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Reznikov K.M.²**COMPLEX CORRECTION OF PSYCHOEMOTIONAL
AND IMMUNOLOGICAL CHANGES IN PATIENTS WITH ACNE**¹NUZ «DKB at st. Voronezh-1» JSC« Russian Railways». 2, lane Zdorov'ya, Voronezh, 394024, Russia²GBOU VPO VSMU named by. N.N. Burdenko of the Ministry of Health of Russia. 10 Studencheskaya str., Voronezh, 394036, Russia.Corresponding author, ¹e-mail: samalyna@yandex.ru**Abstract.****Introduction:** The problem of complex therapy of acne attracts the attention of researchers because it accompanied with significant cosmetic defect and caused serious patient's experiences.**Objectives:** The aim of this study was to find ways to increase the efficacy and safety of treating patients with acne by complex pharmacological correction of its manifestations.**Methods:** The study included 110 people (32 men and 78 women) aged from 17 to 35 years, divided into 5 equal groups (according to the type of therapy) and observed for 6 months. All the patients underwent a comprehensive examination, including calculation of the dermatological index of acne (DIA), psychometric tests as well as an immunological study.**Results and discussion:** Monotherapy with combined topical agents leads to a decrease in DIA (48.75%) and the length of remission for more than 6 months in 46.4% of observations. Phabomotisol decreased DIA count and improved psychometric parameters. Ionized liquid (IL) led to an increase in CD4 + lymphocytes (14.48%) and immunoregulatory index (40.88%), decreased in the number of CD8 + lymphocytes (17.92%). The most effective combination was phabomotisol and IL (negative redox potential): DIA decreased (74.36%), remission of more than 1 year was observed in 22.7% patients.**Conclusion:** Effectiveness therapy with phabomotizol was shown. Effectiveness of IL in the complex treatment of acne in the medium-severe course of the disease is estimated for the first time. Presence of immunotropic properties of IL was established. Possibility of achieving long-term remission without the use of antibiotic therapy was demonstrated.**Keywords:** acne, adolescence, adult, acne complex therapy, psycho-emotional state, pharmacological correction, phabomotizol, ionized liquor, redox potential.**Introduction**

Acne is the most common skin disease. It occurs in about 85-95% of people aged 12-30 years and in 50% of patients – over 25 years [1, 2, 3]. The peak incidence corresponds to the period of social formation and psychological approval of a person [4, 5]. Acne is not a disabling pathology, but it can cause serious emotional disturbances. Patients with acne have a significant range of

psychological changes: anxiety disorders, dysmorphophobia, pathomimia, eating disorders, depression [6, 7, 8]. Severity of depressive symptoms is proportional to the degree of cosmetic defect in most cases [9, 10].

The pathogenetic basis of acne is hyperproduction of sebum, retentional hyperkeratosis of the sebaceous-hair follicle, proliferation of propionbacteria acne and

inflammation [1, 8, 9]. The presence of receptors in the sebaceous glands for neurotransmitters that are released in response to stimulation has also been established. It corresponds to the role of stress in enhancing of acne [9, 10, 11].

A variety of agents for the treatment of acne have been proposed. The main ones are systemic and topical antibacterial preparations of the group of tetracyclines, lincosamides, systemic and topical retinoids, which combined with oral contraceptives [1, 12, 13, 14, 15, 16, 17]. Systemic isotretinoin possesses indisputable efficacy in the cases of severe form of acne [18, 19]. However, many side effects and the absolute teratogenicity of this drug limits its wide application. Systemic antibacterial drugs (tetracycline, doxycycline, minocycline) act only on the ancestor propionibacteria without embracing other pathogenetic mechanisms [1, 2, 11, 16, 17, 20]. Yet they remain the drugs of choice for the treatment in case of moderately severe acne. The drugs are administered for a period of 7 days to several months, but in that case they have a significant negative impact on the microbiocenosis of the intestine and mucous membranes. Previous studies indicate the presence of changes in immunological parameters such as the increase in the content of CD8+ lymphocyte fraction, the decrease in the level of CD3+ and CD4+ populations of T-lymphocytes, the decrease in the immunoregulatory index (IRI=CD4+/CD8+) and the positive effect of immunomodulators in the complex treatment of acne [1, 16, 17, 18, 20]. Antibiotics and agents that affect immunity have several side effects. When they are combined, the pharmacological load and the spectrum of contraindications as well as the frequency of unwanted reactions increase. The greatest number of acne sufferers are teenagers with mild to moderate form [4, 9]. In this age group, it is better to prescribe drugs for topical use due to significant limitations and side effects of systemic drugs. However, the main topical anti-acne preparations (alcohol solutions of clindamycin, erythromycin, benzoyl peroxide, retinoids – adapalene compound) have side effects in the form of erythema, dryness and flaking of the skin. These reasons can cause premature self-canceling of the treatment by a patient.

Understanding the role of immunological, psychosomatic changes in acne as well as positive

assessment of the prospects for the use of appropriate drugs creates the prerequisites for the search of new effective and safe schemes of complex correction of this disease [21, 22]. The effectiveness of the use of psychotropic drugs in a number of patients with acne was proven [23, 24]. Many scientific researches suggested these methods of pharmacological correction for use in practical medicine about 10 years ago [1, 11, 12, 25]. However, there is no data on the use of phabomitol in this disease. Ionized liquids with positive and negative oxidation-reduction potential that are used for the first time in the treatment of acne are currently prescribed to treat eczema and psoriasis in dermatology and to treat purulent wounds in surgery [26].

