

Optimization of the Treatment of Chronic Eczema in the Elderly

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Abstract—The high prevalence and social significance of eczema in the modern world are not in doubt. According to various authors, it takes from 10% to 40% of all cases of skin diseases [1]-[3]. However, in the elderly, eczema accounts for even more than 50% in the structure of skin pathology [4]. This problem is of extreme importance in the modern world, given the fact that, at the moment, the whole world is focused on a significant increase in the number of the elderly. In this sense, the need for dermatological care in people of this category is significantly higher than in people of working age. Many treatment methods have been developed, but medical practice urgently requires the improvement and creation of more effective therapies.

Index Terms—eczema, lichenification, therapy, spirulina

I. INTRODUCTION

Eczema is an inflammatory acute or chronic skin disease of an allergic nature that occurs in patients of different age groups and reaches up to 30-40% of all allergic dermatoses [1]-[3]. According to several studies, the elderly suffer from eczema much more often than patients of young and middle age groups.

The most important mechanism for the development of many skin diseases, including eczema, is lipid disturbance, increased lipid peroxidation and other free radical processes, weakening of the antioxidant defense system, and a change in the synthesis of prostaglandins from polyunsaturated fatty acids. In the blood serum, the amount of LPO products increases, the antioxidant activity of vitamins E, A, and C decreases, the activity of enzymes of the antioxidant system, the functional activity of the microsomal oxidative system of the liver is weakened. Patients with eczema showed a significant increase in LPO processes, manifested by a significant increase in lipid peroxidation products in the blood serum.

It is worth noting that the therapy of eczema in the elderly, however, entails certain difficulties due to the involitional processes of the aging organism, as well as the high likelihood of side effects resulting from the use of drugs. In this regard, it is very important to pay more attention to optimal and adequate external therapy [5].

Currently, against the background of increased neuro-emotional overloads, a tense ecological situation, changes in nutrition, the population is increasingly experiencing symptoms of insufficient adaptation (maladaptation), a decrease in the nonspecific resistance of the body to adverse environmental factors of physical, chemical and biological nature. It is likely the development of various chronic diseases, including skin pathology, is associated with the above-mentioned problem. One of the reasons for maladaptation is the insufficient supply of the body, primarily micronutrients (vitamins, minerals) and minor biologically active components, which are necessary for the normal functioning of the systems that determine the adaptive potential of the body of the antioxidant defense system and detoxification of foreign chemical compounds (xenobiotics). In this regard, issues of increasing the adaptive potential of the body and the search for effective and safe adaptogens are of particular relevance [6].

Among products of natural origin that have an adaptogenic effect on the body, special attention is drawn to the microalgae *Spirulina* (*Spirulina* (*Arthrospira*) *platensis*), which has an extremely high nutritional density. Along with a high (up to 62%) protein content, it contains an almost complete spectrum of carotenoids, essential amino acids, significant amounts of B vitamins, vitamin E, essential gamma-linolenic acid, several trace elements [7]-[9].

Spirulina is a rich source of proteins, vitamins, amino acids, minerals, and other nutrients. Recently, there have been research investigations that describe positive data on the study of the action of drugs made from spirulina algae in various diseases. Among a number of components of the microalgae, its pigment phycocyanin, which is considered as its main biological marker [10], [11], is of the greatest interest. Experimental studies indicate the presence of antioxidant, immunomodulatory and renoprotective properties in spirulina [9], [11].

However, in the available literature, we were not able to find studies on the effect of spirulina on the immune system, as well as antioxidant activity of blood plasma of patients with chronic eczema. Interestingly, some microelements of spirulina (selenium, zinc, manganese, iron, chromium) are part of the intracellular hydrophilic fraction and are apparently associated with proteins. On the other hand, selenium from selenium-containing spirulina and its pigment phycocyanin has a

bioavailability comparable to inorganic forms (for example, sodium selenite) [9].

