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The Clinical, Biochemical and Immunological Parallels of the Clinical Course of Trichophytosis in Patients with Hypothyroid State

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Abstract: The imbalance of the thyroid hormones in patients with trichophytosis can be the cause of the functional and metabolic disorders and a decrease in the immune system, which serve as the basis for chronic disease, as well as the development of severe forms of this disease.

Keywords: trichophytosis, subclinical hypothyroidism, cellular immunity, endogenous intoxication, free radical oxidation.

Introduction: Socio-economic, geo-ecological characteristics and the growing number of risk groups in the population are the main determinants of various variations of the disease and the prevalence of fungal processes around the world [32]. An important place in aggravating the severity of TF, reducing the effectiveness of the treatment is a violation of the functional state of the body, somatic diseases [3, 33, 39], modulation of immunological reactivity [38, 36], depression of detoxification systems that support internal homeostasis and protective and protective skin function [31.35].

The direct connection of changes in the body's immune system with the severity of inflammatory phenomena in the focus and the depth of penetration of pathogens into the skin is proved. Despite numerous studies in this area, immunocorrection for fungal infections of the skin, in particular with zooanthroponictrichophytosis, remains an urgent problem [27]. Cellular immunity is a component of the immune system that provides the vital property of the body - immunological reactivity [18]. However, among the mechanisms of reactivity, the nervous and endocrine systems play an important role. The effect of SH on the immune system of patients with TF is not fully understood, which determines the urgency of the problem. There are practically no data on the state of the cellular immunity link in patients at different stages of TF combined with SH, which served as the basis for this study.

Intensification of FRO, the accumulation of toxic metabolic products such as O2, NO2, NO3, NO, ONOO - against the background of inhibition of the activity of enzymes of the antiradical defense system can serve as important internal factors in the development of secondary immune deficiency and toxemia [34, 40], thereby contributing to the progression of the form TF, the generalization of inflammation and a decrease in the protective and barrier properties of the skin, increased aggressive growth and reproduction of a wide range of strains of pathogenic flora, fungi and protozoa. One of the factors contributing to the development of secondary immunodeficiency is thyroid hypofunction [1, 2, 37].

According to WHO (2005), the Republic of Uzbekistan belongs to the high-risk zone of iodine deficiency and latent subclinical forms of SH [11]. With SH, nonspecific resistance of the body decreases, hormonal regulation and the immune system are disrupted [16, 17]. At the same time, the functional state of the thyroid gland, as one of the possible factors for the progression of various forms of TF, is still not taken into account in dermatological practice, which may be one of the reasons for the protracted course of the disease, the widespread prevalence of this disease, and unsatisfactory

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treatment results. In this regard, the inclusion in the monitoring of the examination of indicators characterizing the function of the thyroid gland will make it possible to differentially approach the choice of treatment tactics, increase the effectiveness of therapy, and explain from new perspectives what mechanisms complicate the process and progression of the clinical course in patients with TF with SH.

Objective: To study the role of subclinical hypothyroidism in the formation of various forms of trichophytosis, taking into account some immunological and biochemical parameters.

Materials and research methods. 150 patients with trichophytosis were examined, including 98 boys (65.3%), 52 girls (34.7%), aged 3 to 17 years. Of these, 90 patients with TF combined with SH.

All patients were diagnosed with TF on the basis of anamnesis, clinical, microscopic (cultural) studies.

It should be noted that, according to WHO (2005), for the diagnosis of SH it is enough to determine the level of TSH in the blood, which should be increased> 5 mU / L and T4 and T3, which should be within the upper limits of the physiological norm - 1 nmol / l and 23.5 nmol / l [10]. In addition, there should not be a visible increase in the volume of the thyroid gland, as well as violations in its structure and size, determined by ultrasound examination.

The basal level of free fractions of thyroid hormones - thyroxine (T4), triiodothyronine and thyroid stimulating pituitary hormone (TSH) was determined by the enzyme-linked immunosorbent assay in the blood serum immunosorbent analyzer "Immunohem" (Czech Repablic), using sets of chemical reagents of the same company.