The purpose of this study is to find the way for the improvement of the effectiveness and safety of treatment in patients with moderate acne by using complex pharmacological correction of psychoemotional, immunological changes and cutaneous manifestations of acne.

Objectives

1. Investigate the possibilities of standard acne therapy.
2. Study the effectiveness of treatment of moderate acne with the use of topical monotherapy.
3. Establish the possibility of including in the complex therapy of acne anxiolytics such as phabomitol and synthesized ionized liquids with different oxidation-reduction potential.
4. Conduct a comparative analysis of various programs for the treatment of acne according to clinical, psychoemotional and immunological indicators.
5. To substantiate the application of the most effective and complex ways for pharmacological correction of psychoemotional, immunological disorders and cutaneous manifestations of acne.

Scientific novelty of the study

The therapeutic efficacy of phabomitol in the correction of psychoemotional changes in acne has been proved for the first time. It has been demonstrated that a combination of standard external therapy with taking phabomitol in a dose of 5 mg 3 times a day during a month effectively corrects psychoemotional changes and cutaneous manifestations of acne.

A positive effect of innovative external therapy (anti-inflammatory lotion containing 3% alcohol solution of chloramphenicol once a day in

the morning 2 to 4 weeks, a peeling lotion containing benzoic acid 1.0, salicylic acid 2.0, camphor alcohol 5-15.0, boric acid 3.0, Streptocide 7.0 and whitening ointment containing zinc, boric acid at 1.5-2.5, 30% hydrogen peroxide 0.5 and zinc ointment 25.0 at night once a day on the skin of the face, excluding the paraorbital area, for 2-4 months) has been established.

The evidence of the immunomodulatory action of a liquid with negative AFP that is administered at a dose of 2 ml/kg of body weight was received by the basis of changes in the immunograms of patients with acne.

New data has been obtained on the positive effect of ionized fluids with positive and negative redox potential on acne eruptions and post-acne changes.

A positive pharmacodynamic interaction of phabomitol and ionized liquid with a negative redox-potential was established, which is expressed in the greater effectiveness of their combination compared to the separate application with the standard external agents. This combination can be considered optimal for reducing the dermatological index of acne (DIA) and increasing the duration of remission. This therapeutic method allows to abandon the use of systemic antibiotic therapy. The incidence of side effects decreases from 81.2% to 4.5% in the case of using complex therapy as a combination of topical agents, phabomitol and ionized fluids with different AFP.

The theoretical significance of the work lies in the development of a system that makes it possible to assess the possibility of changing the therapeutic activity of a pharmacological agent by changing the redox potential of body fluids. For practical medicine, the prospect of a comprehensive correction of acne with the use of phabomitol and liquids with various oxidation-reduction potentials against the background of standard external pharmacotherapy has been proved. This allows to optimize treatment, withdraw from the systemic antibacterial drugs, minimize the frequency of side effects, increase the duration of remission, reduce the cost of treatment, which makes it reasonable to use the proposed scheme of dermatology and cosmetology. New data obtained in this study can supplement the relevant courses in dermatology,

cosmetology, pharmacology, clinical pharmacology.

All the studies were carried out in accordance with the requirements of the current guidelines: the ethical norms of the Helsinki Declaration of 1964, modified by the 41st World Assembly (Hong Kong, 1989) and the 52nd General Assembly of the WMA (Edinburgh, Scotland, UK, 2000), the Lisbon Declaration on the Rights of Patients, (Lisbon, Portugal, 1981), in section V of the Code of Medical Ethics, approved by the XVIII All-Russian Pirogov Congress of Physicians (07.06.1997). All patients signed informed consent, allowing at any time to stop the study.

Personal contribution to the study

Personal contribution consists in the direct participation of the author of the thesis in the study of many scientific sources of Russian and foreign literature, the selection of patients for participation in the study, filling out individual medical records, in systematizing and statistical processing of the data obtained and analyzing the results.

Methods

All patients with papulo-pustular form of acne were on outpatient treatment at the DKB at st. Voronezh-1 RZhD in the period from 2010 to 2014 inclusively. The work was carried out at the Stationary Unit No. 3 of DKB (the Chief Doctor – Doctor of Medical Sciences, Professor Novomlinsky V.V.), the Department of Pharmacology and the Department of Dermatovenereology of the VSMU named after N.N. Burdenko (Rector – Professor I.E. Esaulenko). The results of the examination and treatment of 110 patients of different sexes – 32 men (29.09%) and 78 women (70.9%) with acne of moderate severity were used for the thesis. Diagnosis – Acne vulgaris (L70.0) – was delivered in accordance with the X International Classification of Diseases on the basis of clinical and anamnestic data.

