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OPTIMIZATION IMMUNEPHARMACOTHERAPY OF PYOINFLAMMATORY DISEASES

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Abstract

Introduction: The results of clinical investigation of several pyoinflammatory diseases are presented.

Objectives: On clinical data of various models of pyoinflammatory diseases – deep pyodermia (UCP), chronic salpingooforitis (OHSO), chronic pyelonephritis (CPN), authors found a significant mechanism of influence the pathogenesis on the manifestation of immunopathology, efficacy and mechanisms of pharmacological immunocorrection action.

Methods: The study included 300 patients with purulent-inflammatory diseases of various genesis – UCP, CPN, OHSO. All the patients before and after traditional treatment with mono-and combination of immunomodulators of different origin – Roncoleukin, Licopide, Superlimph, Derinate, Polyoxidonium, Timogen, Galavit were subjected to a standard hemato-immunological examination and additionally model for each nosologic forms of diseases, bacteriological and clinical research. Mathematical analysis of obtained data was determined the significant differences of parameters from a predetermined level, and optionally, key, signal tests, formalized in the form of formulas.

Results and Discussion: A significant impact of three types of the pathogenesis of inflammatory diseases on the nature and severity of the hemato-immunological disorders in patients are established; the effectiveness and mechanisms of action of the modulator Galavit; a lock of a normalizing effect of the traditional treatment of patients; increase activity due to additional assignments of 7 options of monocorrectors and three of their combinations; the ability of modulating drugs affect not only immunological, but also on haematological, bacteriological and clinical characteristics of patients. In results, authors are documented a hole effects the action of immune correcting drugs. A formalized assessment of the variations in clinical and laboratory parameters of patients allowed us to determine diagnostically significant target of each immune factor integrally to compare the effect of individual therapy, to establish mechanisms for the modification of the function of the lymphoid system in mono- and combination immune therapy, due to the inversion of mathematical analysis to identify laboratory evidence for selection of specific variants of complex treatment of patients.

Conclusion: The result of clinical investigation and mathematical analysis of the results achieved was the formulation of a 6-level algorithm to identify and addressing treatment

immunocompromising persons in the form of 7 approved programs for computer-based introduction to computer outcome of laboratory examination of patients.
Keywords: pyoinflammatory diseases, immunotherapy, immunological disorders, formalized assessment.

Introduction

Under natural conditions, when infection develops, it forms a complicated pathogenic complex that includes accumulation of a lien antigens, aggressive factors (endotoxins, acute-phase proteins, low-molecular nucleic acids etc.), and ultra boundary suppression and stimulation of immune reactivity, and also competition between extra- and intra-cellular parasites for defense reaction regulators, cytokines, distortion of metabolic processes (peroxidation of lipids and proteins), dystrophic and other processes. The main method of infectious diseases treatment by antibacterial, antiviral and other drugs that lyse or limit the reproduction of causative agents, haven‘t turned to account because these factors have a series of substantial weaknesses. Firstly, they have no physical ability completely eliminate pathogens; secondly, they stimulate the adaptation of the pathogens, for instance, to antibacterial drugs, and realize corruption distortion of defense reactions towards deficiency, allergization and autoaggression. At the same time, in case of repeated infection of larger causative agents (bacteria) by smaller ones (viruses), when the causative agents are destroyed, the etiology of infection changes, etc. All this requires additional comprehensive therapeutic influence on the mentioned and other mechanisms [1, 2, 3, 4, 5, 6, 7].

Immunotherapy of infections. It implies that in treatment of chronic and poorly responding to conventional therapy diseases, they use vaccines, anatoxins, immunoglobulins, i.e. etiotropic drugs and pathogenetic treatment with use of blood, blood substitutes, plasma, nonspecific immunity stimulators etc. A series of drugs simultaneously have antimicrobial and immune stimulating actions (immunoglobulins, plant extracts etc.). Presently, because of changes in the natures of infectious diseases course, extensive clinical use of drugs that suppress immune reactions (corticosteroids, wide spectrum antibiotics) and increased allergization, it is necessary to free the organism from infectious agents extremely quickly and restore its destroyed homeostasis [8, 9, 10, 11]

By origin, immunotherapeutic drugs subdivide into 4 groups: 1). obtained from blood of various organs of humans and animals (plasma, immunoglobulins, thymus drugs, myelopeptides, interferons, splenin, placenta extract, antilymphocytic serum etc.), 2).obtained from plants (tinctures of eleuterococcus, schizandra etc.), 3).stimulators of microbial origin (pyrogenal, prodigiosan, zymosan, sodium nucleinate, bificol, bacteriophages etc.), 4).synthetic drugs (levamisole, pentoxyl, methyluracil, hemodez, polyoxidonium, licopid, diuciphonum etc.).

By the nature of immunotherapeutic action, immunotherapeutic drugs subdivide into drugs with specific (directed) action – vaccines, anatoxins, immune serums, immunoglobulins, and nonspecific organism resistance stimulators– blood and its preparations, plasma, bificol etc.) [12, 13].

Indications for prescription of immune stimulators are flaccid course of infectious process, its chronization and recurring, sharp long-term suppression of the indices of nonspecific antiinfection resistance and specific immunity in patients. It may also include changes in the nature and increased intensity of pathological changes, threat of secondary infection development and curative use of drugs with immunosuppressing properties [12, 14, 15]. Immunotherapy prescribed in a complex with other medical drugs (antibiotics, sulfanilamides, corticosteroids). Its efficiency depends on the correct assessment of the initial condition of the patient's immune reactivity, the nature and intensity of pathological changes, the choice of optimal drug and dosing schedule. It is also necessary to have an idea about the

action mechanisms of prescribed drugs, their side effects, compatibility with other infection treatment methods, allergic properties etc. Sometimes, vaccine therapy prescribed in case of immune tolerance to a certain AB, may render no positive clinical effect and even aggravate the condition of immune depression; simultaneously, there risk of anaphylactic shock is possible, as well as induction of autoimmune diseases and toxic shock. Blood and plasma transfusion is a good means instrument for stimulation of the patient's reactivity. However, this method of treatment is restrained by stable indications and must be performed on the basis of controlling its effect on the course of the disease, immunity indices and the possibility of allergy. Drugs of etiotropic (immune serums, immunoglobulines, bacteriophages, interferon) and desintoxication action (drugs of blood, plasma, blood substitutes) should be prescribed as early as possible after the onset of the disease. A series of nonspecific stimulators are used at the height of disease and in the convalescence period (pentoxyl, vitamins, methyluracil) or for treatment of complications (ferrocalum, phytin, levamisole). Curative vaccines are added to patients with lingering and chronic forms of disease. The use of polysaccharide preparations is contraindicated for fever conditions. Eubiotics are not prescribed simultaneously with antibiotics and other similar drugs [14, 15, 16, 17].