The study structure included an assessment of immune status. In this case, we used a set of monoclonal systems directed to SDZ + - cells - the total (pan) subpopulation of T-lymphocytes, to CD4 + - cells - a subpopulation of T-helper inducers to SD8 + -cells - T-suppressor-cytotoxic cells, as well as to SD16 + -cells - natural killer cells (EKK) and to CD72 + antigen - a marker of lymphocytes in blood serum. The degree of endotoxemia was assessed by the change in blood parameters of ESC, MWM, which were determined by known methods, according to A. A. Togaybaev et al. [30] and N.I. Gabrielyan, V.I. Lipatova [10]. At the same time, LII was calculated by the formula of Ya. Y. Kalf-Kalif [15], as well as the content of the CIC.

At the same time, indicators characterizing the state of the LPO-AOS processes on the surface of the affected skin were studied. For this purpose, a specially designated damaged skin area of 3-4 cm was chosen and before treatment with antifungal agents, they were irrigated with sterile distilled water in an amount of 5 ml three times.

The production of oxygen radicals was determined by spontaneous chemiluminescence on an HLM1C-01 instrument (Russia) according to the method of Yu. A. Vladimirov and A. I. Archakov [9]. SDE activity was determined by the method of E. E. Dubinina et al. [12].

Results and discussion: When examining the skin of patients with subclinical hypothyroidism, a distinctive feature of those in patients with TF, but without SH, was their pronounced dryness. Also, in these patients, a high frequency of concomitant chronic somatic pathology was observed, which is more associated with disorders of the immune system.

Unlike usual TF in patients with TF combined with SH, the disease began with the appearance of several swollen pink-red spots with sharp borders that appeared slightly above the level of the surrounding skin. Their surface was covered with scales and small vesicles, quickly drying into crusts, almost all patients with SH had itching, while in patients without SH, itching was either absent in 16 (80.0%), or was weakly expressed in 4 (20.0%). (Table 1)

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Table 1: Symptoms of the disease in patients with superficial spotted form of trichophytosis

Symptoms of the disease	**TF+SH, %(n=30)**		**TF, % (n=20)**		**Δ,%**
	abs	%	abs	%	
1	2	3	4	5	6
In the affected areas are found:					
- erythematouspeeling.	10	33,3	5	25,0	8,3
- fusion foci, reaching sizes up to 5-7 cm in diameter.	23	76,7	4	20,0	+56,7
Localization:					
- scalp	2	6,7	2	10,0	-3,3
- headandch. leather	6	20,0	5	25,0	-5,0
- forearmandlowerlegs	6	20,0	1	5,0	+15,0
- torso	8	26,7	11	55,0	-28,3
- face	8	26,7	1	5,0	+21,7
Itching:					
- abs	0	0	16	80,0	-80,0
- mild	24	80,0	4	20,0	+60,0
- expressed	6	20,0	0	0	+20,0
t0-reaction	8	26,7	0	0	+26,7
Inflammatoryreaction:					
-significant	0	0	0	0	0
- insignificant	1	3,3	0	0	+3,3

With the infiltrative form of TF combined with SH, signs of intoxication were more evident, such as increased body temperature in 10 (33.3%) patients, weakness in 15 (30%), loss of appetite in 7 (23.3%), irritability - in 7 (23.3%). In the group of patients with SH, pronounced itching was noted in all patients.

Multiple pustules, papules, and serous peels were observed on the surface of the foci. On examination, the foci were bright red with marked infiltration.

Regional lymph nodes were enlarged - cervical - in 5 (16.7%) patients, axillary - in 5 (16.7%). In this group of patients, pronounced pruritus was noted 25% more, and the incidence of subfebrile body temperature increased by 33.3% more than in patients with TF without SH. (Table 2)

Table 2: Symptoms of the disease in patients with an infiltrative form of trichophytosis

Symptoms of the disease	TF +SH, %(n=30)		TF, % (n=20)		Δ,%
	abs	%	abs	%	
1	2	3	4	5	6
Fociwithinflammatorydiseases:					
- infiltration	30	100,0	20	100,0	0
- hyperemia	0	0	0	0	0
- exudation	0	0	0	0	0
Enlargedregionallymphnodes:					
- cervical	5	16,7	2	10,0	+6,7
- axillary	5	16,7	1	5,0	+11,7
Localization:					
- head	3	10,0	2	10,0	0