The majority of the subjects had an age of 16 to 25 years, which corresponds to literary data on the incidence of acne. Based on the clinical picture and by counting the elements of the rash, we evaluated the condition of the patients and included acne with a moderate degree of severity in the study. For the quantitative evaluation of each type of acne-elements, the dermatological index of acne (DIA) was calculated in points. The

duration of the disease varied from several months to 10 years. During this time, patients either did not seek help expecting spontaneous cure or visited cosmetic rooms. Some of them previously underwent outpatient treatment (with greater or less effectiveness), which did not allow achieving a stable remission. 73.6% (81 patients) of young men and women showed a background somatic pathology – diseases of ENT and gastrointestinal tract, allergic reactions. The criteria for inclusion in the study were: the presence of the disease – acne of moderate severity and post-acne changes (atrophic scars, post-inflammatory pigmentation, breach of skin microrelief), age from 17 to 35 years, written informed consent of the patient. The criteria for exclusion were: indication of the diseases in the acute stage, diabetes mellitus, pregnancy, lactation, individual intolerance of the proposed therapy, disagreement of the patient.

All patients were assigned standard laboratory tests – a general blood test, a biochemical blood test, a hormonal status. Subjects with the revealed endocrine pathology and changes in the content of sex hormones from laboratory data were sent to the appropriate specialists. In addition, the parameters of cellular and humoral immunity (number of T and B lymphocytes, immunoglobulins Ig M, Ig G, Ig A, immunoregulatory index (IRI=CD4 +/CD8+) were estimated additionally. The value of the dermatological index of acne-DIA was calculated by the formula $A + B + C + D$, where A is the score by the number of comedones, B is the number of pills, and C is the number of pustules and D – nodes. The patient's psychometric data was assessed by determining the levels of anxiety and depression on the Tsung scale, State of health, activity, mood.

Regardless of age and sex, patients were randomly assigned to 5 groups (22 patients each) using a randomization table in accordance with the treatment regimen used. In the first group (n = 22) patients were prescribed standard therapy – doxycycline monohydrate tablets ("Unidox Solutab") 100 mg twice a day for 7-14 days, topicals – combination of adapalene with clindamycin (gel "Clenzite-C") 1 time per day for 2-4 weeks, then – adapalene (gel "Clenzite") 2-4 months. A cream with 20% azelaic acid (Skinoren) was applied 2 times a day 2-4 months after the main course of treatment to prevent

exacerbations and post-acne correction. To normalize the intestinal microflora, all patients within 14 days in addition received capsules containing *Lactobacillus acidophilus*, *Bifidobacterium infantis*, *Enterococcus faecium* ("Linex" preparation) 1 capsule 3 times a day. Sunscreen was prescribed if treatment took place in summer.

The second group (n = 22) consisted of patients who did not receive systemic drugs. For topical therapy, combined topical agents were used in the form of an anti-inflammatory lotion containing 3% alcohol solution of chloramphenicol once a day in the morning 2-4 weeks, a peeling lotion containing benzoic acid 1.0, salicylic acid 2.0, camphor alcohol 5-15.0, boric acid 3.0, Streptocide 7.0, and bleaching ointment containing zinc, boric acid at 1.5-2.5, 30% hydrogen peroxide 0.5 and zinc ointment 25.0, at night once a day on the skin of the face, excluding the paraorbital area, for 2-4 months. In addition, a moisturizing lipid-replenishing day cream was prepared from medicinal cosmetics for problem skin and sunscreen for treatment in the summer.

In the third group of patients (n = 22), in addition to the above-described topical combined external agents of standard therapy, phabomotisol was administered at 5 mg 3 times a day for a month.

The fourth group of patients (n = 22) did not receive any drugs internally. For external therapy, the same combination of topical anti-inflammatory agents in the form of lotion, lotion-peeling and whitening ointments were used. Ionized fluids with different AFP were appointed in accordance to the protocol of the study based on the patient's written consent and permission of the Ethics Committee. Anolit – ionized fluid with a positive redox potential (ORP = +600 +900, pH = 6 – 7) was used in the form of applications locally 1 – 2 times daily 2 – 4 weeks. Catholyte – ionized fluid with a negative redox potential (ORP = -400 – 500, Ph = 8 – 9) was administered internally in a dose of 2 mL/kg body weight 1 times a day for 14 days. Ionized fluid was obtained in an electrolytic cell «Karat-M» Tu 3468-001-51702726-2006, certificate of conformance № ROSS RU AJA60V21343, from bottled spring water.

The fifth group used complex therapy including the topical multicomponent agents

described above and containing chloramphenicol, streptocid, benzoic, boric and salicylic acids, camphor alcohol, zinc, and anolyte externally. Fabomotizol in the dose of 5 mg 3 times a day for a month and catholyte in the dose of 2 ml per kg of body weight once a day for 14 days were administered internally.

The results were evaluated before the treatment and after 1, 3 and 6 months of therapy on the basis of patient complaints, their subjective sensations, changes in the clinical picture, dynamics of DIA and psychometric tests, and also on the basis of changes in the parameters of cellular and humoral immunity. DIA was determined before and during treatment – after 1, 3 and 6 months. Psychometric tests were performed before and 3 months after the therapy. The immunogram was evaluated at the beginning of the study and within 20 days after the end of the catholyte intake. The data were recorded and statistically processed. During the statistical analysis, methods of descriptive variational statistics were used. Correlation analysis was used to identify the relationship among the features being investigated. Regression analysis was used to establish the nature of the dependencies of variables. The results were processed in IBM SPSS Statistics v.22 and Microsoft Office Excel 2003 SP3 in the Windows 7 operating system.

