

Broncho-obstructive lung diseases as comorbid conditions in tuberculosis: current strategies for diagnosis and treatment

Ostrovskyy M.M., Makoida I.Ya., Shevchuk-Budz U.I.

Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine

Abstract. This abstract highlights current issues related to the comorbid course of tuberculosis (TB) and chronic obstructive lung diseases, including chronic obstructive pulmonary disease (COPD) and bronchial asthma (BA). Current criteria for the differential diagnosis of these conditions are analyzed, taking into account specific changes in pulmonary function, the type of inflammation, and the architecture of the bronchial receptor apparatus. Personalized approaches to pharmacotherapy are substantiated in accordance with the updated international GOLD and GINA guidelines, particularly strategies for the use of inhaled corticosteroids (ICS) and for minimizing the risk of pulmonary infections. The pathogenetic rationale and clinical relevance of including the mucoactive drug erdosteine in basic treatment regimens and pulmonary rehabilitation programs are demonstrated.

Key words: tuberculosis, COPD, bronchial asthma, GOLD, GINA, inhaled medications, erdosteine.

Background. According to the World Health Organization, COPD and TB remain among the top 10 leading causes of death worldwide, ranking 4th and 10th, respectively [1]. The combination of TB infection and chronic broncho-obstructive pathology significantly aggravates the clinical course of both conditions, accelerates the destruction of lung tissue, and complicates the selection of effective therapy.

The situation is further worsened by the critically low level of patients' adherence to treatment. Medical statistics indicate that adherence to recommendations in BA is only 55.0 %, while in COPD it is 51.0 %, representing the lowest rates among all chronic human diseases [2].

An important factor contributing to disease progression and high mortality in COPD is persistent mucus hypersecretion and the formation of mucus plugs. According to the multicenter prospective COPDGene study, in 73.0 % of patients with COPD, mucus plugs persist in the airways for 5 years, leading to a more rapid decline in lung function, reduced quality of life, increased rates of hospitalization, a higher risk of infectious complications, and increased all-cause mortality [3, 4].

Objective. To illustrate approaches to the differential diagnosis of COPD and BA in patients with pulmonary TB, as well as to substantiate current strategies for the pharmacotherapy of broncho-obstructive syndrome, including the use of ICS and mucoactive agents with

anti-inflammatory effects, based on the current international GOLD and GINA recommendations.

Results and discussion. Differentiation between COPD and BA. Clear differentiation of airway diseases is a primary task for selecting appropriate therapy, including in patients with pulmonary TB. The main diagnostic criteria include:

- A) Etiology and pathophysiology: the development of BA is initiated by sensitizing agents, namely allergens, and is accompanied by atopy, airway hyperresponsiveness, and a predominantly eosinophilic type of inflammation. COPD develops under the influence of harmful agents, such as smoking and pollutants, and is associated with neutrophilic and macrophage-mediated inflammation, without pronounced airway hyperresponsiveness or atopy [5, 6].
- B) Medical history and clinical presentation: BA is characterized by onset at an early age, high variability of symptoms with worsening at night or in the early morning, the presence of comorbid allergic conditions such as rhinitis or eczema, and a positive family history. COPD predominantly manifests after the age of 40 years, has a slowly progressive pattern of symptoms, and is associated with a long history of smoking.
- C) Spirometric parameters: BA is characterized by reversible bronchial obstruction, whereas in COPD the obstruction is persistent/non-reversible, defined as an FEV₁/FVC ratio <0.7 after a bronchodilation test.
- D) Anatomical features and receptor apparatus: in BA, the pathological process, including mucosal edema and smooth muscle spasm, predominantly affects the small airways [7]. In COPD, the large and medium-sized bronchi are mainly involved [8]. It is important to consider airway tone: the large bronchi account for up to 90.0 % of total pulmonary resistance, since their total lumen is significantly smaller than that of the peripheral bronchi [9]. M-cholinergic receptors, located in the large and medium-sized bronchi, are resistant to tachyphylaxis and remain sensitive in patients of all age groups, which makes anticholinergic agents a basic component of COPD therapy [10], in contrast to β_2 -adrenergic receptors of the small bronchi, which show a tendency toward tachyphylaxis and reduced sensitivity in older individuals [11].