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- headandch. leather	5	16,7	2	10,0	+6,7
- face	5	16,7	0	0	+16,7
- forearmandlowerlegs	16	53,3	9	45,0	+8,3
- torso	1	3,3	7	35,0	-31,7
t0-reaction	10	33,3	0	0	+33,3
- weakness	15	50	1	5,0	+45
- lossofappetite	7	23,3	1	5,0	+18,3
- irritability	7	23,3	1	5,0	+18,3
itching:					
- abs	0	0	0	0	0
- mild	0	0	5	25,0	-25
- expressed	30	100	15	75,0	+25

With the development of the infiltrative suppurative form of TF combined with SH, the development of the pathological process was characteristic with the appearance of several flaky spots, round - oval in shape with clear boundaries. The foci were prone to peripheral growth. It is important to point out that in patients with TF on the background of SH, cannon hair was involved in the pathological process by 20.0% more than in patients with TF without SH, a frequency of cases of an increase in cervical and by 16.7% was noted to increase by 53.3%. percent of axillary lymph nodes, 70% more temperature reaction, weakness by 75%, loss of appetite - 80%, headaches - 80%, irritability - 25% more than in patients with TF without SH. (Table 3)

Table 3: Symptoms of the disease in patients with infiltrative suppurative form of trichophytosis

Symptoms of the disease	TF +SH, %(n=30)		TF, % (n=20)		Δ,%
	абс	%	абс	%	
The process involved vellus hair	30	100,0	16	80,0	20,0
Localization:					
- head	23	76,7	7	35,0	+41,7
- headandch. leather	2	6,7	11	55,0	-48,3
- face	1	3,3	1	5,0	-1,7
- forearmandlowerlegs	1	3,3	1	5,0	-1,7
- torso	3	10,0	0	0,0	+10,0
t0 - reaction	27	90,0	4	20,0	+70,0
Enlargedregionallymphnodes:					
- cervical	19	63,3	2	10,0	+53,3
- axillary	11	36,7	4	20,0	+16,7
- headache	27	90,0	2	10,0	+80,0
- weakness	27	90,0	3	15,0	+75,0
- lossofappetite	27	90,0	2	10,0	+10,0
- irritability	12	40,0	3	15,0	+70,0
itching:	0	0	0	0	0
- abs	0	0,0	9	45,0	-45,0
- mild	12	40,0	4	20,0	+20,0
- expressed	18	60,0	7	35,0	+25,0

Therefore, in patients with TF associated with SH, the course of the disease is characterized by violently impaired skin lesions of the scalp, as well as by signs of intoxication of the body.

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Thus, the clinical course of various forms of TF in children, proceeding against the background of SH, is distinguished by a number of features, which makes it possible to distinguish two clinical options (normal and combined with SH). This, in turn, necessitates in-depth scientific research and the selection of therapeutic correction.

Analysis of the results of the study showed that with the superficial spotted form of TF, compared with the control, the difference in the decrease in the total pool of lymphocytes - 1.9% and 3.4% of mature T-lymphocytes (CD3 +) (P <0.05), there is a significant the decrease in the level of a subpopulation of T-helpers - inducers (CD4 +), the difference was 10.9%, T-suppressors (CD8 +) - 3.5%, natural killer cells (NKC) - CD16 - 5.1% and an increase in the marker of B-lymphocytes (CD72) by 3.8%. Due to a disproportionate decrease in CD4 + and CD8 + T-lymphocytes, there was a 14.0% decrease in the integral indicator of immunoregulatory ratios of CD4 + / CD8 +.

With the infiltrative form of TF, there is also a clear dynamics of a decrease in the total number of lymphocytes and T-lymphocyte immunity, increased activity of B-lymphocytes compared with those in the blood of patients with superficial-spotted form of TF, when determining the difference in the level of total lymphocytes - by 4.9 %, T-lymphocytes CD3 + - by 7.6%, CD4 + - 11.5%, CD8 + - by 0.2%, CD16 + - 1.9%, CD72 + - by 4.7%, ratio CD4 + / CD8 + - by 0 , 5%, and compared with the control - by 11.0; 11.5; 3.7; 7.0; 8.0 and 15.2% respectively.