Nonspecific immunomodulation (immunotherapeutic support) of infections

It implies not only correction of immune, but also normalization of hematological, bacteriological, clinical and other indices in patients. Under today's conditions of collective immunity decrease of the humanity, substantial growth of infectious diseases rate, chronization, uncontrolled and irrational use of antibacterial drugs, the problem of immune reactivity modulation acquires special relevance. Diagnostic criteria of control over prescription of immunotropic drugs are implemented through assessment of the complex of clinical and laboratory indices in patients [18, 19, 20]. Clinical and immune criteria of effectiveness are determined by respective specialists with due account for preliminary approbation of the recommended actions. Immunotropic drugs, according to some classifications, divide into groups that induce various effects. These effects are quite numerous and are presented:

1. Stimulation of immune cells formation due to the influence on the hemopoiesis system (colony-stimulating factors).
2. Interaction with specific receptors of immunocompetent cells.
3. Stimulation or suppression of cytokines release.
4. Formation of active (vaccine) or passive (serum) antiinfection immunity.
5. Normalization of microecological status of organism (eubiotics).
6. Provision of energy needs and plastic components for immune reactions (macro-, microelement, vitamins, biological additives, antihypoxic drugs).
7. Activation of the processes of detoxification of immune reaction products (hepatoprotectors, enteral sorbents, afferent methods).
8. Elimination of antigens (adsorbents) from organism.
9. Substitution therapy (thymus drugs, immunoglobulins, white-cell-rich suspension).
10. Direct action on antigens (antiviral drugs) [21, 22].

Objectives: On clinical data of various models of pyoinflammatory diseases – deep pyodermia, chronic salpingooforitis, chronic pyelonephritis, authors found a significant mechanism of influence the pathogenesis on the manifestation of immunopathology, efficacy and mechanisms of pharmacological immunocorrection action.

Materials and Methods

In investigation was included of 300 patients:100 patients suffered from deep pyodermia in the stage of exacerbation (EDP), 100 – from chronic pyelonephritis in the stage of exacerbation (ECPN), 100 women – from chronic salpingooopharitis (ECSO) at the age

from 18 to 60 and 30 healthy patients - momentary donors. The patients in each nosologic form were divided into two equal groups and were undergone a standard treatment and a supplementary one which included a modulators: galavit, roncoleukin, lycopide, roncoleukin with lycopide, superlymph, derinate, superlymph with derinate, polyoxidonium, thymogen, thymogen with polyoxidonium in reglamented doses.

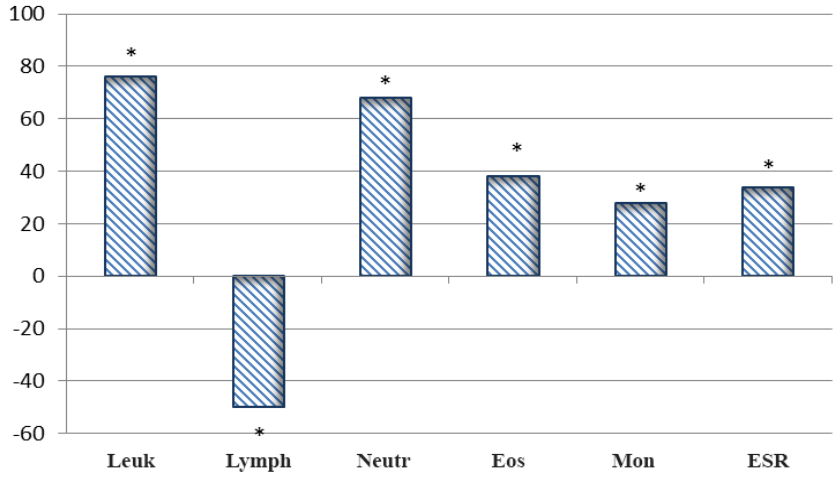
Before and after the treatment the patients were undergone a standard examination to reveal routine hematological markers of inflammation, common immunological factors (population, subpopulation of lymphocytes, serum immunoglobulins, cytokines, absorptional and metabolic ability of phagocytes) and also specific ones for concrete diseases – bacteriological and clinical parameters. As a result, the diagnostic material, taken from skin foci, urine, vaginal secrete, was treated by general methods and pathogenic and saprophyte staphylococcus, colibaccillus, proteus, klebsiella have been sowed and identified. The number of sterile tests was also defined. Clinical parameters included: intoxicational syndrome, subphebrilitis, lymphadenitis, renal colic, leukocyturia, leucorrhea discharge, hypertrophy, adnexa uteri disorders, etc.

The accuracy of the results was provided by the rational arrangement of patients groups, taking into account the criteria of including and excluding, randomization, representation, and statistic processing of data with a proper distribution of parameters: frequency and resulting frequency, graphical. Ranging analysis, formalization of immunopathology and modulation mechanisms by formulas of immune system disorders (FDIC) and targets of correction (FTC) [22, 23, 23, 25, 26, 27].

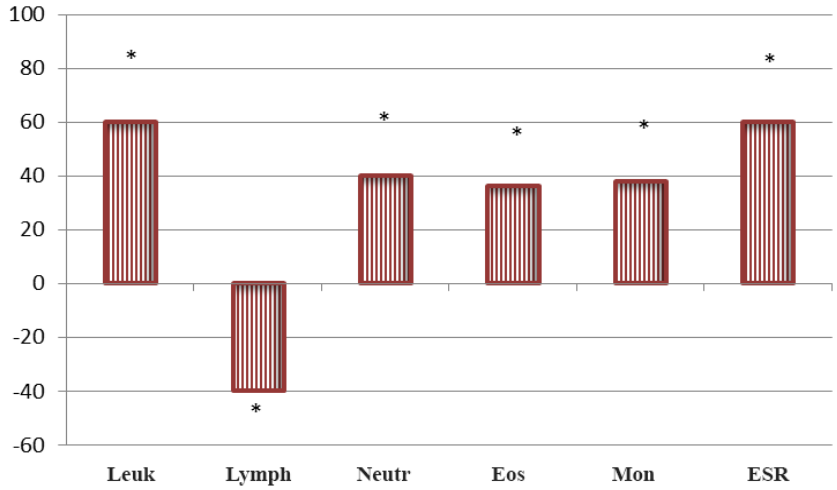
Results and discussion

During our study we have determined a universal standard reaction of routine hematological tests on the inflammatory conditions in patients with EDP, ECPN and ECSO: leukocytosis, neutrophilia, eosinophilia, monocytosis, lymphopenia, ESR acceleration. In the case of PID relatively to TCPN higher leukocytosis and the neutrophilia have been registrated, relatively to ESCO – a sufficiently less monocytosis and ESR have been observed, the patients with ESCO had an advantage over those with ECPN – according to the number of neutrophiles and monocytes.

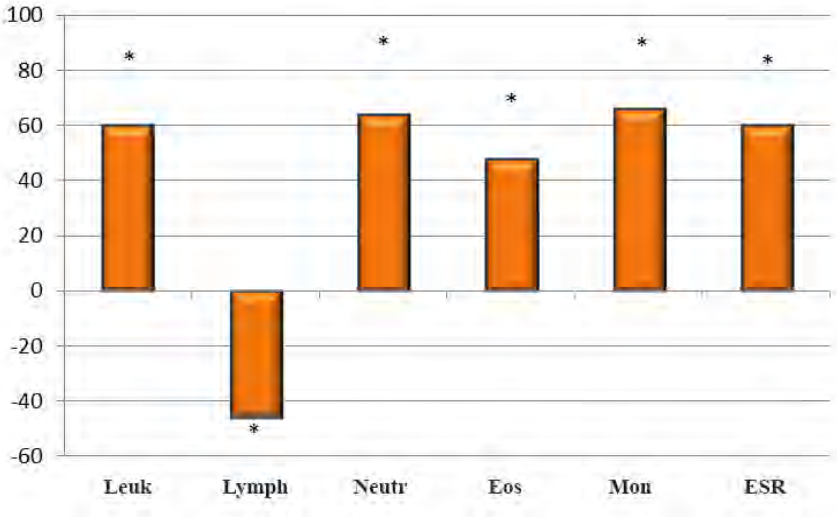
A typical character in all the cases of PID has been expressed in the tendency to disbalance or suppression of T-section immunity, humoral activation, suppression of phagocytes defense, a definite risk of the development of autoagressive and toxic conditions, an accumulation of proinflammatory cytokines, see fig. 1-3.



