American Journal of Science and Learning for Development

ISSN 2835-2157
Volume 2 | No 4 | April -2023

Features of Therapy of Comorbid Conditions in Patients with Tuberculosis

Saipova N. S, Mirodilova F. B, Khashimov F. F., Abboskhonova F. Kh.

Tashkent Medical Academy

Abstract: *The article is devoted to topical issues in the treatment of chronic dermatoses in conditions of comorbidity with cardiovascular diseases, metabolic disorders and tuberculosis of various localizations. The concept of comorbidity and its main types, review data on comorbidity in dermatosis and tuberculosis are presented, the principles of "nodal" therapy are highlighted. The results of our own studies of clinical and biochemical parameters in patients with chronic dermatoses, as well as the results of the use of glutathione in the complex therapy of concomitant diseases are presented.*

Key points: *comorbidity, tuberculosis, chronic dermatoses.*

Relevance. Diagnosis and management of patients with comorbid pathology remain one of the most difficult tasks in clinical practice [21]. Comorbid diseases are a common pathology today, which necessitates their analysis, study of the causes of occurrence and effective treatment [13,14,20]. Comorbidity should be distinguished from “multimorbidity”, both terms being the most popular in the literature [20]. Comorbidity is the coexistence of two and/or more diseases in one patient, pathogenetically and genetically interconnected [8]. Multimorbidity is a combination of several chronic diseases of various origins in one patient without any causal relationships and statistical characteristics. The difference between the terms "polymorbidity" and "comorbidity" lies in the difference in the internal relationship of various diseases. The high prevalence of a combination of diseases cannot be fully explained only by their mathematical addition, the summation of clinical, biochemical, immunological and other manifestations of individual diseases [7,18].

Combined pathologies and the development of comorbidity may be based on the phenomenon of gene pleiotropy (the ability of one gene to influence several phenotypic traits) and typical non-specific pathophysiological mechanisms (impaired membrane function, oxidative stress, endothelial dysfunction, etc.). Comorbidity factors include genetic predisposition, involutive and systemic metabolic changes, chronic infections, inflammation, iatrogenesis, social status and ecology [9,11].

Most often, the list includes CVD, DM, cancer, diseases of the kidneys, lungs, joints, dyslipidemia, and smoking. Usually two (“dyad”) or three (“triad”) diseases are combined, the number of diseases accumulates with age. Arterial hypertension (AH) is most often combined with polyosteoarthritis, IHD, DM, oncological pathology; IHD - with hypertension, diabetes, heart failure; kidney disease - with hypertension; cerebrovascular disease - with dementia, etc. [1,21].

With each subsequent accession of a new disease, against the background of morphofunctional changes in organs and systems during aging and as a result of drug pathomorphosis, new clinical forms arise, more severe, difficult to diagnose with an increased risk of complications and mortality, which forces polypharmacy [1,18]. It is of interest to study comorbidity in patients with common

multifactorial dermatoses, such as psoriasis, lichen planus, eczema, neurodermatosis, pemphigus, and others.

The combination of tuberculosis, one of the most socially significant diseases, with skin diseases dictates the need for special approaches to the treatment of underlying and concomitant diseases, and in case of skin localizations of tuberculosis, in the differential diagnosis of specific (tuberculous) and nonspecific skin pathology.

Against the background of the chronic course of tuberculosis infection, the risk of developing and more aggressive course of concomitant chronic multifactorial dermatosis (CMD), bacterial, viral and mycotic skin infections, as well as drug complications - toxicoderma, allergic dermatitis, etc., increases [4,6,10,12] . According to Ivanko S.I., (2006), skin diseases of non-tuberculous etiology are more common in patients with ITL and FCTL who excrete Mycobacterium tuberculosis, predominantly in men (56.8%) aged 20 to 39 years. The structure of dermatological pathology is dominated by dermatomycosis (45.6%), viral diseases - 28.8% and pruritic dermatoses (17.6%) [3,4,5,6].