Various pharmacotherapeutic methods for the therapy of acne of moderate severity were used in the work.

Results and discussion

The first group (therapy included doxycycline monohydrate and bifidopreparation internally, a combination of adapalene with clindamycin, azelaic acid externally) included 22 patients (6 young people and 16 girls). The dermatological index of acne before treatment ranged from 6 to 10 and averaged 7.1 points. Duration of the disease was from 6 months to 5 years. Six months after the start of standard therapy, DIA on average decreased by 33.12% and corresponded to mild acne in 45.5% of patients (Figure 1).

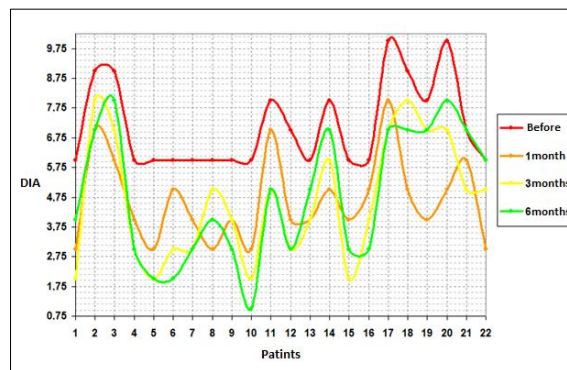


Fig. 1. Dynamics of changes in DIA (scores) in each patient with standard therapy

During the therapy, the following side effects were revealed: redness, dryness, burning, dyspeptic disorders, which were noted by 18 people (81.8%). Standard treatment promoted the onset of remission on average by 2.5 months (Figure 2).

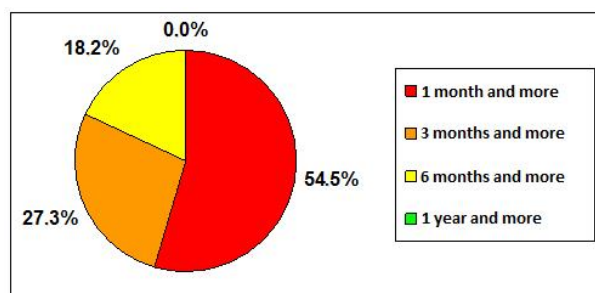


Fig. 2. Duration of remission in patients with acne (standard therapy, %)

When studying the parameters of the immunogram before and after the treatment, serious differences were not found in the patients of the first group, which leads to the conclusion that the standard complex therapy of acne does not significantly affect the parameters of the immune response.

After 3 months from the beginning of the main course of the treatment, positive changes in the indicators of the psychoemotional status of the patients of the first group were recorded. Their dynamics is presented in Table 1.

Table 1

Dynamics of psychometric indicators (M±m, score, %) standart treatment (n=22)

№	Index	Terms of observation	
		Before treatment	After treatment
1	Anxiety	30.91 ± 1.28	28.91 ± 1.07*(93.53%)
2	Depression	39.00 ± 1.52	35.50 ± 1.21*(91.03%)
3	Health	29.36 ± 0.97	35.95 ± 1.09*(122.45%)
4	Activity	27.61 ± 0.74	33.89 ± 1.12* (122.75%)
5	Mood	30.52 ± 0.86	36.18 ± 0.99*(118.55%)

Note: * – p<0.05 compared with the indicators before treatment

Thus, after 6 months from the beginning of the treatment, the DIA index on average decreased by 33.12%, anxiety of patients decreased by 6.47%, depression – by 8.97% and SAN test data improved by an average of 21.25%. Remission for more than half a year was observed in 18.2% of cases and averaged 2.5 months. Adverse effects of therapy were noted by 81.4% of patients (p<0.05).

In 22 patients (5 young people and 17 girls aged 17 to 24 years) of the second group, the duration of the disease was from 1 to 6 years and DIA averaged 7.3 points. For acne therapy, only the above-described combined topical agents were used. One month after the start of the treatment, in 63.6% of patients, DIA decreased to mild acne and six months later decreased by 48.75% (p<0.05). A graphic representation of the dynamics of the DIA is shown in Figure 3.

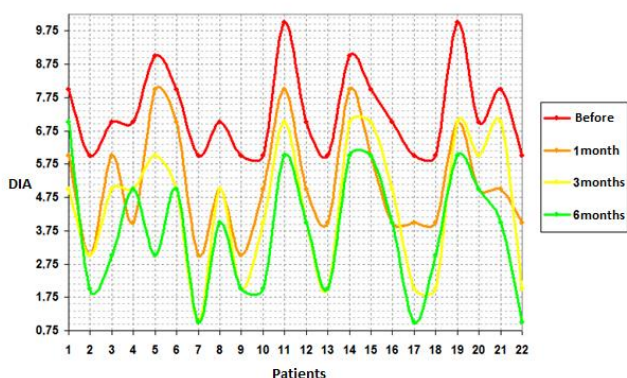


Fig. 3. Dynamics of changes in DIA (scores) in each patient in the appointment of combined topical therapy

The duration of clinical remission exceeded that for the administration of systemic antibiotic therapy and averaged 5.3 months (Figure 4).