A. APP



Б. ECPN



В. ESCO

Fig. 1. Differences in hematological parameters from the normal level in the acute period of PID of various genesis

Note: Leuk. – leukocytes, Lymph – lymphocytes, Neut. – neutrophils, EOS – eosinophils, Mon. – monocytes, ESR – exacerbation sedimentation rate, * – reliability of differences from the norm level at P <0.05, on the vertical axis – % of patients with 2-3 DIF / HIS

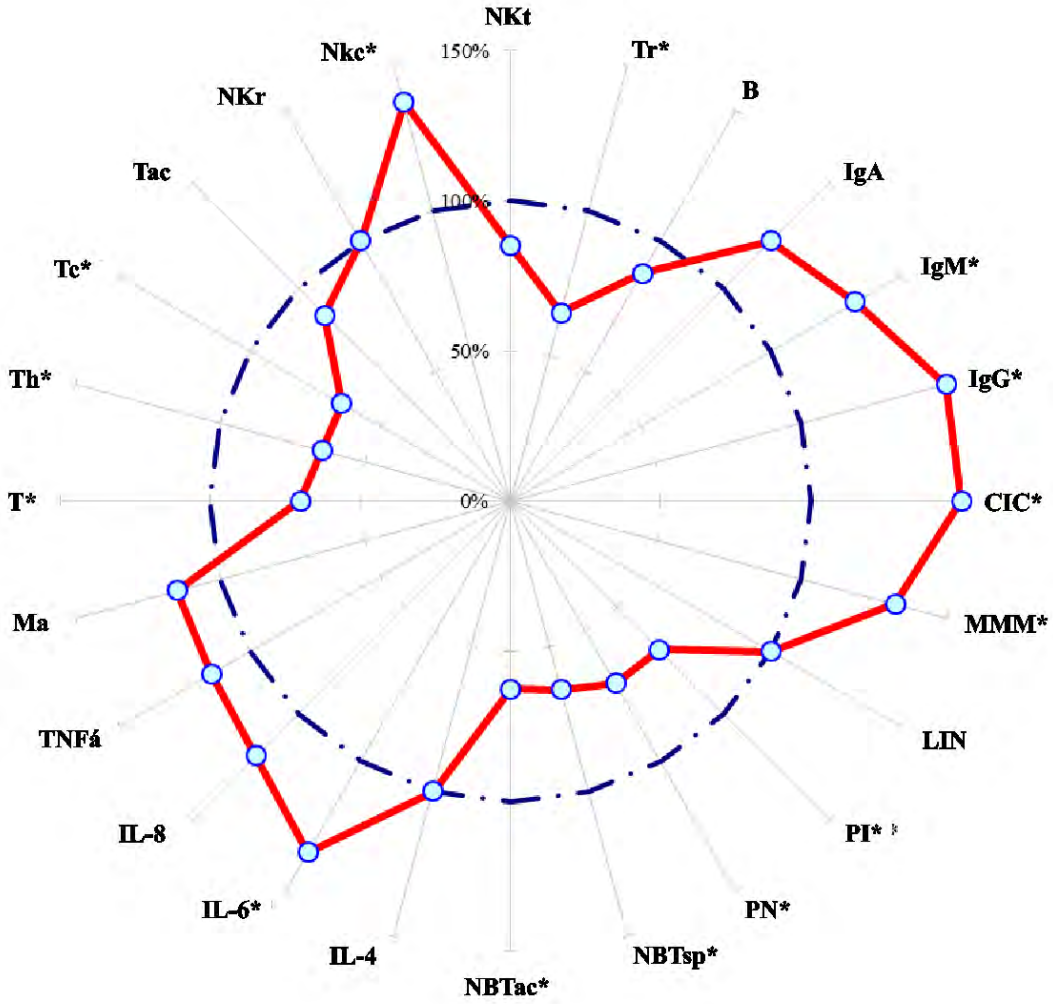


Fig. 2. Graphic visualization of differences in immunologic indexes from the normal level in patients with EDP before the treatment

Note: Tr-T-regulators, B – B-cells, IgA, IgM, IgG – immune globulins, CIC – circulating immune complexes, MMM – molecules of moderate mass, LIN – leucocytes with integreen receptors, PI, PN – phagocyte index and number, NBTsp, NBTac – spontaneous and activated tests with nitro blue tetrasolium, IL-4, IL- 6, I IL- 8 – interleukins, TNFα – tumor necrosis factor, Ma – apoptosis marker, T – T-cells, Th – T-helpers, Tc – T-cytotoxics, Tac – T-active, NKr – natural killers regulators, NKc – natural killers cytotoxics, NKt – natural killers thymus dependent, * – evidence of differences from norm in $p<0.05$, punctual line – normal meaning of parameters of healthy people, broken line – meanings of parameters of sick people