Concomitant dermatoses affect the course of the underlying disease and the effectiveness of the treatment, contribute to the development of undesirable effects of therapy [19]. Drug allergy during PTCT is a serious problem due to the expansion of the spectrum of TB drugs [12,19]. Skin manifestations of drug allergy in patients with tuberculosis are more often noted in men (60%) with fibrous-cavernous and infiltrative tuberculosis of the lungs, secreting Mycobacterium tuberculosis. Most patients are diagnosed with allergic dermatitis - 46.6% and urticaria - 26.6% [4,6].

Attention is drawn to "tuberculides", the essence of which has not yet been disclosed [2,16]. Being united in etiological terms, they are extremely diverse in terms of patho- and histogenetics and require special attention, taking into account the relevance of the problem of studying the pathogenesis of tuberculosis as one of the most urgent problems of infectology [2,15,16]. They note the pathogenetic similarity of such lesions with Poncet's rheumatism, tuberculous-allergic synovitis, arthritis and eye lesions (uveitis, chorioretinitis), especially when they are combined.

A serious problem in comorbid conditions in patients with chronic dermatosis is mycotic, bacterial, viral infections that occur both as a result of general metabolic, immunological, biochemical disorders of the somatic status, and as a result of ongoing therapy with antibacterial and immunosuppressive drugs [3,17]. In this regard, the role of drugs that normalize the immune status of the patient increases significantly. These drugs include a new metabolic drug glutathione.

Purpose of the work: to evaluate the clinical efficacy of glutathione in the complex therapy of skin diseases in conditions of comorbidity with tuberculosis of various localizations and other somatic pathologies.

Materials and methods

Clinical observations were also carried out in 195 patients with TH, who are being treated at the Republican Scientific and Practical Center for Physiology and Prevention of the Republic of Uzbekistan. The studies included socially adapted patients aged 20 to 50 years (including 105 women and 90 men) with skin diseases. Patients were examined according to international standards using general clinical, biochemical, radiological methods of control. Among women, the infiltrative form of pulmonary tuberculosis (ITL) was in 72 (68.5%) patients, the fibrous-cavernous form (FCTL) - in 33 (31.4%). Among men, both clinical forms were diagnosed with approximately equal frequency: 42 (46.7%) and 48 (53.3%), respectively.

Patients with TB received systemic specific anti-tuberculosis chemotherapy for two or more months: for ITL, isoniazid, pyrazinamide were prescribed, in accordance with the standards for the treatment of tuberculosis, for FCT, regimens corresponding to the spectrum of drug resistance were used.

9.5% of patients had chronic obstructive pulmonary bronchitis (COPD), 3.8% had infectious hepatitis, 4.8% had diabetes, 15 (14.3%) had gastritis, and 17 (16.2%)) patients - chronic cholecystitis,

Chronically recurrent dermatoses (atopic dermatitis, psoriasis, microbial eczema, limited neurodermatitis, dyschromia, seborrheic dermatitis) were observed in 29 patients (20.0%), bacterial skin lesions (pyoderma: sycosis, boils, staphyloderma, chronic ulcerative pyoderma, ecthyma), as well as acne and hydradenitis - in 17 men (in total 8.7% of cases). Parasitic diseases (skin leishmaniasis, scabies) were found in 8 (4.1%) patients, viral dermatoses (lichen lichen simplex, herpes zoster) - in 11 (5.6%) patients.

Mycotic lesions of the skin and mucous membranes were more often noted - in general, in 135 (69.2%) patients, in men (30 patients) - these are common forms of multi-colored lichen, mycosis of the feet and large folds, erythrasma (13 patients), as well as candidal balanitis, balanoposthitis, angular stomatitis (17 patients). In women, candidiasis of large folds, angular stomatitis, mycotic eczema of the anogenital region (48 patients in total), and candidal colpitis were more often noted.