So, compared with the control, the difference in the level of total lymphocytes, T-lymphocytes, subpopulations of CD3 + - amounted to 9.0 and 22.2% compared with superficial spotted - 7.1 and 18.8%, with an infiltrative - 2.2 and 11 , 2%, when assessing the CD4 + subpopulation - by 16.8; 5.9 and 5.3%; CD8 + - by 5.0; 1.5 and 1.3%; CD16 + - by 9.4; 4.3 and 2.4%, the ratio of CD4 + / CD8 + - by 27.5; 13.4 and 12.3%; an increase in the marker of B-lymphocytes - by 14.0; 10.2 and 5.5% respectively. (Table 4)

Table 4: Indicators of cellular immunity (in%) in patients with various forms of trichophytosis, M ± m

Forms ofthed isease	Control, n = 20	Superficial spotted, n = 20	Superficials potted + SH, n = 30	Infiltrative , n = 20	Infiltrative+ SH, n = 30	Infiltrative suppuratio n, n = 20	Infiltratives uppuration + SH,n=30
Lymp hocyt es	35,6± 1,7	33,7± 1,80	29,2± 1,55*	28,8± 1,40*	21,6± 1,33*∧	26,6± 1,20*	21,7± 1,23*∧
CD3+	69,3± 3,43	65,9± 4,80	50,7± 4,11*∧	58,3± 3,62*	39,6± 2,77*∧	47,1± 2,85*	28,5± 1,90*∧
CD4+	39,3± 2,52	28,4± 2,17*	21,1± 2,04*∧	27,8± 1,79*	16,4± 1,13*∧	22,5± 1,80*	13,2± 1,16*∧
CD8+	22,1± 1,26	18,6± 1,32	16,2± 1,18*	18,4± 1,30*	14,3± 1,29*∧	17,1± 1,57*	12,6± 1,09*∧
CD16 +	14,7± 2,50	9,6± 0,83	7,8± 0,50*	7,7± 0,62*	5,9± 0,42*∧	5,3± 0,39*	4,1± 0,33*∧
CD72 +	13,4± 1,09	17,2± 1,12*	19,3± 1,34*	21,9± 1,34*	23,5± 1,85*	27,4± 2,48*	35,6± 2,42*∧
ИРИ	1,78± 0,07	1,53± 0,11	1,30± 0,10*	1,51± 0,09*	1,15± 0,07*∧	1,29± 0,08*	1,05± 0,07*∧

Note: * - significantly relative to the control group (* - P <0.05); ∧ - significantly relative to the group without SH (C - P <0.05).

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With the progression of forms of TF, and to a greater extent combined with SH, the level of CD3 +, CD4 +, CD8 +, CD16 +, the immunoregulatory index of CD4 / CD8 decreases, and the B cell count increases - CD72.

Therefore, with the development of various forms of TF, there is a dynamics of a decrease in total lymphocytes and its subpopulation - T-lymphocytes, an immunoregulatory ratio of CD4 + / CD8 +, an increase in the marker of the subpopulation of B-lymphocytes CD72 +, which can be assumed to determine the clinical features of the disease in response to an introduced fungal infection. However, as can be seen from the table. 4 against the background of SH, the immunological reactivity of patients with TF significantly changes, this is confirmed by a statistical, compared with control and compared with some groups of patients without SH, a decrease in the studied subpopulations of T-lymphocytes, an indicator of the immunoregulatory coefficient CD4 + / CD8 + and a subpopulation of B-lymphocytes. So, the total level of T-lymphocytes (CD3 +) in patients with SH in combination with superficially spotted form of TF, compared with the data in patients with a similar disease, but without SH was reduced by - 11.5 and 15.2%, in the group with an infiltrative form - by 7.2% and infiltrative-suppurative - by 4.9%. When assessing the subpopulation of CD4 + - at 7.3; 11.4 and 9.3%; CD8 + - by 2.4; 4.1 and 4.5%; CD16 + - by 1.8; 1.8 and 1.2%; the ratio of CD4 + / CD8 + - by 12.9; 20.2 and 13.5%; an increase in the marker of B-lymphocyte CD72 + - by 2.1; 1.6 and 8.2%, respectively.

A possible reason for the decrease in T-lymphocyte populations and stimulation of B-lymphocytes is an increase in blood circulating immune complexes (CIC), toxic metabolic products, and activation of the phagocytic activity of granulocytes. To confirm this assumption, we studied in a separate series of studies the state of the degree of endogenous intoxication in the blood of patients with various forms of TF, as well as patients with TF in combination with SH. Important indicators of endogenous intoxication are the sorption capacity of erythrocytes (SCEs), medium-weight molecules (MWM), leukocyte intoxication index (LII), and circulating immune complexes (CICs). We conducted a comparative analysis of EI in groups of patients with various stages of TF and similar groups of patients, but with SH.