Updated strategies for basic therapy of COPD and BA according to the updated GOLD 2026 and GINA

2026 recommendations. According to the latest updates of international consensus documents, disease control strategies have undergone substantial changes:

- A) Assessment according to GOLD criteria in COPD: the ABE assessment tool has been revised based on new evidence indicating that even a single moderate or severe exacerbation increases the risk of subsequent adverse events [12]. Patients with a history of at least one exacerbation per year (≥ 1 moderate or severe exacerbation) are automatically classified as Group E, which requires initial treatment with a long-acting β_2 -agonist (LABA) + long-acting muscarinic agonist (LAMA) combination or consideration of triple therapy with LABA + LAMA + ICS in patients with a high blood eosinophil count (≥ 300 cells/ μ L) [12].
- B) Strategy for the use and withdrawal of ICS: the current consensus concept emphasizes the risks associated with unjustified treatment de-escalation [12]. In patients receiving combination therapy with ICS/LABA/LAMA, the ICS component should not be withdrawn, except in cases of inappropriate initial prescription, complete absence of clinical response, or the development of severe or recurrent adverse effects, such as pneumonia [12]. If the blood eosinophil count is ≥ 300 cells/ μ L, ICS withdrawal is likely to result in exacerbations [12]. At the same time, the individual safety profile of the medications should be carefully considered [12]. Risk groups for the development of pneumonia include smokers, individuals aged over 55 years, patients with a history of pneumonia, body mass index < 25 kg/ m^2 , severe dyspnea, or eosinophilia < 2.0 % [12]. A large meta-analysis of 18 randomized controlled trials ($n=49,828$) demonstrated that the use of fluticasone propionate is associated with an increased risk of pneumonia ($rr=1.79$; $p<0.001$) [13]. In contrast, budesonide does not demonstrate such a risk ($rr=1.07$; $p=0.664$) [13], which can be explained by its pharmacological properties: budesonide has substantially higher water solubility (16 versus 0,14 μ g/mL for fluticasone), dissolves much more rapidly in bronchial fluid (6 minutes versus more than 8 hours), and is rapidly absorbed into tissues, thereby significantly reducing the duration of the local immunosuppressive effect on the mucosa, which is particularly important in mycobacterial infection as well [14-16].

Achieving asthma control according to GINA recommendations: in the management of patients aged 12 years and older, Track 1, based on an anti-inflammatory reliever, is recognized as the preferred approach [17]. The use of the budesonide-formoterol combination in the SMART regimen, both as maintenance therapy at Steps 3-5 and for rapid symptom relief as needed, reduces the risk of severe exacerbations by 45.0 % compared with

short-acting β_2 -agonist-based regimens and by 27.0 % compared with as-needed formoterol [18].

Optimization of mucolytic therapy in broncho-obstructive conditions in patients with pulmonary TB: since chronic airway inflammation is accompanied by tissue damage, or alteration, leukocyte infiltration, and exudation with increased sputum viscosity, the prescription of effective mucoregulators is critically important [19]. The use of erdosteine, marketed in Ukraine under the trade name Ermucin, is pathogenetically justified [19]. The drug acts as a potent free radical scavenger, blocks key inflammatory mediators, including IL-6 and IL-8, stimulates an increase in secretory immunoglobulin A, and protects α_1 -antitrypsin from inhibition [19]. Real-world clinical practice studies have confirmed the following effects of erdosteine:

- A) Reduction in the frequency of exacerbations: a two-year course of treatment significantly reduces the number of all COPD exacerbations, and this effect is pronounced regardless of exacerbation history, the presence of cough, GOLD stage 3-4, or concomitant ICS use [19].
- B) Antiviral activity: in laboratory infected models, Ermucin at a dose of 1,000 μ g/mL demonstrated the ability to inhibit the replication of respiratory viruses: SARS-CoV-2 by 91.0 %, respiratory syncytial virus by 94.5 %, and influenza A virus (H1N1) by 47.5 % [19].
- C) Post-COVID rehabilitation. Clinical trials published in the European journal *Minerva Medica* have demonstrated that Ermucin administered at a dose of 300 mg twice daily for 1 month in patients who had recovered from COVID-19 provides a clinically meaningful reduction in cough and dyspnea, defined as a decrease of ≥ 4 points on the St. George's Respiratory Questionnaire, as well as significant restoration of physical activity [19, 20].