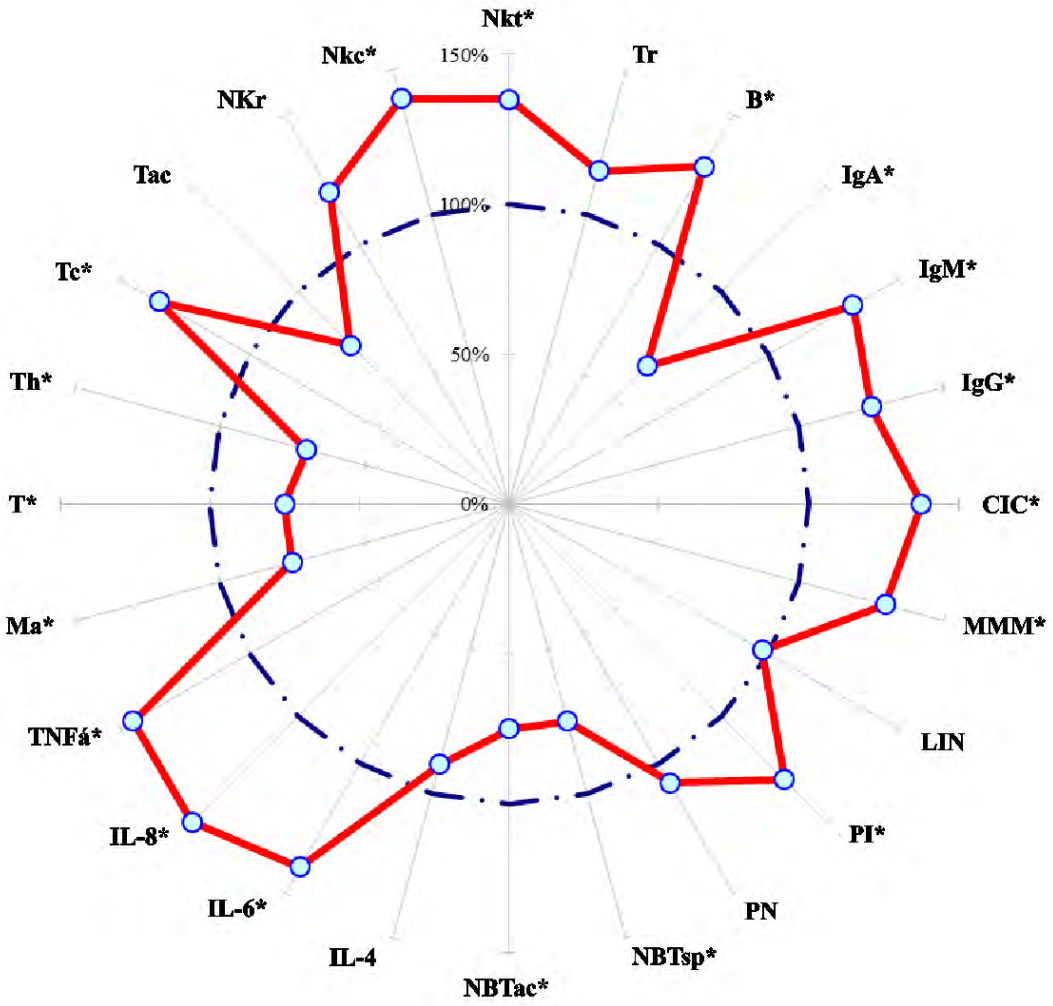


Fig. 3. Graphic visualization of differences in immunologic indices from norm in patients with ECPN before the treatment

Note: Tr-T-regulators, B – B-cells, IgA, IgM, IgG – immune globulins, CIC – circulating immune complexes, MMM – molecules of moderate mass, LIN – leucocytes with integreen receptors, PI, PN – phagocyte index and number, NBTsp, NBTac – spontaneous and activated tests with nitro blue tetrasolium, IL-4, IL- 6, I IL- 8 – interleukins, TNFα – tumor necrosis factor, Ma – apoptosis marker, T – T-cells, Th – T-helpers, Tc – T-cytotoxics, Tac – T-active, NKr – natural killers regulators, NKc – natural killers cytotoxics, NKt – natural killers thymus dependent, * – evidence of differences from norm in $p<0.05$, punctual line – normal meaning of parameters of healthy people, broken line – meanings of parameters of sick people.

While assessing the dynamics of moderate numbers of immunological indices from normal significance, and the outcomes of frequency and resulting frequency analysis, the most variations have been revealed in patients with ECPN (50), ESCO (45), EDP-38 tests. The determination of the level of immunologic indices changes has shown its moderate expressiveness in IDP cases and sufficient – in ECPN and ESCO cases.

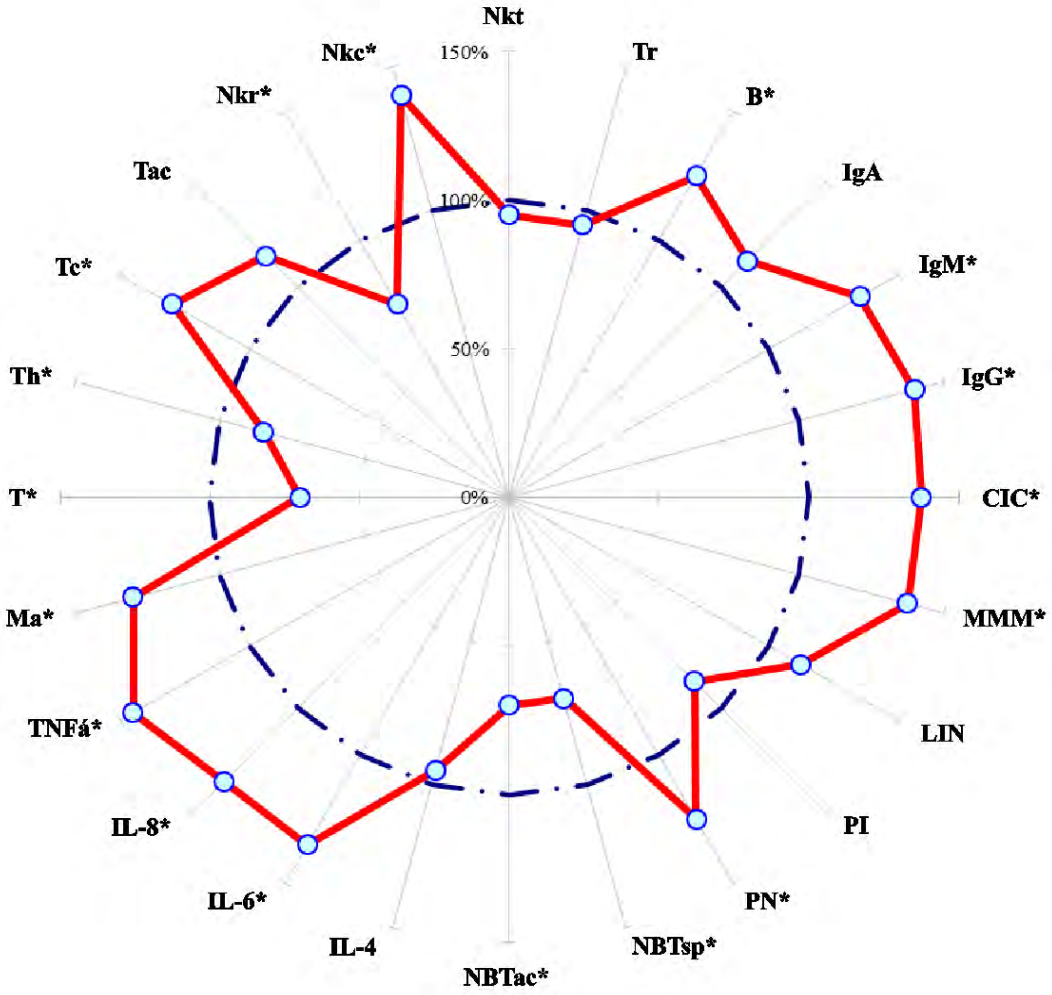


Fig. 4. Graphic visualization of differences in immunologic indices from norm in patients with ESCO before the treatment

Note: Tr-T-regulators, B – B-cells, IgA, IgM, IgG – immune globulins, CIC – circulating immune complexes, MMM – molecules of moderate mass, LIN – leucocytes with integreen receptors, PI, PN – phagocyte index and number, NBTsp, NBTac – spontaneous and activated tests with nitro blue tetrasolium, IL-4, IL- 6, I IL- 8 – interleukins, TNFα – tumor necrosis factor, Ma – apoptosis marker, T – T-cells, Th – T-helpers, Tc – T-cytotoxics, Tac – T-active, NKr – natural killers regulators, NKc – natural killers cytotoxics, NKt – natural killers thymus dependent, * – evidence of differences from norm in $p<0.05$, punctual line – normal meaning of parameters of healthy people, broken line – meanings of parameters of sick people

A detailed study of the immunologic mechanisms in concrete nosologic forms of pyoinflammatory diseases (PID) has revealed their dependence from pathogenesis. Thus FDIS decoding showed, that in EDP there was observed the accumulation of markers of the autoimmune processes (CIC), cytotoxic natural killers and anti-inflammatory cytokine (IL4). In ECPN – activation of humoral section of immunity in B-cells and MCM, the increase of cytotoxic lymphocytes, in TSCO – the presence of inflammation, disbalance of immunoglobulins of class G and T-cells. The data obtained have the evidence that despite the typical immunological body reaction on the general inflammation, there are concrete pathologies, dependent upon pathogenesis of diseases having a diagnostic significance.

