbation phase has pain, 15% - dysmenorrhea, 36.8 - increase the basal rate during menstruation, at 32.2% there is an increase of leukocytes in the smears (Table. 10).

Table 10.

Clinical effectiveness of different treatment regimens of patients with chronic adnexitis in the exacerbation phase (% of patients).

| № | Treatment | Relapses exacerbations (> 1 during the year) | Increasing leukocytes in the smears | Increasing of basal temperature during menstruation | Pain syndrome | Dysmenorrhea | The secretary dysfunction (whites) |
|----|--------------------------------|--|-------------------------------------|---|--------------------|--------------|------------------------------------|
| 1. | Standard treatment (ST) | 32,2 | 32,2 | 36,8 | 36,8 | 15,0 | 40,0 |
| 2. | ST + «Gepon» | 12,5 ^{*1} | 25,0 | 25,0 ^{*1} | 18,8 ^{*1} | 18,8 | 25,0 ^{*1} |
| 3. | ST + «Longidaza» suppositories | 6,7 ^{*1} | 20,0 ^{*1} | 20,0 ^{*1} | 20,0 ^{*1} | 13,3 | 13,3 ^{*1,2} |
| 4. | ST + «Longidaza» injections | - ^{*1-3} | 13,3 ^{*1-3} | 13,3 ^{*1,2} | 20,0 ^{*1} | 13,3 | 13,3 ^{*1,2} |

The maximum decrease in clinical manifestations observed after the application of an additional «Longidaza» in the form of injections, after the appointment of the drug were no relapses of diseases in 13.3% of patients was observed and dysmenorrhea, increase in white blood cells in the smears and increase basal temperature.

With multiple correlation matrix the Spearman between exponent of immune, metabolic status and clinical manifestations were significant, both positive and negative connections, testified of the interdependence of laboratory and clinical long-exponent.

A number of indicators have the greatest number of these relation: concentration in the blood plasma FNO α , C3 component complement system, α_1 -antitrypsin, and cervical-vaginal lavage - the concentration of IL-18, the activity of superoxide dismutase.

In patients with chronic adnexitis in the exacerbation phase has been a violation of a number of indicators of immune status, as in system, and at the local level, at the same time it is carried out the standard pharmacological correction in these patients does not allow fully resolve as the immune, so and metabolic status, which dictates the desirability of research and testing in clinical trials of more pharmacological agents and methods immunorehabilitation patients with chronic adnexitis in the exacerbation phase, in this connection, we have

established Immune efficacy of «Gepon» and «Longidaza» in patients with chronic chronic adnexitis in the exacerbation phase. In the end, we used the drug «Gepon» and «Longidaza» in two dosage forms - suppositories and injectable form.

Use in addition to standard pharmacotherapy chronic adnexitis in the exacerbation phase «Gepon» helped normalize blood levels only α_1 -antitrypsin, while the use of «Longidaza» in the form of suppositories further normalizes the concentration of CRP, INF α and C3 component of the complement system. This is the use of an additional «Longidaza» injection enabled normalized larger number of indicators at the system level.

The use of «Gepon» does not have a normalizing effect on the changed indicators were in vaginal-cervical lavage women with chronic adnexitis in the exacerbation phase, whereas the use of «Longidaza» as suppositories normalizes studied indices of metabolic status, whereas injectable normalizes a level of α_2 -macroglobulin and INF α .

The use of «Gepon» corrects inside the erythrocytes malonic dial level and sorption capacity of erythrocyte, «Longidaza» in the form of suppositories - further sorptive capacity glycoalyx, while the use of «Longidaza» in the form of injections normalize sorption properties of erythrocytes.

Thus, on the basis of the research we can recommend to use in practical public health sketch

pharmacologists immuno-metabolic rehabilitation in patients with chronic adnexitis in the exacerbation phase using «Longidaza» in the form of injections. Less effective, it corrects the disturbed immune parameters and oxidative status of the treatment regimen with the use of this drug in the form of suppositories.

RECOMMENDATION

Taking into account the results expressed in the form of the article, we can, but to formulate the recommendations and prospects of further development of the theme:

– In order to mitigate immune and oxidant disturbances in patients with chronic adnexitis in the exacerbation phase in the form of injection (3000 IU intramuscularly 1 time per day for 5 days) is possible the use of exacerbation «Longidaza».

– To obtain objective facts on the severity of Immune disorders in patients with chronic adnexitis in the exacerbation phase usefully be measured in the blood plasma concentration FNO α , C₃-component system someone plementa, α_1 -antitrypsin, and cervical-vaginal lavage - the concentration of IL-18, the activity of superoxide dismutase.