Clinical manifestations of dermatoses against the background of pulmonary tuberculosis were characterized by prevalence and torpid course. Biochemical parameters and lipid composition were studied in 29 patients with comorbidities (TL+CMD), control studies were performed in 20 healthy volunteers. Patients showed a significant increase in the level of ALT 29.77±13.9 (control - 19.96±4.45), AST - 29.96±11.7 (control - 20.88±3.30) compared with the control , as well as the content of cholesterol - 5.04 ± 0.33 (in control - 4.11 ± 0.1) mmol / l, TG, 1.33 ± 0.09 (in control - 1.12 ± 0.06) mM/l, increase in LDL - 3.03±0.28 (in control - 2.95±0.02) mM/l, and VLDL - 1.12±0.1 (0.66±0.04) mM /l, with a decrease in HDL - 0.87±0.1 (in control -1.19±0.03) mM/l.

Thus, in patients with chronic dermatosis and tuberculosis, in general, multiple comorbid conditions (AH, HD, DM, etc.) and similar changes in lipid metabolism are observed, which makes it possible to choose targeted drugs.

Glutathione was prescribed in the complex treatment of 23 patients with TB+ CMD aged 20-60 years and 29 patients with CMD without concomitant tuberculosis.

The drug was administered intravenously at a dose of 600 mg once a day for a week. The first group included the following nosologies: psoriasis-5, lichen planus-5, acantholytic pemphigus-3, eczema-5 neurodermatosis-5. In the second group, 29 patients (psoriasis - 10, LP (lichen planus) - 5, AKP (acontolytic pemphigus) - 3, eczema - 6, neurodermatosis - 5) with comorbid diseases of CVS, type 2 diabetes, HD (hypertension) (table 1)

Psoriasis (5 patients). We used glutathione in the complex therapy of intertriginous and widespread psoriasis vulgaris with large focal plaque manifestations, with pustular psoriasis, erythroderma and PA (psoriatic arthritis) in patients with TL, TKiS against the background of anti-tuberculosis therapy. Concomitant diseases: type 2 diabetes, ischemic heart disease, hypertension, COPD, obesity

LP (5 patients) glutathione was prescribed in the complex therapy of LP (typical papular form - in 3, warty - in 2). Widespread rashes were localized on the trunk, limbs, on the oral mucosa (oral mucosa). Concomitant diseases: chronic gastritis, hepatitis, cholecystitis, varicose symptom complex, obesity, type 2 diabetes, (Grishpan's syndrome - type 2 diabetes mellitus, arterial hypertension in a patient with fibrous-cavernous tuberculosis).

Acantholytic pemphigus (3 patients). Glutathione was prescribed in combination with GCS therapy (vulgar-2, seborrheic-1). Concomitant diseases and complications of therapy: Itsenko-Cushing's syndrome, hypertension, type 2 diabetes, candidal stomatitis, angular dermatitis, urogenital candidiasis (candidiasis colpitis).

Eczema (5 patients), including varicose eczema - in 2 patients aged 74 and 65 years, in 1 case in combination with erysipelas, with the formation of trophic ulcers of the leg. Concomitant diseases: IHD (ischemic heart disease), GB (hypertension), NK (circulatory failure), varicose symptom complex, chronic hepatosis (non-alcoholic fatty liver disease), obesity of the 2nd degree.

Neurodermatosis (5 patients), including atopic dermatitis (diffuse neurodermatitis) - 3, pruritus - 2 (at the age of 56 and 68 years). Concomitant diseases: chronic gastritis, cholecystitis, malabsorption

syndrome, spring-autumn hay fever, sinusitis, atopic bronchial asthma, coronary artery disease, atherosclerosis of cerebral vessels, cerebral type IRR, obesity.

Mycosis of the skin and mucous membranes in general was observed in all patients, including mycosis of large folds in 4, mycosis of the feet in squamous and intertriginous form was found in 14, onychomycosis in 6, bacterial infections of the skin in 9, secondary pyoderma against the background of CMD and diabetes mellitus), alcoholism (ecthyma, pyoderma ulcer, boils), diseases of the sebaceous and sweat glands (acne and hidradenitis).