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Therefore, the main objective of this research is to identify the correlation between skin disorder, immune systems, lipid peroxidation and antioxidants system in eczema in the elderly, and as a result, to create a dosage form, an ointment containing urea, dimexide, and a topical hydrophilic strong corticosteroid with a reduction in the possible side effects of a corticosteroid to a minimum. For this purpose, the following tasks are proposed:

- To evaluate the processes of lipid peroxidation and antioxidant activity in patients with eczema in the elderly.
- To study the effect of spirulina on the main indicators of cellular, humoral and phagocytic parts of the immune system and lipid peroxidation processes in contact allergic dermatitis in an experiment.
- To evaluate the clinical effect of spirulina in eczema patients and their effect on the skin condition, immune status, and lipid peroxidation processes.
- To develop dosage forms for external use using spirulina.

The technical result consists in increasing the effectiveness of the treatment of chronic eczema and reducing the time of regression of the pathological manifestations of dermatosis in the elderly.

In this paper, for the first time, the effect of spirulina on the main indicators of cellular, humoral and phagocytic immunity units and lipid peroxidation processes in contact allergic dermatitis in an experiment will be studied. Moreover, the possibilities of the activating effect of spirulina on the antioxidant defense system of patients, manifested in a decrease in the accumulation of lipid peroxidation products (MDA) in the blood plasma of patients, will be clarified. Finally, for the first time, the clinical efficacy of spirulina preparations in the general and external treatment of eczema will be studied.

II. MATERIALS AND METHODS

The objective of the invention is to develop means for external use, in which the conditions for the quick and powerful action of corticosteroids on various parts of the pathological process in the skin are organically created, and the risk of side effects is minimized. The product

contains celestoderm, urea, boric acid, lanolin, petrolatum, zinc oxide, dimexide, and spirulina.

A. Ingredients

- 1) *Petroleum jelly*
Officially available liquid paraffin, colorless oily liquid, storage in a well-sealed container.
- 2) *Lanolin*
Officially released animal wax, purified lanolin in the form of an ointment base, stored in sealed containers.
- 3) *Spirulina*
In capsule, tablet form, or powder form.
- 4) *Celestoderm*
Official hormonal ointment (betamethasone) in tubes.
- 5) *Zinc oxide*
Fine white amorphous powder.
- 6) *Boric acid*
Colorless, scaly-like, and fatty to the touch crystals, which are poorly soluble in cold water and well soluble in hot water, in glycerin.
- 7) *Urea*
Slightly yellowish oily liquid with a faint odor, reminiscent of garlic.

It is known that the drug base itself provides the healing properties of the drug. So, hydrophilic bases, having high osmolar activity, do not have a damaging effect on healthy tissues and selectively absorb exudate, as well as limit the absorption of CS, due to which drug action is manifested directly in the lesion with the most sparing effect.

The hydrophilic base of the ointment, urea in combination with dimexide, significantly enhances the anti-inflammatory and anti exudative effects of celestoderm. In patients with chronic dermatoses, a thickening of the stratum corneum of the epidermis is observed, which creates certain obstacles to the effect of the drug on the pathological processes in the underlying layers of the skin. The feasibility of including urea in a preparation for external use is determined by its keratolytic and moisturizing effect, as well as the effect of enhancing penetration of drugs into the skin. And finally, dimexide significantly enhances the transdermal permeability of drugs and has anti-inflammatory, anti-allergic and antipruritic effects. A unique combination of biologically active compounds (proteins, B, C, E vitamins, polyunsaturated fatty acids, carotenoids, chlorophyll, phycocyanin) in the biomass of spirulina provides anti-inflammatory and antioxidant properties, accelerates the healing, regeneration, and epithelization of tissues. Urea and boric acid exert antibacterial and fungicidal action, which prevents complications such as the development of a secondary pyococcal or fungal infection, which is not uncommon during prolonged use of CS (which is especially important when using the drug in the area of large skin folds of the body).

It should be noted that a decrease in the concentration of CS by more than 3 times in the ointment we are developing does not lead to a decrease in efficiency in

comparison with the original unchanged ointment. This reduces the risk of side effects of topical strong corticosteroids.

B. Preparation and Dosage

Lanolin, petroleum jelly, celestoderm are mixed, following which urea, boric acid, spirulina, and zinc oxide are sequentially added to the mixture. After thorough mixing, dimexide is added and everything is mixed until a homogeneous mass is obtained.