An analysis of the results showed that with the progression of TF in the blood, the level of toxic metabolic products increases. So, in comparison with the data in the control, toxic metabolic products increase in the blood of patients with superficial spotted form leading to an acceleration of the ESC process - by 15.8%, an increase in MWM - by 5.8%, the number of leukocytes (mainly granulocytes), as evidenced by an increase in LII - by 9.4%, and an increase in the CIC - by 15.0%. At the infiltrative stage of TF, in comparison with the control, the SSE indicator exceeded 25.5%, MSM - 38.0%, LII - 67.0% and CEC - 96.9%, and compared with surface spotted - by the form of TF the SSE indicator - by 9.7%, MSM - by 30.5%, LII - by 52.7% and the CEC - by 71.1%.

So, in comparison with the data obtained from patients with the superficial spotted form of TF and patients against the background of SH with the same pathology, the level of ESC exceeded by 9.4%, MWM - by 23.0%, LII and CIC - by 35.5% and 43.0%. When comparing ESC, MWM, LII and CIC of a group of patients with an infiltrative and infiltrative form against the background of SH, in the latter they were higher by 14.2%, 75.8%, 136.5% and 65.8%.

We obtained similar data when comparing the degree of EI between groups of patients with infiltrative-suppurative and infiltrative-suppurative against the background of SH. In patients with SH, the ESC was higher - by 14.8%, MWM - by 49.1%, LII - by 33.5%, and CIC - by 79.0%.

In general, as shown by the results of studies, indicators of the degree of endogenous intoxication in patients with TF on the background of SH were significantly higher than in patients with TF without this pathology (Table 5).

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We found the maximum level of activation of proteolysis processes in patients with infiltrative suppurative form of TF. Compared with the control, the indicators of ESC, MWM, LII, CIC exceeded - by 39.9%, 81.0%, 114.1%, 203.8%, respectively, compared with the group of patients with superficial-spotted form - by 24 , 1%, 71.1%, 95.7%, 164.1%, and compared with the group of patients with an infiltrative form - by 44.0%, 31.1%, 28.2%, 54.3%, respectively EI indicators under study.

Table 5: EI in the blood of patients with various forms of trichophytosis and SH

Формы заболевания	ESC, %	MWM, gp/ml	LII, ЕД	CIC, gp/ml
Control, n=15	38,6± 3,11	0,242± 0,02	0,85± 0,05	57,8± 4,39
Surfacespotted, n=20	54,3± 3,40*	0,02± 0,256	0,93± 0,06	66,5± 4,65
Superficialspotted + SH, n=30	63,8± 4,25	0,315±0,02*∧	1,26± 0,09*∧	95,1± 7,19*∧
Infiltrative, n=20	64,1± 5,29*	0,334± 0,03*	1,42± 0,08*	113,8± 8,35*
Infiltrative +SH, n=30	78,3± 6,47*	0,450±0,03*∧	2,20± 0,11*∧	188,7±12,41*∧
Infiltrativesuppurative, n=20	78,5± 5,51*	0,438± 0,04*	1,82± 0,09*	175,6±11,34*
Infiltrativesuppurative +SH, n=30	93,3± 6,17*	0,653±0,05*∧	2,43± 0,15*∧	314,3±15,70*∧

Note: * - significantly relative to the control group (P <0.05); ∧ - significantly relative to the group without SH (P <0.05).

Therefore, the studies showed that with the progression of forms of TF in the patient's body, the products of impaired metabolism increase, which apparently determines the severity of the clinical course of the disease, especially the immunological reactivity in the patients examined by us. At the same time, of particular interest to us is the study of EI indicators in patients with various forms of TF on the background of SH.

In dermatological practice, in recent years, special attention has been paid to studying the role of free-radical reactions in the pathogenesis of trichophytosis.It has been shown that the cells of TF patients (monocytes, macrophages, polymorphonuclear and endothelial cells) generate an excess of activated oxygen species (AOS), which is one of the important causes of the destruction of the epidermis and dermis, microcirculatory, vascular and hemosthesiological and rheological disorders of the blood with the development of inflammatory process. Of particular interest is the study of the role of NO and its metabolites in inflammatory processes. In inflammatory neutrophils, monocytes and edematous fluid cells during inflammatory processes, overexpression of NO synthase is observed, which may be the result of an increase in anti-inflammatory cytokines - TNF-α (tumor necrosis factor), IL-1 (interleukin) and IL-6 and other inflammation factors.