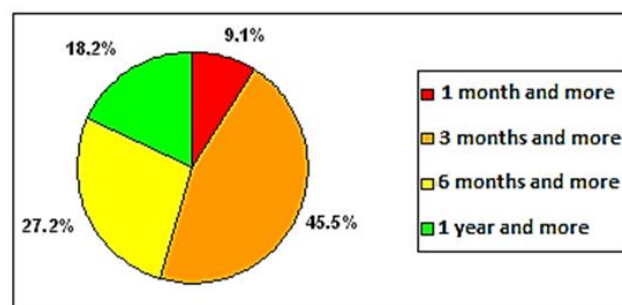


Fig. 4. The duration of remission in patients with acne in the appointment of combined topical therapy, %

Side effects of the therapy (flaking, erythema and dry skin sometimes) were noted by patients in 2 cases (9.1%).

When studying the parameters of the immunogram before and after the treatment, no significant differences were found in the patients of the second group. Thus, acne therapy with standard combined topical drugs did not affect the immune status indicators of the subjects.

After improvement of the clinical picture of the disease, according to the data of the anxiety, depression and SAN scales, positive changes were observed: in the majority of patients, anxiety and depression indicators decreased and SAN increased (Table 2).

Thus, as a result of therapy with combined topical agents, anxiety of patients decreased by 11.06%, depression by 12.71%, SAN test data improved by an average of 28.3%. The DIA indicator on average decreased by 48.75%. Remission of more than 6 months was observed in 46% of cases. The side effects of the therapy were sometimes noted by 9.1% of patients (p<0.05).

Table 2

Dynamics of psychometric indicators (M±m, score, %) of patients with the appointment of combined topical therapy (n=22)

№	Index	Terms of observation	
		Before treatment	After treatment
1	Anxiety	31.64 ± 1.26	28.14 ± 0.98* (88.94%)
2	Depression	37.55 ± 1.40	32.77 ± 1.83* (87.29%)
3	Health	28.68 ± 0.95	37.14 ± 0.92* (129.48%)
4	Activity	27.44 ± 0.92	35.48 ± 0.98* (129.3%)
5	Mood	29.23 ± 1.04	36.87 ± 1.02* (126.14%)

Note: * – p<0.05 compared with the indicators before treatment.

Changes in the clinical picture and psychoemotional status of patients with acne when phabomositol was included in the program of the treatment. In the third group (n = 22), including 7 young people and 15 girls aged from 18 to 27 years, in addition to combined external therapy, phabomotisol was administered internally in a dose of 5 mg 3 times a day for a month. The duration of the disease varied from 6 months to 5 years. The average index of DIA was 7.1 points. After 6 months of therapy, the DIA index decreased by 56.41% (p<0.05) and was equal to 1 in 36.4% of patients. The skin was almost pure. All patients noted the disappearance of fatty gloss on the face, which is associated with the normalization of sebum and the effect of lightening the skin. A graphic representation of the intensity of the rash in patients receiving external therapy in combination with phabomotisol is shown in Figure 5.

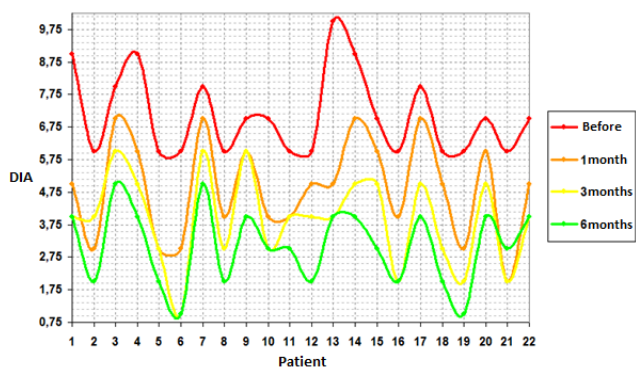


Fig. 5. Dynamics of changes in DIA (scores) in each patient treated with phabomotisol

A sufficient effectiveness of treatment is confirmed by a decrease in the frequency of side effects. Most of the subjects did not make any complaints. Redness and dryness of the skin were sometimes noted only by 2 patients treated in the autumn-winter period. The duration of remission also increased (p <0.05) and averaged 5.2 months (Figure 6).

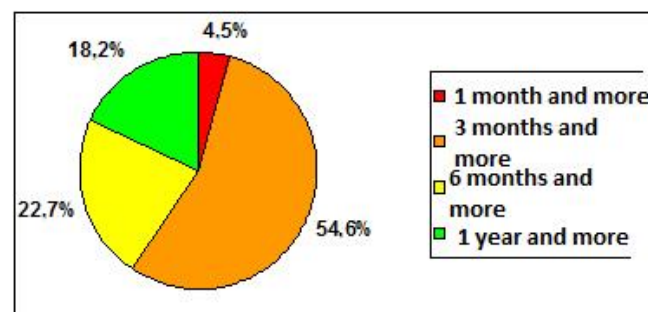


Fig. 6. Duration of remission in acne patients treated with phabomotisol, %

According to the received data, the main indices of the immunograms of the subjects were not changed significantly. Mathematical processing of the obtained results showed no significant effect of the inclusion in the therapy of phabomotisol on the immune status of patients of the third group.

The results of therapy indicate a decrease in anxiety rates by 20.55%, depression by 12.81% and an increase in SAN scores by an average of 32.03% (p<0.05). These changes in the psychometric parameters of patients in the third group are presented in Table 3.