Description of the ointment: ointment of a yellowish color for external use. Side and toxic effects from the applied ointment are absent.

Storage: the ready ointment is stored in well-corked bottles in a cool, dark place.

The proposed ointment can be made in any pharmacy institution with an available recipe guaranteeing the quality of the preparation.

C. Methods

A study was conducted with the participation of patients with eczema of the elderly (the main group of 90 patients), as well as a control group (50 healthy individuals), in the clinic “Shipager”, Semey, Kazakhstan.

The intensity of lipid peroxidation processes was judged by the content of lipid peroxidation products – Diene Conjugates (DC) and Malondialdehyde (MDA). To assess the state of the antioxidant defense system, we determined the activity of antioxidant defense enzymes – Superoxide Dismutase (SOD), Glutathione Peroxidase (GPO), glutathione reductase in peripheral blood.

A study of immunological parameters included determining the number of T-lymphocytes and their subpopulations. The level of Circulating Immune Complexes (CIC) and cytokines in blood serum will also be determined.

Experimental studies were performed on 120 laboratory animals – guinea pigs; on the model of contact allergic dermatitis, the effects of spirulina were studied: its effect on the manifestations of allergic contact dermatitis, the immune and antioxidant status of guinea pigs.

III. EXPERIMENTAL INVESTIGATION

Under our supervision, there were 78 patients. The age of patients ranged from 61 to 87 years, women - 31, men - 47. The duration of the disease ranged from several months to several decades. All patients were divided into 2 groups by random sampling. Patients of the first group received the ointment we developed 2 times a day for 3 weeks in combination with complex therapy, including calcium gluconate 0.5 g per day, a tablet of chloropyramine 0.025 g 3 times a day for 3 weeks. Patients of the second group received Celestoderm ointment twice a day for 3 weeks in combination with general therapy similar to patients of the 1st group.

Patients complained of rashes on the skin of the palms and dorsum of the hands, forearms, dorsum of the feet and legs. The pathological process was symmetrical, with fuzzy borders. The skin in the lesions was hyperemic,

infiltrated, in some places, there were phenomena of lichenification, cracks and pinpoint micro erosion. Moisture in the foci was slightly expressed, mainly there was dry skin, and subjectively intense itching, tightness, and dryness of the skin. It should be noted that the features of eczema in the patients we observed were the absence of vesicles and weeping in all the examined patients, mild swelling and, in most cases, passive erythema. The pronounced infiltration and lichenification, cracks and dryness of the skin came to the fore.

Studies were performed in both groups before treatment and at the end of treatment. The clinical manifestations of chronic eczema were assessed by identifying the main symptoms of the disease: erythema, edema, excoriation, lichenification, papules, dryness, peeling, cracks, itching. The severity of the skin process was assessed by the dermatological index of the scale of symptoms (DISS), which can be calculated as the sum of the severity of the indicated symptoms of the disease calculated in points: The severity of symptoms was evaluated in points: absence - 0; slight severity - 1; poorly expressed - 2; strongly expressed - 3. The reliability of differences between the studied parameters was determined using paired and unpaired Student’s t-test.

IV. RESULTS AND DISCUSSIONS

The study showed that with the beginning of the use of the ointment we have developed, patients noted a significant reduction in itching, a decrease in irritability, and an improvement in sleep. In most cases, a clear clinical effect was observed already 3-4 days after the start of complex treatment using the developed ointment. Along with subjective symptoms, objective symptoms significantly decreased. By the 8th-11th day from the start of treatment, the resolution of erythema and edema in the foci, a significant decrease in excoriation, infiltration, and lichenification, peeling in the foci of the lesion were noted.