– Use in the educational process of medical universities the knowledge about the reacting immunocorrective and antioxidant effects «Longidaza» and «Gepon» in terms of exacerbation of chronic adnexitis.

CONCLUSIONS

After the standard treatment in patients with chronic adnexitis in the exacerbation phase has not reached the level of healthy donor concentration in plasma IL-18, C₃, C₄ components of the complement system, α_1 -antitrypsin, α_2 -macroglobulin, C-reactive protein in vaginal-cervical lavage concentrations of stable metabolites of nitric oxide, IL-10 and α_1 -antitrypsin, α_2 -macroglobulin and endoglobular concentrations of malonic dial.

Use in addition to standard pharmacotherapy of chronic adnexitis «Gepon» (in a dosage of 10 mg per 1 times a day for 5 days) helped further to normalize at B level α_1 -antitrypsin, inside red blood cells to correct the level of malonic dial and total sorption capacity blood cells without significant effects on performance at the local level.

Appointment of patients with chronic adnexitis in the exacerbation phase, in addition to the standard treatment regimen, «Longidaza» in the form of suppositories (in a dosage of 1 suppository 3000 per recti 1 times a day for 5 days) complement normalizes blood plasma concentration of C-reactive protein, INF α and C₃ component of the complement system, sorption capacity glicocalyx red blood cells,

and vaginal-cervical lavage almost all the studied indicators of metabolic status.

Using an additional «Longidaza» injection (in a dosage of 1 suppository 3000 intramuscularly 1 time per day for 5 days) in patients with chronic adnexitis in the exacerbation phase helped normalize the greater number of indicators at the system level: sorption properties of red blood cells, and at the local level only level α_2 -macroglobulin and INF α .

Using «Gepon» normalizes 16.6% of the indicators (2.8 times more effective than standard therapy), and the use of «Lonegidaza» in the form of suppositories - 28.6% (4.9 times more effective than standard therapy), which reduced the number of indicators other than the level of the norm to 77.6 and 65.6%. At the same time the using of «Longidaza» in the form of injections in patients with chronic adnexitis in the exacerbation phase allowed normalized larger number of indicators, making lower the number of modify to 58.8% (6.1 times more effective than standard therapy).

References

1. Atykanov A.O., Osmonova M.B. Assessment of a condition of processes of peroxide oxidation of lipids and system of antioxidatic protection in a blood plasma at women with inflammatory diseases of appendages of uterus. *Bulletin of the Kyrgyz-Russian Slavic University*. Vol. 14, № 9 (2014): 25-27. [[eLIBRARY](#)] [[Full text](#)] (in Russian)
2. Klenina N.M., Rykalin E.B. Pharmakoepidemiological analysis of antimicrobial therapy of salpingoophorites in hospitals of the Saratov region. *Bulletin medical Internet conferences*. Vol. 4, № 5 (2014): 799. [[eLIBRARY](#)] [[Full text](#)] (in Russian)
3. Konoplya A.A., Gazazyan M.G., Karaulov A.V. Use of immunomodulators in the complex treatment of chronic salpingoophoritis. *Obstetrics and gynecology*. № 4 (2010): 75-78. [[eLIBRARY](#)] (in Russian)
4. Kagramanova ZH.A., Suslov V.S., Gusev T.S. Clinicoimmunological rationale for immunotherapy in patients with acute inflammatory diseases of the uterine appendages. *Bulletin Russian obstetrician-gynecologist*. № 5 (2006): 29-32. [[eLIBRARY](#)] (in Russian)
5. Sharafutdinova N.H., Mustafin G.T., Kandarov D.F. Reproductive health and behavior of women according to survey and medical examination. *Medical bulletin of Bashkortostan*. Vol. 9, № 1 (2014): 17-21. [[eLIBRARY](#)] [[Full text](#)] (in Russian)
6. Vafakulova U.B. Factors of health of the womans in futile marriage in republic Uzbekistan. *The Modern high technologies*. № 4 (2005): 39. [[eLIBRARY](#)] [[Full text](#)] (in Russian)
7. Loktina I.P. Application a polioksidoniya as a part of complex therapy of inflammatory diseases of an urogenital path. *Consilium Medicum*. № 6 (2009): 22-24.

[\[eLIBRARY\]](#) [\[Full text\]](#) (in Russian)

8. Simonova A.N., Ivlichev A.V., Yemlyanenko T.V. Comparative assessment of a condition of a coagulative hemostasis at pyoinflammatory diseases of bodies of a small pelvis at women. *Bulletin medical Internet conferences*. Vol. 4, № 5 (2014): 588.