Conclusions. The comorbid course of TB and broncho-obstructive lung diseases requires accurate differential diagnosis, taking into account the specific features of chronic inflammation, its type, and pulmonary function abnormalities.

Current therapy for COPD and BA, including in patients with pulmonary TB, is based on the personalized approach outlined in the GOLD and GINA consensus documents. The choice of the ICS component should take into account the need to minimize the risk of pulmonary infections, including mycobacterial infection. In this context, budesonide may be preferable to fluticasone due to its faster absorption and higher solubility [12, 13, 17].

The inclusion of erdosteine in basic COPD treatment regimens, including in patients with pulmonary TB, as well as in post-COVID rehabilitation programs, is a pathogenetically justified approach that provides simultaneous mucolytic, anti-inflammatory, antioxidant, and antiviral effects [19].

References

1. World Health Organization (WHO). The top 10 causes of death (Data 2022-2023). WHO Fact Sheets.
2. Hansen R., Seifeldin R., Noe L. Medication adherence in chronic diseases. *Transplant. Proc.* 2007; 39 (5): 1287-1300.
3. Diaz A.A., et al. Airway mucus plugs and mortality in COPD: the COPDGene study. 2023.
4. Tian X., et al. Mucus hypersecretion and long-term outcomes in chronic airway diseases. 2015.
5. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention. 2026.
6. Milne S., Mannino D., Sin D.D. Asthma-COPD overlap and chronic airflow obstruction: definitions, management, and unanswered questions. *J. Allergy Clin. Immunol. Pract.* 2020 Feb; 8 (2): 483-495.
7. van den Bosch W.B., James A.L., Tiddens H.A.W.M. Structure and function of small airways in asthma patients revisited. *Eur. Respir. Rev.* 2021 Jan 19; 30 (159).
8. Tanabe N., Shimizu K., Terada K., et al. Central airway and peripheral lung structures in airway disease-dominant COPD. *ERJ Open Res.* 2021 Mar 22; 7 (1).
9. Usmani O.S., Dhand R., Lavorini F., Price D. Why we should target small airways disease in our management of chronic obstructive pulmonary disease. *Mayo Clin. Proc.* 2021 Sep; 96 (9): 2448-2463.
10. Shelley R., et al. Receptor distribution in human airways. *Ann. Intern. Med.* 2004; 140: 802.
11. Donohue J.F., et al. Anticholinergic therapy in progressive airway diseases. *Chest.* 2002; 122: 47.
12. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of COPD. 2026. Available at: <https://goldcopd.org>.
13. Zhang Q., Li S., Zhou W., et al. Risk of pneumonia with different inhaled corticosteroids in COPD patients: a meta-analysis. *COPD.* 2020 Aug; 17 (4): 462-469.
14. Richardson H., Alferes De Lima Headley D., Clarke C., et al. The effect of different inhaled corticosteroid and long-acting bronchodilator combinations on the airway microbiome in patients with severe COPD: a randomised trial (MUSIC). *Eur. Respir. J.* 2025; 66 (4): 2500287.
15. Edsbäcker S. Pharmacological differences between inhaled corticosteroids. *Pulm. Pharmacol. Ther.* 2008; 21 (2): 247-258.
16. Lodise T.P., et al. Local immunosuppression and pneumonia risks with ICS. *Int. J. Chron. Obstruct. Pulmon. Dis.* 2020 Nov 11; 15: 2889-2900.
17. Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA). 2025. Available at: <https://ginasthma.org>.
18. Rabe K.F., Atienza T., Magyar P., et al. Effect of budesonide in combination with formoterol for reliever therapy in asthma exacerbations: a randomized controlled, double-blind study. *Lancet.* 2006; 368 (9537): 744-753.
19. Cogo R. Erdosteine: a new therapeutic weapon beyond the PEACE. *Trends Med.* 2012; 12 (3): 133-142.
20. Feshchenko Yu.I., Ostrovskyy M.M., Varunkiv O.I., Horovenko N.H. Improved quality of life and dyspnea with erdosteine in COVID-19 patients after hospital discharge. *Minerva Respiratory Medicine.* 2022 Feb 10.