

## NEW APPROACHES TO THE TREATMENT OF PATIENTS WITH SEBORRHEIC DERMATITIS

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**Abstract.** The article presents results of complex treatment of 55 patients with seborrheic dermatitis (SD) at the age of 26–48 years. Patients with SD are divided into two groups, homogeneous by age, sex, clinical forms, severity, laboratory parameters. Patients of group 1 in the cold period of the year (November-March) were administered cholecalciferol (vitamin D3) and synbiotic (combined probiotic) DermaPro in the background of complex traditional therapy. Patients of group 2 received only traditional treatment. Clinical remission and significant improvement were detected in group 1 patients (88.2%) more often compared with the similar result in group 2 patients (52.4%). Relapses of the disease were detected in 23.6% of patients in group 1 and 50.0% in patients in group 2 within one year. The appointment of patients with SD cholecalciferol and DermaPro led to an increase levels of 25(OH)D by 81.5% and cathelicidin LL-37 by 78.4%, normalization and improvement of gut microbiota in 88.2% of cases. The use of traditional therapy resulted in only normalization and improvement of intestinal biocenosis in 28.5% of patients.

**Key words:** vitamin D3, probiotic, clinical and laboratory efficacy, treatment, seborrheic dermatitis.

**Introduction.** Seborrheic dermatitis (SD) is a common chronic inflammatory skin disease associated with increased secretion of sebum, a change in its qualitative composition. Yeast-like fungi *Malassezia* spp. is supposed to be the main cause of SD, however, the amount of these lipophilic microorganisms is often within normal limits on the skin of patients [1, 2]. Genetic predisposition, hormonal status change, gastrointestinal tract and the nervous system diseases, dysfunction of the epidermal barrier may provoke the disease [3, 4].

New therapeutic technologies which allow to reduce rapidly the sign of the SD main symptoms (itching, skin lesions and scales, redness, plaques and hair loss) have emerged during the last decade. Medicines containing topical glucocorticosteroids, antifungal and antimicrobial substances, zinc pyrithione, selenium sulphide and others are used in treatment most often [5, 6]. When carrying out complex treatment, the availability of the body

with vitamin D, the state of innate immunity and the gut microbiota of the patients have not been taken into account until now. The prognosis of some patients remains unfavorable, which is caused by insufficient effectiveness or resistance to traditional therapy, frequent recurrence, despite the successes achieved in the treatment of dermatosis. The search for new approaches to treatment continues, as these issues are an actual problem.

### **2. Purposes, subjects and methods:**

**2.1. Purpose.** The purpose of the present study was to estimate the effectiveness of SD patients' therapy which is held using vitamin D and a probiotic containing *Lactobacillus ramosus* GG.

**2.2. Subjects.** The study included 55 patients with SD at the age of 26-48 years (35 men and 20 women). Patients didn't have concomitant diseases at the stage of exacerbation or decompensation, primary hyperparathyroidism. Patients didn't take antifungal drugs, corticosteroids, anticonvulsants, vitamins within the last three months. All patients voluntarily signed informed consent to participate in the study.

Patients showed a variety of clinical SD signs, caused by the localization and type of the rashes, the prevalence of the skin process. The disease's

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severity degree was established on the base of the SDASI calculations (Seborrheic Dermatitis Area Severity Index [7]). In average SDASI was  $10.3 \pm 1.6$  points among the patients. Exacerbation of dermatitis occurred in 76.4 % of cases in autumn and winter, the disappearance of rashes or significant improvement in 85.4 % of patients in summer. 67.3 % of patients showed insufficient intake of foods rich in vitamin D (sea fish, eggs, milk). Associated diseases of the GIT and hepatobiliary system were diagnosed in 52.7 %, clinical manifestations of dysbiosis in 65.4 % of patients (discomfort or mild aching, blunt regular abdominal pain, flatulence). Laboratory signs of large intestine dysbiosis (decrease in the number of bifidobacteria and lactobacilli, aerobic E. coli typical, an increase in the number of saprophytic and opportunistic bacteria – epidermal staphylococcus, enterobacter, cyrobacter, yeast-like Candida fungi) were detected in 100 % of patients.

**2.3. Methods.** Patients with SD are divided into two groups. The group 1 consisted of 34 patients (24 men, 10 women), the average age was  $36.4 \pm 2.2$  years, SDASI -  $10.6 \pm 1.8$  points. The group 2 consisted of 21 patients (11 men, 10 women, the average age was  $37.5 \pm 2.5$  years, SDASI –  $10.1 \pm 1.7$  points. Both groups of patients were homogeneous by age, sex, clinical forms, severity, laboratory parameters.