Determined by a high level of NO formation in patients with inflammatory and infectious processes, as noted by us in the review of the literature (1.3), correlates with the severity of clinical and laboratory parameters, disease activity. Nitrogen monoxide itself is not a strong oxidant, therefore, it can be assumed that its damaging effect is mediated primarily by peroxynitrite (ONOO), which is formed by the interaction of superoxide (O2) and nitrogen monoxide along the NO + O2 - ONOO pathway. However, to date, literature data regarding the formation of ONOO in the pathogenesis and clinic of TF are practically absent.

In connection with the foregoing, one of the important tasks of our studies was to evaluate the activity of the NO-system and the associated processes of intensification of lipid peroxidation (LPO), the activity of the superoxide dismutase enzyme (SDE) on the skin surface in patients with various forms of TF associated with SH.

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An analysis of the studies showed that the level of NO on the skin of patients was determined by the form of TF, however, the development of the form of TF on the background of SH aggravated the formation of NO even more.

So, in patients with a superficial form of TF, the NO content exceeded the control data 4.72 times, in patients with TF combined with SH - 4.81 times, with infiltrative - 7.0 times, and combined with SH - 8, 0 times, with an infiltrative suppurative form - 11.12 times, and combined with SH - 13.7 times. At the same time, on the surface of the skin of patients, depending on the form of TF, and especially with its development on the background of SH, there is overexpression of ONOO, superoxidion (O2) and the activity of the enzyme NR. So, with a superficial form of TF, the ONOO level exceeded the control data by 12.0 times, with an infiltrative one - by 16.7 times, with an infiltrative-suppurative form by 42.5 times, the content of O2 - by 2.2; 2.9; 4.6 times, NR activity - 1.3; 1.7; 2.8 times.

On the background of SH with the surface form of TF, these indicators exceeded the data of those in the control - 12.4; 2.5; 1.54 times, with infiltrative - 25.5; 3.6; 2.0 times, with infiltrative suppurative form - 58.7; 5.9; 3.8, respectively, of the studied indicators. It can be assumed that the overexpression of ONOO and O2 is due to the high activity of NADPH oxidase and the intensification of FRO, which is confirmed by the progressive dynamics of an increase in CL products on the surface of the affected skin in patients with TF in accordance with the progression of the form of the disease. Moreover, as in previous studies, on the background of SH, these reactions increase. So, the activity of NADPH oxidase was higher and the CL level was significantly higher than the control values in patients with the superficial form of TF - by 49.1% and 130%, and in the infiltrative form - by 167.9 and 233.6%, the infiltrative-suppurative form - by 517.0 and 389.9%, and against the background of SH with superficial - by 71.5 and 183.1%, by infiltrative - by 275.5 and 239.1%, by infiltrative-suppurative - by 701, and 576.1%.

An important factor in the initiation of lipid peroxidation, an increase in O2 activity, is a deep depression of the activity of the SDE enzyme, which in patients with superficial, infiltrative, and infiltrative suppurative forms of TF was lower than the control data by 16.9; 22.9; 43.4%, respectively. On the background of SH, the activity of SDE in the study groups was even lower in patients with a superficial form of TF; against the background of SH, the activity of SDE was lower by 19.3 compared with the control in patients with an infiltrative and infiltrative suppuration form - by 34.9 and 53.0 respectively.

Therefore, the studies showed a significant increase in the level of NO2, which is associated with an increase in the content of ONOO, O2, activity of NR, NADPH oxidase, and CL on the background of a depressed SDE enzyme activity. The increase in NO, it can be assumed, was associated with the activation of iNOS –induced form of NO synthase, the marker of which is NADPH-dependent nitrate reductase. As a result of the inhibition of the activity of SDE, the main enzyme for the neutralization of O2, which is stimulated by the activity of NADPH oxidase, was one of the important reasons for the formation of excessive amounts of activated forms of oxygen (AFO), which is confirmed by the increased content in the washings of ultralow glow products - CL. At the same time, apparently, the reaction conditions of compound O2 with NO and the formation of a reactive and highly cytotoxic compound — ONOO — are provided. With the formation of ONOO, O2, we associate the development of the inflammatory process and skin damage in patients with TF. It can be assumed that, due to reduced skin resistance and local immunity in patients with SH, the development of various forms of TF proceeded according to an unfavorable scenario - a more pronounced violation of the processes of NO, AFO and antioxidant status in damaged skin than in patients without the form of TF combined with SH (table 6).