Basic therapy for dermatoses and comorbidities was carried out according to the treatment standards of the Ministry of Health of the Republic of Uzbekistan (2021).

In the complex of external therapy for erosive and ulcerative lesions of the oral mucosa (oral mucosa) with LP (lichen planus) and pemphigus, Timogel was used in the form of applications on the elements on the gums and tongue for resorption. Lesions on the skin were lubricated with Timogel gel in combination with Neoderm cream. The clinical efficacy of treatment was assessed in the comparison groups according to the method of treatment.

Table 1. Distribution of patients with dermatoses in the compared treatment groups

	Psoriasis	LP	Neurodermitis	Exema	Pemphigus
Anti-tuberculosis drugs. Glutathione 600 mg 1 time / day No. 5-10. Outwardly: Neoderm, thymogel, fukortsin, etc., taking into account morphological changes					
1 group, n=23 (CMD + TB + other diseases)	5	5	5	5	3
Glutathione IV 600 mg 1 time / day No. 5-10. Outwardly: Neoderm, thymogel, fukortsin, etc., taking into account morphological changes					
2 group , n=29 (CMD + other diseases)	10	5	6	5	3
Traditional treatment. Outwardly: Neoderm, thymogel, fukortsin, etc., taking into account morphological changes					
Control (CMD + other diseases), n=41	10	10	10	6	5
GCS therapy (according to indications in all groups): 11 patients (pustular psoriasis, PsA, acantholytic pemphigus, erythroderma)					

The effectiveness of therapy was assessed 1) according to "utility criteria" - the dynamics of clinical manifestations, regression of local symptoms of inflammation and subjective sensations, the development of unwanted side effects 2) in terms of quality of life - reduction of suffering (elimination of itching, soreness), restoration of working capacity and social communication; 3) according to the influence on the course of concomitant diseases - the reduction or disappearance of clinical symptoms and the normalization of laboratory parameters; 4) according to the assessment of direct and indirect costs of treatment - inpatient treatment, drug provision, loss of time, restriction of labor and social activities.

Medical efficacy was assessed by the ratio of positive (clinical recovery, improvement) and undesirable (minor effect, complications) treatment outcomes. The effectiveness of the method (Ek, Et, En, Et + n) was calculated as (a + c) = 100%, where a is the desired, c is an undesirable outcome for each method

To determine the effectiveness of various methods of treatment, the results were analyzed according to the scheme proposed by G.P. Kotelnikov, A.S. Spiegel. A contingency table was compiled, in which possible adverse outcomes were given, indicating insufficient efficacy of pharmacotherapy (Table 3). Recommended key indicators were calculated.

Table No. 2 The frequency of positive and undesirable outcomes of treatment

Condition Criteria	K p=41 trade treat	1-group P=29	2group P=23
		glutation	
Clinical recovery Absence of new rashes, complete regression of rashes (reduction of PASI, EASI SCORAD by 90% of the original), lack of sensation, restoration of physical activity and social and social activities No complications or side effects of treatment	20 (48,8%)	15 (51,7%)	16 (69,6%)
Clinical Improvement Absence of new lesions, reduction of inflammatory symptoms (weeping, xerosis, infiltration (reduction of PASI, EASI, SCORAD by 75% of the original), reduction of subjective sensations, restoration of physical activity and social and social activities Side effects of corticosteroids (cushingoid, osteoalgia, hypertension)	12 (29,2%)	10 (34,5%)	4 (17,4%)
Minor improvement absence of new rashes, partial regression of elements - a decrease in the area of the lesion by 25%, a decrease in subjective sensations, the absence of a complete remission, relapses, acne, GCS withdrawal syndrome with a decrease in dose, cushingoid, hypertension, etc.	9 (21,9%)	4 (13,8%)	3 (13,04%)
A + B (a - desirable, c - undesirable outcome in the control group, (sg, dg), (stg, dtg) - in the comparison groups)	32+9	25+4	20+3
Risk of outcomes, a/(a+c) (in%), st/(st+dt), df/sn+dn) stn,/(stn+dt)	78,0%	86,2%	86,9%
Relative risk, sg / (sg + dg) / a / (a + c) (in%)		1,1	1,1
Absolute risk reduction, CAP= s/(s+e)-a/(a+c), %		8,2%	8,9%
Relative risk reduction, ROR wor \u003d (s / (s + d) - a / (a + c)) / (a / (a + c))%		10,2%	11,4%
Odds ratio OR, (a/c)/(s/d) for each group		0,58	0,53