TABLE I. CHANGES IN CLINICAL SYMPTOMS DUE TO THERAPY

Changes in clinical symptoms		Erythema	Edema	Infiltration	Crusts	Exfoliation	Cracks
Group 1	Before therapy	29	13	25	29	29	27
	Disappeared	14	13	19	25	29	27
	Decreased	12	0	5	4	0	0
	No change	3	0	1	0	0	0
Group 2	Before therapy	29	12	26	29	28	28
	Disappeared	6	8	7	16	20	21
	Decreased	14	4	8	9	7	6
	No change	9	0	11	4	0	1

Changes in clinical symptoms during therapy were characterized as follows: congestive erythema, infiltration, and lichenification observed in most patients responded especially poorly in the second group; in the vast majority

of patients, these clinical manifestations decreased slightly. In the first group, in all patients with edema in the lesion focus, its full resolution was noted, while in the second group, swelling completely disappeared in half of the patients (57.1%), decreased in 35.7% and remained unchanged in 7.0%. The more effective therapy was for such manifestations as infiltration and lichenification. In the first group, in all patients (except for one case), complete healing of cracks, rejection of crusts, and complete disappearance of peeling in the lesion focus were noted. In the second group, crusts completely disappeared only in half of the patients (55.1%), peeling in 71.4%, infiltration, and lichenification in 29.9%, and cracks in 77.8%.

The corresponding favorable shifts of clinical symptoms that occurred under the influence of treatment found their significant ($p < 0.05$) reflection in the decrease in the values of the dermatological symptom score index (DSSI). So, in the first group, there was a decrease in the level of DSSI by 12.3 ± 0.29 . In the second group, the value of the DSSI fell by only 6.7 ± 0.3 . That is, with the initially similar clinical severity of the disease, the severity of positive clinical dynamics in patients of the first group receiving complex therapy in combination with the ointment developed by us was almost doubled, compared to the second group.

Thus, the use of the ointment we have developed as part of the complex therapy of chronic eczema increases the effectiveness of the treatment of this disease, causing a more pronounced regression of the symptoms of the disease, reducing its severity and improving the quality of life of patients. This method is suitable for the treatment of patients with chronic eczema in the elderly, convenient for use in outpatient practice and does not require hospitalization of patients.

The therapy, which included the ointment we have developed, is clinically significantly more effective than therapy that includes pure celestoderm.

Earlier treatment was diverse but ineffective. Advantan, sinaflan, fluorocort, zinc, sulfur-tar ointments, etc. were used.

The use of this complex for external treatment in the elderly with chronic lichenified eczema allows the disappearance of inflammatory phenomena: erythema of edema and infiltration, the disappearance of excoriation, lichenification, dry skin and healing of cracks in the lesion, and, as a result, the full restoration of the normal structure skin.

Example 1: Patient N., 67 years old, senior citizen, medical history No. 563 from 11/12/18. Diagnosis: Chronic eczema. Complaints: intense itching, dryness, a feeling of tightening of the skin, the pathological process is localized on the skin of the hands, forearms, and legs. The patient has been sick for more than 10 years. Previous treatment was diverse but ineffective.

The pathological process is represented by erythema and skin infiltration of the back surface of the hands, forearms and lower legs, powerful lichenification in the wrist and ankle joints, dryness, excoriation, and cracks on the lateral, dorsal and palmar surfaces of the fingers.

Laboratory: General blood test: Hb - 140 g/l, Er. - $4.5 \times 10^{12}/l$, L - $9.4 \times 10^9/l$, s - 73%, e - 3%, l - 20%, m - 4%, ESR - 19 mm/h. General urine analysis: without features. Biochemical analysis of blood: total protein - 56 g/l, thymol test - 1.4 units, sugar - 4.2.

The patient underwent external treatment using the ointment we developed. The ointment was applied to the lesions 3 times a day. External therapy was combined with complex therapy, including calcium gluconate, 1 tablet 3 times a day, chloropyramine 1 tablet 2 times a day. The good tolerability of the drugs was noted. The first signs of improvement were noted already on the 3rd day of treatment: erythema, excoriation, and dry skin decreased. A significant decrease in infiltration and lichenification in the foci, healing of cracks were observed on the 7th-9th day of observation. Complete disappearance of itching and excoriation, erythema in the foci were noted on the 15th day of treatment, and complete regression of clinical manifestations and restoration of the normal structure of the skin occurred 3 weeks after the start of therapy.