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Table 6: Dynamics of NO, AFO, and SDE activity in skin washes in patients with various forms of TF, M ± m

Formsofthe disease	Control, n = 20	Superficialspotted, n = 20	Superficialspotted + SH, n = 30	Infiltrative, n = 20	Infiltrative + SH, n = 30	Infiltrativesuppuration, n = 20	Infiltrativesuppuration + SH,n=30
NO^-, mcmol/l	3,31± 0,09	15,62± 0,93*	15,93± 0,81*	23,16± 1,74*	26,41± 1,85*	36,82± 2,70*	45,34± 3,19*∧
$ONOO^-$, mcmol/l	0,13± 0,01	1,56± 0,08*	1,61± 0,07*	2,17± 0,09*	3,31± 0,13*∧	5,52± 0,38*	7,63± 0,42*∧
$O2^-$, nmol/l	0,42± 0,02	0,94± 0,07*	1,05± 0,06*	1,22± 0,09*	1,53± 0,09*∧	1,95± 0,12*	2,48± 0,15*∧
NR,мкmol/ min/l	1,51± 0,05	1,96± 0,14*	2,33± 0,08*∧	2,55± 0,11*	3,06± 0,12*∧	4,28± 0,32*	5,78± 0,38*∧
NADPH-оксидаза, nmol/min/l	0,53± 0,03	0,79± 0,05*	0,91± 0,06*	1,42± 0,09*	1,99± 0,13*∧	3,27± 0,20*	4,25± 0,36*∧
CL, imp/sec	36,25± 2,81	83,41± 5,87*	102,6± 6,19*∧	120,9± 9,25*	155,9± 11,3*∧	177,6± 12,26*	245,1± 17,8*∧
SDE, ME/l	0,83± 0,03	0,69± 0,05*	0,67±0,03*	0,64± 0,04*	0,54± 0,03*∧	0,47± 0,03*	0,39± 0,02*∧

Note: * - significantly relative to the control group (* - P <0.05); ∧ - reliably relative to the group without SH (∧ - P <0.05)

Thus, the studies showed that with TF on the surface of damaged skin there is a high level of O2, NO, ONOO activity of HP, NADPH-oxidase, the content of super-weak luminescence products - CL, against the background of depression of the reaction rate of the AOS-SDE enzyme. These indicators are still violated to a large extent with the progression of TF forms - superficial, infiltrative, infiltrative suppuration, which indicates the importance of FRO processes in the pathogenesis and development of the severity, clinical course of the disease, the need for treatment methods taking into account their activity.

In this work, special attention was paid to the study of the symptoms and clinical course of various forms of trichophytosis in patients with SH. It can be assumed that more pronounced clinical symptoms of the disease, a high frequency of intoxication symptoms are associated with a deeper violation of skin resistance, a decrease in the immune system, the development of proteolysis processes, metabolic disorders in the blood, high activity of FRO, and impaired activity of antiradical defense enzymes. In patients with TF on the background of SH, the processes of immunosuppression of T8 lymphocytes of CD8, T - helper lymphocytes of CD4, the content of activated cytotoxic T-lymphocytes of CD8, natural killer cells (NK cells) - SD16 are enhanced to a greater extent, against the background of an increase in subpopulations of B-lymphocytes (CD72). These facts give reason to believe that with an increase in the severity of the disease, they create conditions for reducing tolerance to the action of infection, increasing inflammatory reactions of an allergic or autoimmune