Patients of the group 1 were prescribed colecalciferol (vitamin D3) in the cold period of the year (November-February) and synbiotic (combined probiotic) DermaPro on the background of complex traditional therapy. Nolecalciferol was taken at a dose of 2000 IU once a day during 6 weeks with vitamin D deficiency (level of 25(OH)D in the range of 51–74 nmol/l). The medicine was recommended at a dose of 3200 IU once a day during 8 weeks with a transition to 2000 IU for 2 weeks in case of vitamin D deficiency (level of 25(OH)D less than 50 nmol/L). The patients took DermaPro for one capsule during 14–21 days (taking into account the degree

of dysbiosis). The Patients of the group 2 received only traditional treatment – oral antihistamines (levocetirizine, phenocarol), vitamins of group B (vitamin B6, biotin, Neurovitan), antifungal drug itraconazole (in case of widespread and resistant to therapy), topical corticosteroids, topical inhibitors calcineurin, shampoos with antiproliferative, antifungal, keratolytic components.

Clinical and laboratory results were compared after the treatment with various methods in order to study the effectiveness of the therapy. The results of the treatment were assessed using the following clinical criteria: clinical recovery, significant improvement, improvement, no effect. The determination of the level of 25(OH)D and cathelicidin LL-37 in serum was carried out by the method of enzyme immunoassay. The standard bacteriological method of faeces examination was used to assess the state of the intestinal microflora.

The obtained data were processed with the determination of the arithmetic mean (M), the standard deviation ( $\delta$ ) using the STATISTICA for Windows 5.5 software system. Differences between groups were established using the ANOVA test and Mann-Whitney U. The criterion for statistical reliability of the findings was the value  $p < 0.05$ .

The study was conducted according to the international bioethical standards.

**Conflict of interests.** There is no conflict of interests.

**3. Results and discussion.** The clinical results (*table 1*) established that the clinical remission was 2.7 times more frequent among the patients of the group 1 (38.2%) than among the patients of the group 2 (14.3%). Significant improvement took place more often with the patients who received the therapy with vitamin D3 and probiotic (52.9%) than those who got the traditional therapy (38.1%). Improvement was more often registered in group 2 (33.3%) comparing to the same indicator in patients of the group 1 (accordingly, 8.8%). The therapy was

*Table 1*  
Results of the treatment of patients with seborrheic dermatitis by various methods

Results of the treatment	Patients, groups	
	1, n = 34 abs. / %	2, n = 21 abs. / %
Clinical remission	13 / 38,2	3 / 14,3
Significant improvement	17 / 50,0	8 / 38,1
Improvement	4 / 11,8	7 / 33,3
Lack of effect	–	3 / 14,3
Total	34 / 100,0	21 / 100,0

ineffective only for the patients of the group 2 (14.3%). Positive results were achieved in 100.0% of patients in group 1 and 85.7% among the patients in group 2. However, clinical remission and significant improvement were more often determined among the patients who were treated according to the developed method (88.2%), comparing with the similar results among the patients who received the traditional therapy (52.4%, respectively).

Regression of the main clinical symptoms of Seborrheic dermatitis under the influence of therapy occurred after different times. The more rapid disappearance of subjective and objective manifestations of dermatosis was revealed in patients who received supplemental vitamin D3 and probiotic. Shorter time to regression of erythema and scaling in patients of the group 1 ( $5.1 \pm 0.5$  and  $6.3 \pm 0.7$  days,  $p < 0.05$ ) comparing to the patients of the group 2 ( $9.4 \pm 0.9$  and  $10.1 \pm 1.0$  days) attracts the attention. Analysis of the decrease in SDASI in patients of different therapeutic groups also revealed the advantage of the developed differential treatment. Reduction of SDASI in 4.2 times was noted in patients of the group 1 (main), while in the group 2 – in 1.7 times.

Observation of patients within one year after treatment revealed relapses of the disease in 8 (23.6%) patients of the group 1 and 11 (50.0%) patients in the group 2.

The patients of the group 1 experienced a significant increase in serum 25(OH)D level ( $p < 0.05$ ) after treatment reaching the target level (75–150 nmol/l, according to the guidelines for Central European countries [8]) and cathelicidin LL-37 ( $p < 0.05$ ), whereas in the patients of the group 2 – the values of both indices practically did not change (*table 2*).

on the qualitative and quantitative composition of the intestinal microbiota of the complex approach with additional use of cholecalciferol and DermaPro. It was expressed in restoring the level of obligate microflora to reference values, reducing the number of facultative, eliminating pathogenic microbes. In patients of the group 2, intestinal dysbacteriosis persisted in most cases (71.4%), the indices improved or normalized in patients with the first degree of dysbiosis in the background of a diet. The use of therapy with vitamin D3 and synbiotic led to normalization or significant improvement in the quantitative and qualitative composition of the gut microflora in most patients.