Since the assessment and direct comparison of action effectiveness in the differentiated complex immunotherapy PID of different genesis with galavite between various

nosoforms of disorders due to clear reasons was incorrect, the analysis was done according to the correctors own effect, independent from the immunotropic activity of a traditional disease treatment. For this purpose we used a corresponding mathematic method. The data obtained are presented on figures 5-7 and in formulas of targets of galavite immunocorrection (FTI).

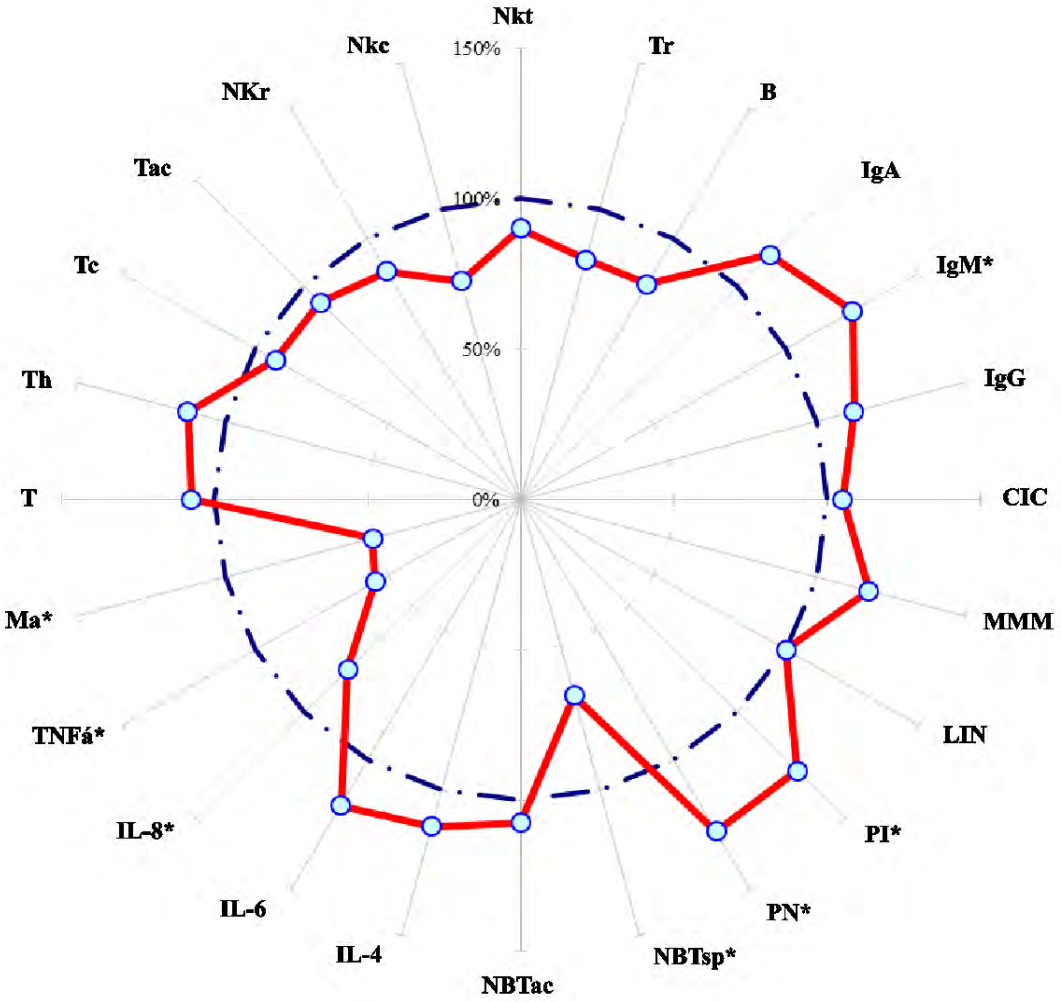


Fig. 5. Graphic visualization of galavite's own effect in patients with EDP

Note: Tr-T-regulators, B – B-cells, IgA, IgM, IgG – immune globulins, CIC – circulating, MMM – molecules of moderate mass, LIN – leucocytes with integreen receptors, PI, PN – phagocyte index and number, NBTsp, NBTac – spontaneous and activated tests with nitro blue tetrasolium, IL-4, IL- 6, IIL- 8 – interleukins, TNFα – tumor necrosis factor, Ma – apoptosis marker, T – T-cells, Th – T-helpers, Tc – T-cytotoxics, Tac – T-active, NKr – natural killers regulators, NKc – natural killers cytotoxics, NKt – natural killers thymus dependent, * – evidence of differences from normin, $p<0.05$, punctual line – normal meaning of parameters of healthy people, broken line – meanings of parameters of sick people.
Circumference – normal parameters of patients after traditional treatment