Table 3

Dynamics of psychometric indicators (M±m, score, %) of acne patients treated with fabomotisol (n=22)

№	Index	Terms of observation	
		Before treatment	After treatment
1	Anxiety	31.64 ± 1.39	25.14±0.73* (79.45%)
2	Depression	34.77 ± 1.49	30.32 ± 0.91* (87.19%)
3	Health	27.59 ± 0.94	36.69 ± 0.92* (132.98%)
4	Activity	28.91 ± 0.88	37.55 ± 0.82* (129.87%)
5	Mood	26.98 ± 0.91	35.95 ± 0.88 *(133.24%)

Note: * – p<0.05 compared with the indicators before treatment.

Mathematical processing of the obtained data indicates more significant changes in the clinical picture of this group than in the previous groups: DIA decreased by 56.41% (p<0.05), remission of more than 1 year was observed in 18.2% of cases, the side effects of the therapy were sometimes noted by 9.1% of patients (p<0.05). A significant decrease in anxiety scores was detected – by 20.55% (p<0.05). Analyzing the presented results, we came to the conclusion that this effect can be explained by the inclusion of phabomotisol in the treatment program. The effectiveness of therapy for acne disease when included in the treatment of ionized fluids.

According to the design of the study, the number of patients in the fourth group corresponded to the previous (n = 22) – 6 young people and 16 girls aged 18 to 26 years. The duration of the disease varied from 1 to 7 years. The dermatological index of acne was consistent with the diagnosis and averaged 6.9 points. In addition to the combined topical drugs, according to the study protocol, patients were assigned ionized fluids: anolyte (ORP = + 600 + 900, pH = 6-7) was used locally for inflammatory elements 1-2 times a day for 2-4 weeks and catholyte (ORP = -400-500, pH = 8-9) was administered internally in a dose of 2 ml / kg body weight once a day for 14 days.

After half a year of observation and treatment in 50% of cases, the skin was practically clean, the dermatological acne index was equal to 1-2 points. On average, the number of rashes decreased by 61.84% (p <0.05). A graphic representation of the positive effect of treatment

on the dynamics of DIA of each patient of the fourth group is shown in Figure 7.

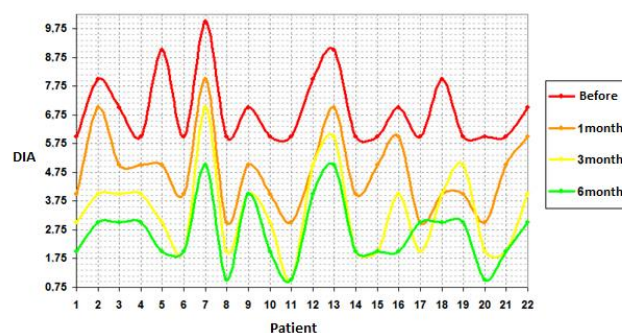


Fig. 7. Dynamics of changes in DIA (scores) in each patient patients when included in the treatment of ionized fluids

Only 1 person (4.5% of cases) during the treatment experienced redness and dryness of the skin. The remission of patients of the fourth group averaged 5.5 months (Figure 8).

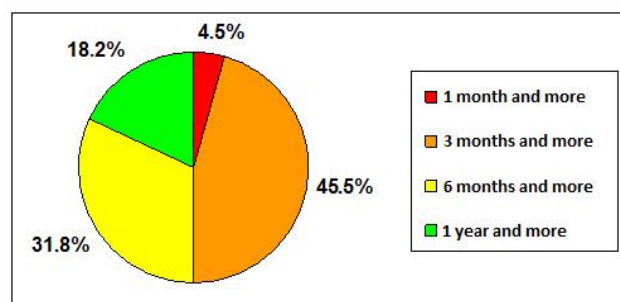


Fig. 8. Duration of remission of patients with acne when included in the treatment of ionized liquids, %

Analysis of the patients' immunograms revealed significant positive changes after the treatment: CD8 + lymphocyte count decreased by 16.9%, CD4 + lymphocyte count increased by 13.52%, immunoregulatory index (IRI) increased by 38.73% ($p < 0.05$).

After the therapy, anxiety and depression levels on the Tsung scale were significantly reduced. The dynamics of the investigated parameters is presented in Table 4.

Thus, as a result of the therapy, DIA

decreased by 61.84% ($p < 0.05$), the average duration of remission was 5.5 months. Side effects of the therapy were observed in 4.5% of cases. Mathematical processing of data made it possible to reveal more positive dynamics of the results of psychometric tests after the treatment in this group than in previous groups: anxiety of patients decreased by 22.53% ($p < 0.05$), depression – by 19.11% ($p < 0.05$), the indices for the SAN test improved by an average of 49.03% ($p < 0.05$).

Table 4

Dynamics of psychometric indicators (M±m, score, %) in patients with the inclusion of ionized fluids (n=22)

№	Index	Terms of observation	
		Before treatment	After treatment
1	Anxiety	31.27 ± 1.27	24.23 ± 0.70* (77.47%)
2	Depression	36.86 ± 1.33	29.82 ± 0.77* (80.89%)
3	Health	28.05 ± 0.78	42.64 ± 1.17* (152.03%)
4	Activity	29.27 ± 0.81	43.41 ± 1.1* (148.3%)
5	Mood	28.52 ± 0.9	41.86 ± 0.97* (146.77%)

Note: * – $p < 0.05$ compared with the indicators before treatment.