In the course of treatment, there was a positive dynamics of clinical manifestations in both comparison groups, a decrease in the PASI, EASI, SCORAD index by 75% compared with baseline values, a reduction in the epithelization of erosions in case of skin lesions and oral mucosa (oral mucosa), a decrease in subjective sensations and an increase in quality of life of patients. In patients with tuberculosis, there was an improvement in well-being, a decrease in symptoms of intoxication, cough

In the course of therapy, no adverse reactions to drugs of the complex of specific therapy and accompanying therapy were detected. The ongoing therapy is applicable to the management of patients with concomitant pathology of CCC, NK (circulatory failure) and GBS. In both groups, patients showed positive dynamics of biochemical parameters of blood. In general, the ongoing treatment has reduced the amount of drug therapy. (tab. №2)

Table 3. Dynamics of clinical symptoms in patients with dermatoses during therapy (terms in days, M+m).

Index	Control, n=41	HMD+KZ Glutathionee, n=29	HMD+TB+CZ Glutathione, n=23
No new elements	10,18±2,72	9,98±2,63	9,98±2,63
Regression of rashes:	18,7± 5,55	16,4±5,53	15,9±5,02
Erythema, infiltration, hyperkeratosis (papules, plaques)	15,2±6,43	12,86±5,66	12,4±3,43
Epithelization of erosions on the skin	10,3±1,08	6,3±0,47	-
Epithelialization of erosions on mucous membranes	18,7±5,55	5,4±1,23	-
Rejection of crusts, pigmentation	14,0±3,23	11,0±1,41	-
Decreased oozing, exudation	7,9±0,93	6,26±0,46	6,0±0,4
Decreased dryness, lichenification	10,75±2,22	10,5±1,5	10,3±1,08
Reducing the intensity of itching	11,4±3,62	10,1±2,8*	9,9±2,55
General state normalization	10,9±2,03	7,6±0,90	9,6±2,71
Reducing intoxication	10,5±1,5	7,8±0,92	8,3±0,88
The increase in physical activity	14,3±3,30	11,3±0,8	13,5±2,23
Drug complications (toxicoderma, hepatitis, hypertension), abs. (%)	3 (7,3)	3 (10,3)	-
Station duration. to lay down. dermatoses, day	20,3±5,32	17,6±5,26	17,1±5,05
Remission duration	10 day to 12 month.	10 day to 12 month.	10 day to 12 month.
Number of relapses during the year	1-3	0-3	0-2

Note. * – $p<0.05$.

Conclusion. In most cases, there was a clinical recovery and a significant clinical improvement (preferably a positive outcome). The results obtained allow us to conclude that the effectiveness of treatment with the appointment of glutathione and combined topical preparations was 86.2-86.9% and was higher than in the control group using traditional methods of treatment. The risk of complications with these methods is minimal, the odds ratio does not exceed 1.