Thus, the use of the ointment 3 times a day during the entire observation period was accompanied by good dynamics of the regression of clinical symptoms, the disappearance of skin itching and moisturization of the skin, which ultimately made it possible to achieve complete clinical recovery in the observed patient.

Example 2: Patient S., 68 years old. Relapse occurred 5 years ago after a long 20-year remission. In the first 3 years, the disease passed with severe island-inflammatory phenomena, microvesiculation, exudation and weeping in the lesion foci. In the past 2 years, there have been practically no remissions; severe itching, insomnia, irritability have been worrying. In the lesions on the skin of the hands, forearms, shoulder, on the back of the neck, lower back and thighs, foci of erythema, infiltration, lichenification, dry skin, hemorrhagic crusts and cracks on the palms and back surfaces of the hands are observed. Repeated treatment on an outpatient and inpatient basis in the GDVD was unsuccessful.

General blood test: Hb - 130 g/l, Er. - $3.95 \times 10^{12}/l$, L - $10.4 \times 10^9/l$, s - 65%, e - 5%, l - 22%, m - 8%, ESR - 21 mm/h. General urine analysis: without features. Biochemical analysis of blood: total protein - 58 g/l, protein fractions: albumin - 56%, globulins: α_1 - 1.5%, α_2 - 7.1%, β - 12.0%, γ - 18%.

The patient was treated using our proposed method. By the end of the first week of treatment, there was a noticeable improvement, decreased itching, excoriation, erythema, and infiltration in the foci. By the end of 2 weeks, cracks, dry skin and lichenification in the foci decreased. Complete clinical recovery occurred around the 25th day of treatment.

V. CONCLUSION

An external treatment method for chronic lichenified eczema that includes traditional therapy has been proposed. It is characterized by that an ointment is additionally prescribed, containing: lanolin, petrolatum, celestoderm, spirulina, urea, boric acid, zinc oxide, and

dimexide in the following ratio of components, % by weight:

Rp: Lanolini – 15.0
Vaselini – 10.0
Celestoderm V – 15.0
Spirulina platensis – 20.0
Urea – 8.0
Boric acid – 1.0
Zinc Oxide – 4.0
Dimexide – 3.0

MSD: apply the ointment 2 times a day, for 3 weeks.

The proposed method for the external treatment of chronic eczema consists in using the ointment developed by us, which includes: urea – keratolytic, moisturizing effect; glucocorticosteroid celestoderm – which reduces a variety of inflammatory and toxic-allergic reactions in the soft tissues that occur in chronic allergic dermatoses; spirulina – carries out anti-inflammatory and antioxidant effects; dimexide – anti-inflammatory and penetrating effect. The invention relates to medicine, namely to dermatology and venereology and can be used for external treatment of patients with chronic dermatoses both in a hospital and in an outpatient setting. The use of this complex for the external treatment of chronic eczema allows you to quickly reduce inflammation, moisturize the skin, resorb infiltrates, and to achieve the disappearance of cracks and dry skin.

The use of the developed external treatment for chronic eczema in the elderly allows the disappearance of inflammatory skin phenomena, and as a result, the restoration of the normal structure of the skin.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

The research investigation was performed under the supervision of Professor Nurmukhambetov Z. (1952-2019), Semey Medical University, Semey, Kazakhstan. 3rd year PhD student Ibrayeva T. developed the experimental program and conducted the investigation, as a result invented the ointment for the therapy of chronic eczema in the elderly. The investigation involving the patients was performed in the clinic “Shipager” with the help of Doctor Nurmukhambetov A., a CEO of the clinic. Doctor Bazarbekov Y. provided the literature and the

statistical data associated with the public health and welfare. All authors had approved the final version.

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Zhumash Nurmukhambetov (1952-2019) had been a head of the Department of Dermatovenereology in Semey Medical University, Kazakhstan, for the last 15 years. A great number of research investigations, academic papers and articles were written and medical inventions were developed under the supervision of Professor Nurmukhambetov. He raised the studies of dermatovenereology in Semey city as well as in whole Kazakhstan to the new level. He will always and forever be in the memories of his students, colleagues, patients, and friends.