The use of phabomotisol and ionized fluids with positive and negative AFP in complex acne therapy.

According to the protocol of the study, the number of patients in the fifth group who received complex therapy was 22 people – 8 young people and 14 girls aged 18 to 28 years. The duration of the disease varied from 1 to 10 years. Before the start of therapy in this group, the dermatological index of acne averaged 7.1 points. In addition to combined topical agents and anolyte externally, patients were prescribed phabomotizol in a dose of 5 mg 3 times a day for a month and catholyte in a dose of 2 ml / kg body weight once a day for 14 days internally.

A month after the start of the treatment in 68.2% of cases, DIA decreased to light acne by 30.77% ($p < 0.05$). After 3 months, 36.4% ($p < 0.05$) of the rash virtually disappeared (DIA 1-2). On average, the number of rashes decreased by 56.41% ($p < 0.05$). After a half of a year of the observation and treatment, 81.2% of patients did not complain, because the skin was practically clean of the acne-elements. Only comedones were present in the seborrheic zones. The level of decline in DIA as a whole

was 74.36% ($p < 0.05$). In all, one patient (4.5%) was noted to have tightness of the skin (sometimes). A graphic depiction of the decrease in the intensity of acne eruptions in patients of the fifth group is shown in Figure 9.

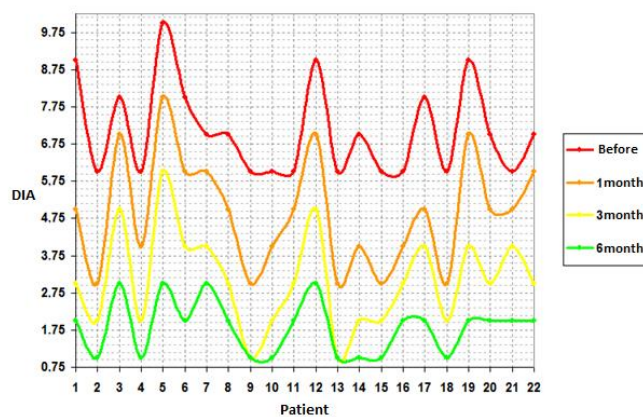


Fig. 9. Dynamics of changes in DIA (scores) in each patient treated with phabomotisol and ionized fluids

The results obtained also demonstrate an increase in the duration of remission, which averaged 6.1 months and 22.7% of patients continued for more than 1 year (Figure 10).

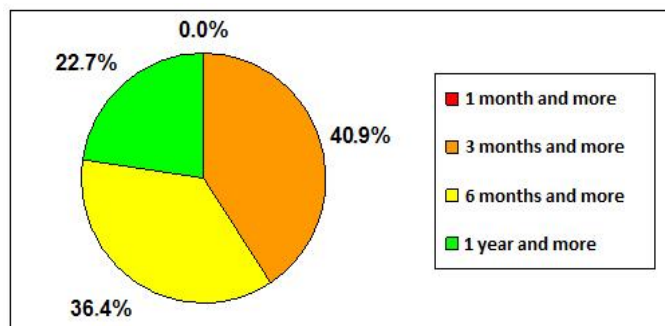


Fig. 10. The duration of remission when included in the treatment of acne phabomitol and ionized fluids, %

After inclusion in the treatment regimen of acne phabomitol and ionized fluids, the patient's immunograms changed significantly (table 5): the number of CD4 + T-cells increased by 14.48%, the immunoregulatory index increased by 40.88%, the number of cytotoxic CD8 + lymphocytes decreased by 17.92% ($p < 0.05$).

Table 5
Dynamics of changes in immunological indices (M±m, UD, %) of patients treated with phabomitol and ionized fluids (n=22)

№	Indicators immunity	Terms of observation		Percent changes
		Before treatment	After treatment	
1	Leukocytes	6.26 ± 0.35	6.07 ± 0.17	96.7
2	Lymphocytes	25.41 ± 1.66	28.55 ± 1.46*	115.17
3	CD3+	71.93 ± 1.67	73.16 ± 1.16	101.91
4	CD19+	9.53 ± 0.91	10.90 ± 0.79	107.78
5	CD4+	36.31 ± 1.69	41.05 ± 1.71*	114.48
6	CD8+	27.32 ± 1.14	22.50 ± 0.85*	82.08
7	Immunoregulatory index	1.36 ± 0.10	1.89 ± 0.11*	140.88
8	NK	10.07 ± 1.06	10.01 ± 0.76	98.96
9	Phagocytic activity of neutrophils	59.55 ± 1.47	63.68 ± 1.35*	88.22
10	IgG	13.34 ± 0.67	11.79 ± 0.44*	86.84
11	IgM	1.87 ± 0.13	1.63 ± 0.08*	88.29
12	IgA	2.40 ± 0.18	2.10 ± 0.14	11.71

Note: * – $p < 0.05$ compared with the indicators before treatment.

According to the obtained data on the change in the psychoemotional state of patients (Table 6), as a result of treatment of patients in the fifth group, anxiety rates decreased by 25.68% ($p < 0.05$), depression by 15.17% ($p < 0.05$), The results of the SAN test improved by 52.75% ($p < 0.05$).