[\[eLIBRARY\]](#) [\[Full text\]](#) (in Russian)

9. Wollcott R., Fisher S., Tomas V., Kuble W. Randomized, prospective, controlled study of laparoscopic tube patency. *Fertility and Sterility*. Vol. 72, № 5 (2003): 879–884. [\[Full text\]](#)

10. Shperling N.V., Vengerovsky A.I., Shperling I.A. Principles of pain syndrome therapy in salpingo-oophoritesю Gynecologies, obstetrics and perinatology. Vol. 13, № 1 (2014): 35-40. [\[eLIBRARY\]](#) [\[Full text\]](#) (in Russian)

11. Smirnova L.E. New approaches to prophylaxis and treatment of infectious and inflammatory complications after abortions with use of medicine Longidaza®. *Pharmatek*. № 12 (2012): 53-56. [\[eLIBRARY\]](#) [\[Full text\]](#) (in Russian)

12. Samtsov A.V., Luchina E.N. Clinical experience with of hyaluronidase-based drugs: Combination therapy for skin scarring deformities. *Experimental and Clinical Dermatology and Cosmetology*. № 6 (2012): 28-32. [\[eLIBRARY\]](#) [\[Full text\]](#) (in Russian)

13. Avdoshin V.P., Andryukhin M.I., Pulbere S.A. et al. Assessment of clinical effectiveness of the medicine Longidaza® in complex treatment of patients with chronic prostatitis. *The Efficient pharmacotherapy*. № 43 (2012): 22-25. [\[eLIBRARY\]](#) [\[Full text\]](#) (in Russian)

14. Smirnova L.E., Umakhanov M.M., Torchinov A.M. Efficacy of longidaza in combined therapy of peritoneal commissures of pelvic organs in endometriosis. *Pharmateka*. № 4 (2012): 48-51. [\[eLIBRARY\]](#) [\[Full text\]](#) (in Russian)

15. Shmyreva V.F., Ivanov A.S., Fedorov A. A. et al. Medical and biological research of Longidaza. Part 2. *Glaucoma*. № 1 (2012): 6-11. [\[eLIBRARY\]](#) [\[Full text\]](#) (in Russian)

16. Belenova I.A., Bondareva E.S. Increase efficiency of treatment of chronic complex square gingivitis in the children by means of the local immunomodulators. Bulletin of the new medical technologies. *Electronic resource*. № 1 (2013): 92 [\[eLIBRARY\]](#) [\[Full text\]](#) (in Russian)

17. Kolenko Yu.G. Substantiation of using immunomodulators in complex treatment of erosive and ulcerative lesions of oral mucosa. *The Modern medicine: topical issues*. № 23 (2013): 85-91. [\[eLIBRARY\]](#) [\[Full text\]](#) (in Russian)

18. Abramova S.N., Konoplya A.A., Bystrova N.A. Pharmakoterapiya of a chronic salpingoophoritis with use of a gepon and longidaza. *The Medical immunology*. Vol. 17, special issues (2015): 254. [\[eLIBRARY\]](#) [\[Full text\]](#) (in Russian)

19. Abramova S.N., Lazareva G.A., Konoplya A.A., Omasharifa Zh. P. Efficiency of immunomodulator at treatment of the chronic salpingoophoritis in the exacerbation stage. *Systems analysis and management in biomedical systems*. Vol. 12, № 4 (2013): 1027-1030. [\[eLIBRARY\]](#) [\[Full text\]](#) (in Russian)

20. Benisevich V.I., Idelson L.I. Formation of peroxides of nonlimiting fatty acids in an envelope of erythrocytes at a disease Markiafava-Mikeli. *Questions of the medical chemistries*. Vol. 19, № 6 (1973): 596-599. [\[Abstract\]](#) (in Russian)

21. Korolyuk M.A., Ivanova L.I., Mayorova I.G. et al. Method of definition of activity of a catalase. *Clinical laboratory diagnosis*. № 1 (1988): 16-19. [\[eLIBRARY\]](#) (in Russian)

22. Golikov P.P. Nitrogen oxide in clinic of urgent diseases. Moscow: Medpraktika, 2004. 137. [\[eLIBRARY\]](#) (in Russian)

23. Klebanov G.I., Babenkova I.V., Teselkin Yu.O. Assessment of anti-oxidizing activity of a blood plasma with application of vitelline lipoproteins. *Clinical laboratory diagnosis*. № 5 (1988): 59-62. [\[eLIBRARY\]](#) (in Russian)