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nature. Apparently, a special place in this process is given to reducing the subpopulations of T4DM, T8DM, which play an important role in the development of the inflammatory process. It has been established that a decrease in the CD8 subpopulation is involved in the cytotoxic effect of most antigen-specific target cells, CD4 in the antigen-specific cellular and / or humoral immune response, are targets for NK cells (CD16), cells with multiplying intracellular infections, in our study conditions in patients with trichophytosis, the cooperation of subpopulations of T and B lymphocytes is more disturbed, especially in groups of patients with a severe form of this disease on the background of SH, as evidenced by the data a decrease in the immunoregulatory index CD4 / CD8. In the reduction of cooperation in the cellular component of immunity, an important place is taken by the CIC, and the products of proteolysis by MWM [29]. Increasing as a result of an increase in decay products with the progression of mycoses, pathogenic flora, they increase the content of neutrophilic leukocytes, basophils, eosinophils, monocytes in the circulating blood, as a result of which, it should be assumed that in patients with trichophytosis, especially with combined SH pathology, LII and ESC increase.

An increase in ESC can be regarded as a consequence of enhanced surface membrane sorption of red blood cells, circulating antigens and aimed at removing them and circulating immune complexes from the blood. A decrease in the level of important subpopulations of the T-cell immunity and an increase in B-lymphocytes, against the background of increasing toxemia, may be due to the aggressiveness of the infection and a decrease in the reactivity (tolerance) of tissues. Important indicators of this process are FRO activity, antiradical defense enzymes. An increase in FRO (O2, NO, NO3, ONOO) can be associated with activation of the mycological process and pathogenic flora, as well as the presence of a high content of leukocytes in the affected skin [19, 20, 25]. All cells of the body to one degree or another participate in protection from someone else's as effector factors of the immune response. An increase in FRO infections is more related to their cytolytic effect on tissues. It is proved that the higher the AOS enzymes, the less the effect of infection through the FRO mechanism to damage the skin.However, due to its excessive activity of phagocytes, mainly granulocytes (neutrophilic, eosinophilic), FRO products can be expressed even more to the tissue, which, instead of a positive effect, can have a damaging effect on normal tissues and cause an aggravation of the pathological process [21, 5, 13].

Neutrophilic leukocytes and monocytes are able to capture, kill and digest a variety of extracellularly multiplying infectious agents, due to the direct action of FRO on them [6, 8]. In this regard, neutrophilic white blood cells play a decisive role in the destruction of extracellular parasitic microbes. Monocytes determine the outcome of chronic inflammation and free the body from intracellular parasitic microbes [7]. Unlike polymorphonuclear leukocytes, as is known, monocytes are able to regulate somatic cells infected with microbes, thus interrupting the reproduction of intracellular infections [23]. Insufficient phagocytic activity of monocytes, which is more often observed in SH [14], may be one of the important causes of the protracted course of the disease in the patients with trichophytosis under study. Moreover, NADPH oxidase is responsible for the formation of O2, [22, 24], nitrate reductase (NR) - for overexpression, in pathological processes NO, NO2, NO3, ONOO [28, 26]. In this connection, it can be assumed that an important factor in the more pronounced initiation of FRO in patients with trichophytosis against the background of SH was overexpression of the NADPH oxidase and HP enzymes on the surface of damaged skin, as well as low activity of the SDE enzyme, which inactivates O2 [4].

CONCLUSIONS

Subclinical hypothyroidism complicates the clinical course of trichophytosis, contributing to the occurrence of common multifocal lesions on smooth skin and scalp, the increase in cases of infiltrative and suppurative varieties of trichophytosis, frequent combination with other somatic diseases, and the development of general symptoms of intoxication.

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Iodine deficiency in patients with trichophytosis significantly enhances the imbalance in the cellular immunity, which is manifested by a statistically significant decrease in a subpopulation of T-lymphocytes (CD3), T-helper cells (CD4), T-cytotoxic lymphocytes (CD8), natural killer cells (CD16) on the background expression of b-lymphocytes (CD72).

With trichophytosis in the blood, a more pronounced increase in the products of proteolysis in the acute phase of inflammation is observed, which determine the degree of toxemia on the surface of the affected skin, FRO processes (increase in O2 - NO2 (NO2 and NO3), overexpression of NR and ONOO are determined. There is an increase in endogenous intoxication indicators of ESC, MWM, LII, CIC. The degree of detected disorders depends on the severity of the clinical course of trichophytosis, and is more pronounced in patients with subclinical hypothyroidism.

Thus, further study of the clinical course of zooanthroponictrichophytosis, participation in the development of the pathological process of micro - and macroorganisms will allow us to develop new effective methods of treatment of this disease.

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