Analyzing the presented results, it can be concluded that a pronounced clinical effect (a decrease in DIA by 74.36%) and the longest remission (an average of 6.1 months) were observed with the inclusion of phabomitol and

ionized fluids in the combination of topical acne therapy.

Comparative analysis of acne treatment results using different therapy programs.

One of the main indicators of the effectiveness of the treatment is the magnitude of DIA, which characterizes the degree of positive changes in skin condition. Analysis of the obtained data shows that in the fifth group the decrease in the intensity of the precipitation was maximal: after 6 months, decreasing by 74.36%.

Table 6

Dynamics of psychometric indicators (M±m, scores, %) in patients treated with phabomotisol and ionized fluids (n=22)

№	Index	Terms of observation	
		Before treatment	After treatment
1	Anxiety	31.68 ± 1.46	23.55 ± 0.58*(74.32%)
2	Depression	34.45 ± 1.38	29.23 ± 0.90*(84.83%)
3	Health	29.23 ± 1.32	44.55 ± 1.25*(152.41%)
4	Activity	30.18 ± 1.05	45.67 ± 0.95*(151.32%)
5	Mood	28.40 ± 1.16	43.89 ± 1.04* (154.54%)

Note: * – p<0.05 compared with the indicators before treatment.

In the appointment of IL with negative AFP, in conjunction with phabomotisol, the maximum increase in the total SAN index was observed by 52.75% in patients of the fifth group and the decrease in anxiety scores by 25.68% (p <0.05), which is associated with a positive pharmacodynamic interaction of the drugs. In addition, the conducted correlation analysis demonstrated the dependence of the amount of dermatological index of acne and indices of the psychological profile, in particular – values of the scale of anxiety. Among patients who received phabomotisol and ionized fluids, an increase in the correlation coefficient was revealed (Table 7), which indicates an increase in the relationship between DIA indices and anxiety after the therapy.

Table 7

Spearman correlation coefficients for anxiety and DIA

Number	Before treatment	After treatment
Group 1	0.261	0.001
Group 2	0.198	0.357
Group 3	0.303	0.424*
Group 4	0.332	0.311
Group 5	0.315	0.398

Note: * – Correlation is significant at the level of 0.05 (two-sided).

In the results of the research, the effect on the immune processes of a combination of ionized liquid with negative AFP and a psychotropic drug was demonstrated. The absence of significant changes in the immune response, when standard

drugs and phabomotisol are included in the treatment program, allows us to state that IL with negative AFP has an immunotropic action.

One of the important indicators of the effectiveness of therapy is the duration of remission. The data of the study convincingly testify that remission for more than a year occurred in 22.7% of patients in the fifth group and in no one as a result of the application of a standard therapy regimen. As a result of the inclusion in the treatment program of acne phabomotisol and ionized fluids with different AFP on the background of combined topical drugs, the incidence of side effects decreased from 81.2% to 4.5% of cases.

Conclusion

The thesis presents the results of studying the effect of preparations of a complex pharmacotherapeutic regimen for the correction of immunological, psychoemotional changes and cutaneous manifestations of acne on the course of the examined dermatosis. In the course of the study, an effective way of standard topical combined agents not including retinoid-like substances on the pathological processes in the hair follicle and skin manifestations of acne was suggested. Given the role of stress in the implementation of the cascade of pathogenetic mechanisms of acne, including changes in the local and systemic immune response, new tools have been proposed to correct psychoemotional and immunological changes in patients with acne.

The effectiveness of the assignment of ionized liquids, which we use for the first time in

complex therapy of moderate acne, has been proved in the work. The physicochemical properties of the ionized liquid with negative AFP made it possible to assume the presence of its immunotropic properties, which was confirmed in the course of the study. In addition, it was proved that the therapeutic effect, expressed in the reduction of cutaneous manifestations of acne and the onset of a prolonged remission, was achieved without the use of systemic antibiotics with the minimum frequency of side effects.

Summing up, we can draw the following conclusions:

1. The use of standard therapy provides a reduction in the DIA index by 33.12% and does not lead to a stable remission. Side effects of therapy are recorded in 81.8% of cases.

2. When using monotherapy with combined topical agents, the DIA index decreases by an average of 48.75%, remission for more than a half of a year is achieved in 46.4% of cases.

3. The inclusion in the treatment of moderately severe acne of fabomotizol at a dose of 5 mg 3 times a day during the month positively affects the clinical picture of the disease and the psychometric parameters of patients (DIA after 6 months decreases by 56.41%) and does not affect the immune status. Undesirable effects of the therapy are recorded in 9.1% of patients.

4. The use of an ionized liquid with negative AFP at a dose of 2 ml / kg of body weight 1 time per day for two weeks in patients with acne leads to an increase in CD4+ lymphocytes by 14.48%, an immunoregulatory index by 40.88% and a decrease in the number of CD8+ cytotoxic lymphocytes by 17.92%.

5. The maximum decline in the DIA index (by 74.36%) and long-term clinical recovery (remission of more than a year in 22.7% of cases) with a minimum incidence of side effects (in 4, 5% of cases) was achieved by including in the treatment program phabomotisol and ionized liquids with different redox potential.

Conflicts of interest

The authors have no conflict of interest to declare.

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