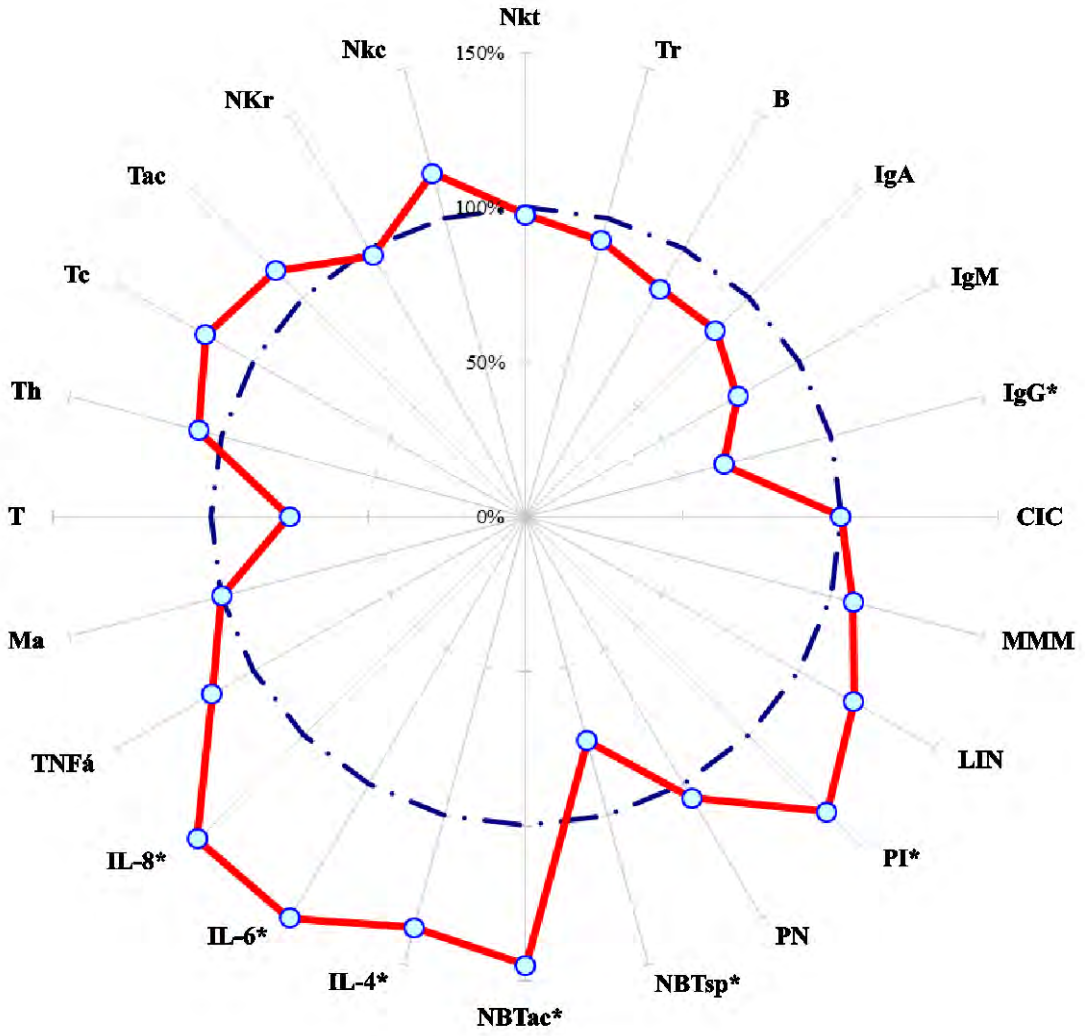


Fig. 6. Graphic visualization of galavite‘s own effect in patients with ECPN

Note: Tr-T-regulators, B – B-cells, IgA, IgM, IgG – immune globulins, CIC – circulating immune complexes, MMM – molecules of moderate mass, LIN – leucocytes with integreen receptors, PI, PN – phagocyte index and number, NBTsp, NBTac – spontaneous and activated tests with nitro blue tetrasolium, IL-4, IL- 6, I IL- 8 – interleukins, TNFα – tumor necrosis factor, Ma – apoptosis marker, T – T-cells, Th – T-helpers, Tc – T-cytotoxics, Tac – T-active, NKr – natural killers regulators, NKc – natural killers cytotoxics, NKt – natural killers thymus dependent, * – evidence of differences from norm in $p<0.05$, punctual line – normal meaning of parameters of healthy people, broken line – meanings of parameters of sick people

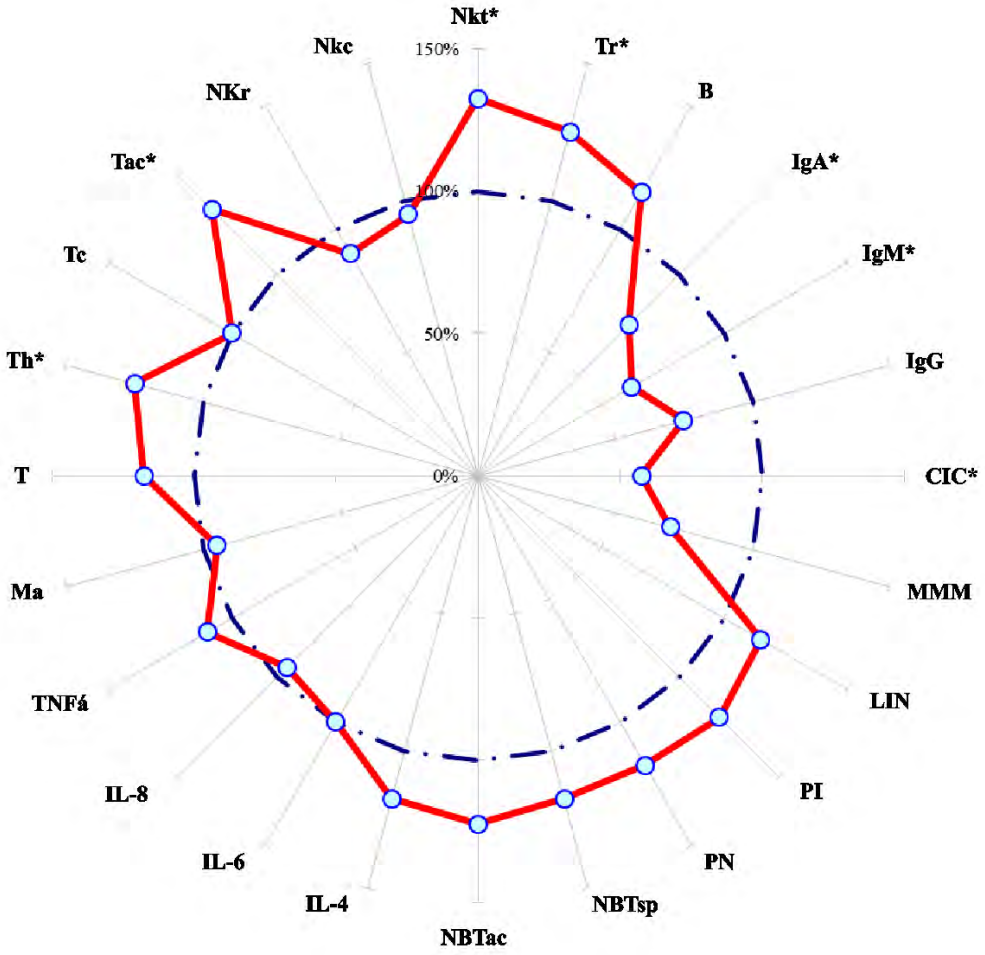


Fig. 7. Graphic visualization of galavite's own effect in patients with ESCO

Note: Tr-T-regulators, B – B-cells, IgA, IgM, IgG – immune globulins, CIC – circulating immune complexes, MMM – molecules of moderate mass, LIN – leucocytes with integreen receptors, PI, PN – phagocyte index and number, NBTsp, NBTac – spontaneous and activated tests with nitro blue tetrasolium, IL-4, IL- 6, I IL- 8 – interleukins, TNFα – tumor necrosis factor, Ma – apoptosis marker, T – T-cells, Th – T-helpers, Tc – T-cytotoxics, Tac – T-active, NKr – natural killers regulators, NKc – natural killers cytotoxics, NKt – natural killers thymus dependent, * – evidence of differences from norm in $p<0.05$, punctual line – normal meaning of parameters of healthy people, broken line – meanings of parameters of sick people

It was found out that under the galavite influence the patients with EDP have undergone some evident changes from the initial level 5 laboratory indices in 24 studied. The concentrations of IgM, phagocytes number have increased but NBTsp, the level of FNO and cells with apoptosis marker have decreased. The key targets of modulator in EDP were $TNF^-_3Ma^-_3IgM^+_2$.

In patients with ECPN the same preparation resulted in a significant dynamics from the initial level of 7 immunologic tests – a phagocyte index NBTac, IL-4, -6, -8 with a stimulating vector and NBTsp, IgG –with suppressing. The main points in the immune system of galavite modulator in ECPN were tests ($PI^+_3NBTsp^+_3$ IgG^-_3).