The results of the study indicate that patients with seborrheic dermatitis require the appointment of vitamin D3 and a synbiotic, which not only increased the effectiveness of therapy and the rapid regression of clinical manifestations (a decrease of SDASI by more than 75%), but also the normalization of most laboratory indicators. All patients tolerated the treatment well.

Detection of anti-inflammatory and immunosuppressive activity of vitamin D has opened up new possibilities for the therapeutic use of this substance and its analogs for the control of inflammatory skin diseases supposedly associated with hyperproduction of cytokines (psoriasis, atopic dermatitis, urticaria, scleroderma) [9, 10, 11]. Data on the use of vitamin D in patients with SD don't exist in the available literature, although in 92.3% of patients a deficiency / insufficiency of the vitamin (at 20% in practically healthy individuals) was detected [12]. The choice of the optimal dose of vitamin D3 depends on the initial concentration of 25(OH)D in the blood. Calculation of the daily dose of vitamin D3 was carried out depending on

Table 2

*Dynamics of vitamin D status and innate immunity in patients with seborrheic dermatitis during the treatment*

Parameters	Patients, groups	
	1, n=34	2, n=21
25(OH)D, nmol/l	$53.06 \pm 4.30^*$ $96.29 \pm 7.18$	$57.33 \pm 4.50$ $63.15 \pm 5.11$
Cathelicidin LL-37, ng/ml	$18.1 \pm 1.9^*$ $32.3 \pm 2.7$	$19.2 \pm 2.1$ $21.4 \pm 2.2$

**Note:** the numerator indicates pre-treatment indicators, the denominator indicates after treatment; differences are significant between the indices in the group for  $p < 0.05$  – \*.

Comparative analysis of the results of the study of faeces on intestinal dysbacteriosis in patients with SD after the treatment (*table 3*) showed the most pronounced corrective effect

the initial concentration of 25(OH)D according to the scheme developed by Garland et al. (2011) [13]. The doses fully satisfied the recommendations of the International Endocrinology Society.

Table 3

*The state of the intestinal microbiota in patients with seborrheic dermatitis in the course of treatment*

Parameters	Patients, groups	
	1, n=34 abs. / %	2, n=21 abs. / %
Dysbacteriosis of the intestine	4 (11.8)	15 (71.4)
Normalization of intestinal biocenosis	24 (70.6)	2 (9.5)
Improvement of bacteriological parameters	6 (17.6)	4 (19.1)

One of the "nonclassical" effects of the D-hormone, along with the inhibition of cellular proliferation and angiogenesis, an anti-inflammatory effect, is the stimulation of the production of antimicrobial peptides (cathelicidins, defensins) [14]. To date, it is believed that the role of vitamin D in the pathogenesis of allergic diseases is due to its regulatory effect on the immune system, participation in antimicrobial protection and the barrier function of the skin and mucous membranes [15, 16]. The appointment of colecalciferol in patients with seborrheic dermatitis confirms the modulating effect of vitamin D on the functioning of innate immunity on the basis of a significant increase the level of LL-37 in the blood of patients by a factor of 1.8.

Probiotics acquire great importance in the treatment of seborrheic dermatitis, taking into account their normalizing effect on the state and balance of intestinal microflora, immunity and immune response - modulation of the Th1 / Th2 response, inhibition of Ig E synthesis, stimulation of Ig A production, antimicrobial peptides, macrophages and so on [17, 18]. High importance and leading positions in the number of communities of symbiotic microorganisms of "healthy" people of all age groups of lactobacillus led to a choice for correction of dysbiotic disorders in SD of the DermaPro synbiotic [19].

The drug consists of a probiotic (lactobacillus) and a prebiotic (fructo-oligosaccharide).

Lactobacillus rhamnosus GG, included in the preparation 1.5 billion CFU, prevent the proliferation of pathogenic microorganisms in the intestine and help restore the balance of useful microflora, eliminate dysbiosis and normalize digestion, immune response. It should also take into account the normalizing effect of vitamin D on the state of the intestinal microflora [20].

The obtained results of the research allow us to state that the use of vitamin D3 (cholecalciferol) and synbiotic DermaPro in the complex treatment of diabetes is an effective and safe method of therapy.

#### Conclusions:

1. The use of vitamin D3 and synbiotic in the treatment of SD contributed to an increase in the effectiveness of complex therapy – remission and significant improvement were noted in 88.2%, relapses in 23.6% of patients compared to those in patients receiving only traditional therapy (52.4 % and 50.0 %).

2. The appointment of patients with SD cholecalciferol and DermaPro led to an increase in blood levels of 25(OH)D by 81.5% and cathelicidin LL-37 by 78.4%, normalization of gut microbiota in 88.2% of cases.

3. The use of drugs that have a normalizing effect on the vitamin D status and the level of cathelicidin LL-37 of blood, intestinal microbiocenosis is a new pathogenetic grounded approach to the therapy of patients with SD.

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