In most patients, a significant regression of rashes was noted within 10-14 days, in most cases - until the symptoms, itching and discomfort completely disappeared. The most pronounced effect was observed when Neoderm was combined with thymogel, which is due to the action of components that complement each other (clotrimazole, clobetasol, neomycin, metronidazole, timoptin). Along with the positive dynamics of skin manifestations of dermatosis on the background of tuberculosis, in the process of complex therapy, a positive effect on comorbid diseases was noted - the dynamics of general clinical and radiological symptoms of tuberculosis improved, and there were no undesirable effects of therapy.
In the course of treatment with glutathione, the majority of patients showed positive dynamics of biochemical parameters of the blood, there were no intolerance to drugs and allergic reactions. Thus, the inclusion of Glutathione in the complex of treatment of patients with chronic multifactorial

dermatosis, comorbid pathology of internal organs and tuberculosis makes it possible to optimize the tactics of managing comorbid patients. (Table No. 3)

Literature.

1. Asfandiyarova N.S. Multiple chronic diseases // Clinical gerontology, 3-4, 2018, -57-64.
2. Bellendir E.N. Modern understanding of the pathogenesis of extrapulmonary tuberculosis / / Scientific works of the All-Russian Scientific and Practical Conference / ed. Yu. N. Levasheva. SPb., 2006. -S. 225-226.
3. Gorbuntsov V.V. Malassezia skin. Lecture.//Dermatovenereology. Cosmetology. Sexopathology.-2010-1-2.-125-153.
4. Dermatoses as a special variant of concomitant pathology in patients with respiratory tuberculosis / S. A. Ivanko, S. E. Borisov, Yu. scientific tr. Conf. dedicated to the 45th anniversary of the Department of Tuberculosis of the Saratov State Medical University. - Saratov, 2006. - P. 94–98.
5. Zhovtyak P.B., Grigoriev S.S., Letaeva O.V. The structure of comorbid pathology in patients with various forms of lichen planus of the oral mucosa // Modern problems of science and education. - 2015. - No. 4;
6. URL: https://science-education.ru/ru/article/view?id=20732
7. Ivanko, S. A. Modern characteristics of dermatoses in patients with respiratory tuberculosis// IV scientific and practical conference in memory of Professor A. L. Mashkileison: Sat. scientific tr. conf. - M., 2006. - S. 48–50.
8. Kaminskaya G.O., Abdullaev R.Yu., Komissarova O.G. Features of lipid metabolism in patients with pulmonary tuberculosis with concomitant diabetes mellitus type 1 and 2//Tuberculosis and lung diseases.- 2016.-volume No. 94.-No. 9.-65-72.
9. Klyukvina N.G. The problem of comorbidity in systemic lupus erythematosus. Regular issues of "RMJ" No. 7 dated 04/21/2015 p. 370
10. Makulbekova S.K. Polymorbidity in patients and their role in diagnosis and treatment (literature review). Vestnik KRSU. 2015. V. 15, No. 11. P. 100–102.
11. Mitrushkina, features of the manifestation of dermatoses in patients with HIV infection and tuberculosis // Tuberculosis and lung diseases.- 2019.- Volume 97, No. 1
12. Comorbidity and multimorbidity in the medical practice: A literature review / L. Collaku,M. Resuli, I. Gjermeni, M. Tase. Alban Med J. 2017. Vol. 4. P. 55–59.
13. Charlson ME, Pompei P, Ales KL, McKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chron Dis 1987;40(5): 373-383.
14. Porovsky Ya.V., Tetenev F.F. Comorbidity in medical practice. Siberian Medical Review. 2015. No. 4. P. 5–13. Serbina I. M. Comorbidity in alopecia areata. // Dermatology and venereology. - No. 2 (80) 2018.- P. 67-70.
15. Tlish M.M., Popandopulo E.K. Etiopathogenetic aspects of the development of microbial eczema (review). /Saratov scientific medical journal.- 2018.-vol. 14.-4-651-656.
16. Chuzhov A.L. Clinical and morphological features and diagnosis of various forms of skin tuberculosis. Diss. Candidate of Medical Sciences, St. Petersburg.-2009
17. Shevyakov M. A., Uspensky Yu. P. Features of diagnosis and treatment of candidiasis of the upper digestive tract in patients with metabolic syndrome // Experimental and Clinical Gastroenterology 2017; 143(7): 161–166).