In women suffering from ESCO under the influence of galavite modulator has been achieved a mathematically significant change of 7 indices but their spectrum turned out to be different. The number of Th, Tac, Tr, NKt, IgA, -M concentrations have increased, CIC – have decreased. The main effect of the corrector has been produced on $NKt^+_3CIC^-_3IgM^-_3$.

These results show that the key targets in the immune system of the galavite modulator in patients with IDP, ECPN, ESCO have been different.

Preliminary studies have shown that the traditional therapy PID, in general, did not provide a complete correction of the changed clinical laboratory indices as a supplementary method of treatment a galavite modulator has been used.

Table 1

Rating assessment of differentiate treatment effectiveness in DIP in ranges

Treatment	Indices				N.L.	Summa of ranges	Effectiveness	Nosoform of PID
	Hem. M N	Bact. M N	Clin. M N	Imm. M N				
TT	1 2	1 2	1 1	3 2	4	17	6	
+Gal	1 1	1 2	1 1	3 1	3	14	4	EDP
TT	1 2	1 2	1 1	3 2	4	17	6	
+Gal	1 1	1 2	1 1	3 1	3	14	4	ECPN
TT	2 3	3 2	1 3	3 2	3	22	5	
+Gal	1 3	2 1	1 1	3 1	3	16	2	ESCO

Note: TT – traditional treatment, Gal – galavite, Hem – hematologic, Bact – bacteriologic, Clin - clinical, Imm – Immunologic indices, MN – mobile and normalizing effects, N.L. – number of strong correlation links, 1 2 – maximal and moderate ranges of effectiveness.

Due to the table data, a supplementary role of galavite at the background of the traditional treatment of all the PID nosoforms according to the outcome rating has provided an evident increase of its effectiveness in hematological, bacteriological, immunological and clinical indices. Besides, the preparation activity was higher in ESCO patients.

While analyzing the obtained data, we have documented the phenomena of typical variations formation of hemato-immunological inflammation markers, independent from PID pathogenesis. They were in the form of leukocytes masses, granulocytes, monocytes, accelerated ESR, disbalance or suppression of some immunity sections and the induction of the diagnostically significant laboratory changes on the subpopulation, interleukin, immunoglobulin levels, given in the formulary forms.

We have also determined qualitatively and quantatively differentiated clinic laboratory effects of combinations of traditional treatment with galavite, dependant from the pathogenesis of disorders and analyzed parameters.

It was also found that the traditional uncorrected treatment of different nosoforms of DGT as a whole proved to be insufficiently effective, and in particular – differentiated according to the effect on the grouped and individual indicators of patients. At the same time, normalization of clinical, bacteriological, and less often hematological and immunological parameters was observed, which puts additional immunotherapy of patients on the agenda. As its variants, modulators of various origins were chosen; stimulants of local and systemic immunity; its various links [28].

As a result of the application of formalized analytical approaches, the clinical and laboratory effectiveness of complex treatment of patients was shown to increase and the declining overall rating of its variants was determined. With UCP: 1 – roncoleukin with lycopide, 2 – lycopide, 3 – galavite, roncoleukin; with ECPN: 1 – superlymph with derinatom, 2 – galavite, 3 – derinate, 4 – superlimph; with ESCO: 1 – polyoxidonium, 2 – thymogen with polyoxidonium or galavite, 3 – thymogen. The effectiveness of one

traditional treatment in all cases was less pronounced.

Phenomena for achieving a new quality with a combination of modulators of different origin and mechanism of action relative to monoactivity have been established, as well as increasing the formation of standard formulas of immune system disorders of strong correlation links in the process of complex treatment of patients, tabl. 2, 3.

Table 2

Signal targets in the lymphoid system of differentiated immunotherapy of PID of various genesis

Treatment	FIT	FISD
EXTENSION OF DEEP PYODERMIA		
Traditional treatment	$B^{+}{}_{3}Tc^{+}{}_{3}NBTsp^{+}{}_{3}$	$IL8^{+}{}_{3}NKc^{+}{}_{3}Ma^{+}{}_{3}$
+roncoleukin	$Tac^{+}{}_{3}IgG\ {}_{3}T^{+}{}_{3}$	$IgM^{+}{}_{3}\ CIC^{+}{}_{2}Tac^{+}{}_{2}$
+lycopide	$FI^{+}{}_{3}NBTac^{+}{}_{3}IL6^{-}{}_{3}$	$Tr^{+}{}_{3}IgA^{+}{}_{3}Tc^{-}{}_{2}$
+galavit	$IL4^{+}{}_{3}TNF\ {}_{3}Ma^{+}{}_{3}$	$IL6^{+}{}_{3}NBTsp^{+}{}_{3}IL4^{+}{}_{3}$
+roncoleukin +lycopide	$NBTsp^{+}{}_{3}Tc^{+}{}_{3}Th^{+}{}_{3}$	$NKc^{+}{}_{3}IgG^{+}{}_{3}IL4^{+}{}_{3}$
EXTENSION OF CHRONIC PYELONEPHRITIS		
Traditional treatment	$T^{+}{}_{3}IgA^{+}{}_{3}\ CIC\ {}_{2}$	$NKc^{+}{}_{3}IgM^{+}{}_{3}TNF^{+}{}_{2}$
+superlimph	$Tr^{+}{}_{3}B^{+}{}_{3}Tc^{+}{}_{3}$	$Tr^{+}{}_{3}IgM^{+}{}_{3}NKt^{+}{}_{3}$
+derinate	$NBTsp^{+}{}_{3}FN^{+}{}_{3}NKr^{+}{}_{3}$	$T\ {}_{2}FI^{+}{}_{3}IgG^{+}{}_{3}$
+galavit	$FI^{+}{}_{3}IL4^{+}{}_{3}Tr\ {}_{2}$	$FI^{+}{}_{3}IL4^{+}{}_{3}Tr^{+}{}_{3}$
+superlimph +derinate	$Th^{+}{}_{3}Tr^{+}{}_{3}\ CIC\ {}_{3}$	$B^{+}{}_{3}FI^{+}{}_{3}Tc^{+}{}_{3}$
EXTENSION OF CHRONIC SALPINGFOORITIS		
Traditional treatment	$Tac\ {}_{2}IgM^{+}{}_{2}Th\ {}_{2}$	$IL8^{+}{}_{3}NKc^{+}{}_{3}Ma^{+}{}_{3}$
+thymogen	$Th^{+}{}_{3}Tc^{+}{}_{3}\ NKr^{+}{}_{3}$	$IgM^{+}{}_{3}\ CIC^{+}{}_{2}Tac^{+}{}_{2}$
+polyoxidonium	$Tr^{+}{}_{3}NBTsp^{+}{}_{3}FN^{+}{}_{3}$	$Tr^{+}{}_{3}IgA^{+}{}_{3}Tc^{-}{}_{2}$
+galavit	$FN^{+}{}_{3}IL4^{+}{}_{3}NKt^{+}{}_{3}$	$TNF^{+}{}_{3}B^{+}{}_{3}FI^{+}{}_{3}$
+thymogen +polyoxidonium	$Th^{+}{}_{3}NBTac^{+}{}_{3}MSM^{-}{}_{3}$	$NKc^{+}{}_{3}IgG^{+}{}_{3}IL4^{+}{}_{3}$

Note: TT – traditional treatment, Gal – galavite, Hem – hematologic, Bact – bacteriologic, Clin - clinical, Imm – Immunologic indices, MN – mobile and normalizing effects, N.L. – number of strong correlation links, 1 2 – maximal and moderate ranges of effectiveness.

Detailing the targets of correctors and creating programs for computers has allowed to formulate a simplified method of selecting active drugs for individual nosoforms for key laboratory markers. A six-level algorithm for the detection and treatment of immunocompromised contingents has been singled out and protected.

The first, prelaboratory, preliminary, on the basis of the questionnaire, the certificate for the computer program No. 2014519643.

The second, auxiliary on the basis of immunotropic treatment, the certificate for the computer program № 2015612811.

The third, unified on the basis of the formulas of the immune system disorders, the certificate for the computer program №2015614977.

The fourth, summarized on the basis of grouped indicators, certificate for the computer program No. 2015612811.

The fifth, detailed, based on a complete analysis of the immune status, certificate for the computer program No. 2014619846.

The sixth, personalized, based on the formulas of immunocorrection targets, the certificate for the computer program No. 201466056 and 2016619036.

Table 3

Additional laboratory indications for the selection of differentiated immunotherapy PID

Nosoform	Recommended treatment	Critical values of benchmarks
APP	Traditional treatment	**B**<0,2*10^{9}l,**Tc**<0,14*10^{9}l**, NBTsp**<2,9 CU
	+roncoleukin	**Tac**<0,04*10^{9}l, **T**<0,5*10^9, **IgG**>18,0 g/l
	+lycopide	**FI**<24,3%, NBTac<7,5%,**IL6**<пкг/ml
	+galavit	**IL-4**<5,5pkg/ml, **TNF**>0,32 pkg/ml, **Ma**>0,14*10^{9}л
	+roncoleukin+ lycopide	**B**<0,2*10^{9}l,**Tc**<0,14*10^{9}l, **NBTsp**<2,9%
ECPN	Ttraditional treatment	**T**<0,5*10^{9}l, **IgA**<0,5g/k, **CIC**>45,9 CU
	+superlimph	**NKr**<0,11*10^{9}l, **NKt**<0,18*10^{9}l, **IL4**<6,6 pkg/ml
	+derinate	**T**<0,03*10^{9}l, **Tc**<0,14*10^{9}l, **B**>0,6*10^{9}l
	+galavit	**FI**<24,3%, **IL4**<6,6 pkg/ml **Tr**<0,19*10^{9}l
	+superlimph+derean t	**Th**<0,38*10^{9}l, **Tr**<0,03*10^{9}l, **CIC**< 45,9 CU
ESCO	Ttraditional treatment	**Tac**>0,2*10^{9}l, **Th**>1,82*10^{9}l, **IgM**<0,6 g/l
	+thymogen	**Th**<0,38*10^{9}l, **Tc**<0,14*10^{9}l, **NKr**<0,11*10^{9}l
	+polyoxidonium	**Tr**<0,03*10^{9}l, **NBTsp**<2,9%, **FN**<2,4 mt
	+galavit	**FN**<2,4 mt, IL**4**<6,6 pkg/ml, NKt<0,18*10^{9}l
	+thymogen+ polyoxidonium	**Th**<0,38*10^{9}l, **NBTsp**<2,9%, **MSM**>9,1 CU

Conclusion

1. Patients with exacerbation of deep pyoderma, chronic pyelonephritis, and salpingooophoritis were found to have standard hematological changes (leukocytosis, neutrophilia, eosinophyllosis, monocytosis, lymphopenia, accelerated ESR), immunological (imbalance of cell, humoral, phagocytic defense, accumulation of CIC, MSM, pro-inflammatory cytokines), metabolic (suppression of antioxidant system factors, stimulation – free radical oxidation of lipids and proteins). Key formulas of laboratory disorders in patients have been determined, with the help of the diagnostic value coefficient.

2. Three clinical models with PID have shown a qualitative typical character of the immunopathology – a tendency to disbalance and suppression of T-section immunity, the activation of humoral, the suppression of phagocyte, the increased risk of autoaggressive and toxic conditions development, the accumulation of the proinflammatory cytokines.

3. It has been revealed a diagnostically significant influence of pathogenesis of each disorder on the concrete character and expressiveness of the immunopathology which was shown in individual FDIS patients: in EDP –$CIC^+_3NKc^+_3Il6^+_3$; in ECPN – $B^+_3MMM^+_2Tc^+_3$; in ESCO – $TNF^+_3IgG^+_3T^-_2$.

4. Traditional nonimmunotropic treatment of PID causes uneven normalization of clinical and laboratory status: with APP (acute purulent pyelonephritis) – significant (> 66%) elimination of changes in bacteriological, clinical and secondary (33-66%) – hemato-immunological indicators; with ECPN – significant – bacteriological, secondary – immunological, insignificant (<33%) – hematological, biochemical, clinical tests; at ECSO – average – bacteriological, immunological and insignificant – hematological and clinical parameters of patients.

5. A differentiated distribution of galavite action was established for laboratory parameters of patients with different PID: hematologic – significant for all nosoforms; on immunological – the average for ECPN, inessential – with APP and ECSO. The key effect of the modulator in the immune system with APP appeared to be oriented toward pro- and anti-inflammatory cytokines, CD95 + lymphocytes; with ECSO – in PI, IL4, Tr; at ECSO – on PN, IL4, NKt.

6. Additional application of differentiated immunocorrection in complex treatment of APP increases its final clinical and laboratory significance with the following decreasing rating of individual drugs: 1-roncoleukin + lycopide, 2-lycopide, 3-roncoleukin, 4-galavit, 5-traditional therapy.

7. Additional appointment of patients with ECPN immunocorrectors causes stimulation of the overall activity of complex treatment with the following rating of individual effects: 1-derinate + superlimph, 2-galavite, 3-derinate, 4-superlimph, 5-traditional therapy.

8. Additional inclusion in the conventional treatment of ECSO immunotropes potentiates its resulting efficacy with the following rating of the declining efficacy of specific drugs: 1-polyoxidonium, 2-thymogen + polyoxidonium or galavite, 3-thymogen, 4-traditional therapy.

9. With the combination of modulators in patients with PID, it is not mechanical summation of the properties of individual drugs that is realized, but an increase in the overall efficiency and transformation of the reference targets of the complex with respect to mono-actions. Thus, in case of APP, roncoleukin + lycopid causes activation of neutrophil metabolism, accumulation of regulatory subpopulations of T cells; with ECPN, superlymph + derinate – increase in the level of Th, NBTac and decrease in MSM; at ECSO timogen + polyoxidonium – stimulation of NBTsp, the number of Tc and Th.

10. As an auxiliary method of selecting the optimal variants of immunotherapy for purulent-inflammatory diseases, it is proposed to detail, with the help of the diagnostic value coefficient, formalized targets of action (FIT) of individual correctors and their combinations for determining signal laboratory markers.

11. A six-stage method for identifying immunocompromised individuals and choosing the optimal differential therapy for purulent-inflammatory diseases (an electronic assistant to a doctor) was developed based on the introduction of digital results of a laboratory examination of patients in a computer.

Conflict of Interest

The authors have no conflict of interest to declare.

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