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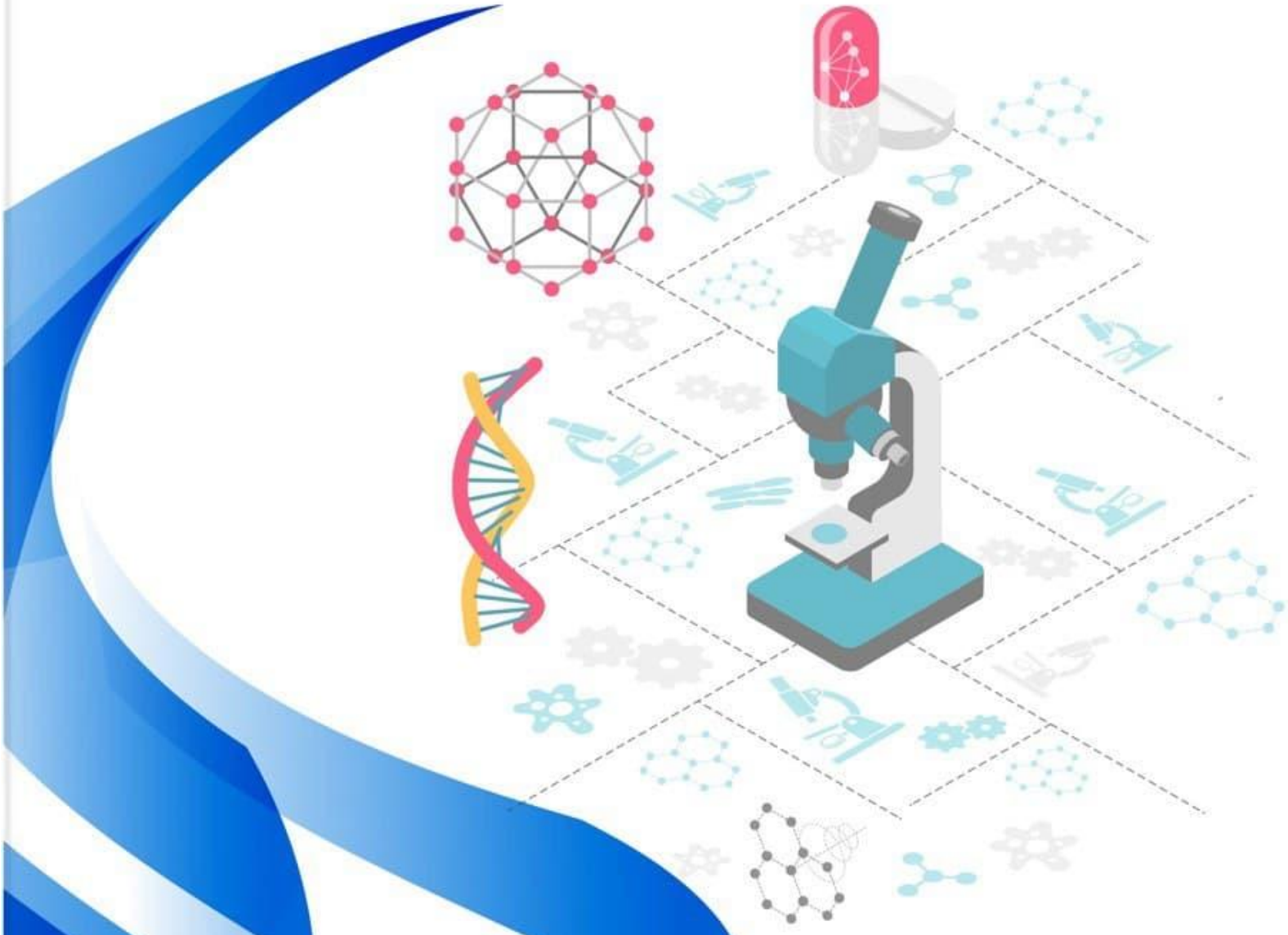

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FEATURES OF MANAGEMENT OF PATIENTS WITH COPD ASSOCIATED WITH COVID-19

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Abstract: Objective: Based on literary sources, to present modern data on the problem of comorbidity of chronic obstructive pulmonary disease (COPD) and the new coronavirus infection COVID-19.

The review summarizes and systematizes modern concepts about the association of COPD and COVID-19 and highlights the most important aspects of this problem - epidemiological, pathogenetic, clinical. Particular attention is paid to the management of patients with COPD in the context of the COVID-19 pandemic, based on the accumulated research experience and international guidelines.

The need for further clinical studies on the problem of comorbidity of COPD and COVID-19 is shown, which will allow a detailed study of the mechanisms of mutual aggravation of associated pathology, to clarify the effect of SARS-CoV-2 on the respiratory system and the course of COPD taking into account the phenotype of the disease, to determine effective treatment methods and improve the prognosis of patients with COPD who have had the new coronavirus infection COVID-19.

Keywords: comorbidity, COVID-19, chronic obstructive pulmonary disease.

The physician must clearly understand the tasks of managing a patient with COPD associated with the new coronavirus infection COVID-19. According to the provisions of GOLD (Global Initiative for Chronic Obstructive Lung Disease), the list of drugs for daily therapy depends on the patient's definition in accordance with the integrated assessment of the disease in one of the groups - A, B, C, D and includes long-acting bronchodilators (β2-agonists, anticholinergic drugs), according to indications - inhaled corticosteroids, phosphodiesterase-4 inhibitors. During an exacerbation, which is defined as a deterioration in the condition leading to increased drug therapy, antibacterial drugs, mucolytics, and oxygen therapy are additionally prescribed.

Guidance on treatment and follow-up for patients with COPD during the pandemic has been provided by both GOLD and the UK National Institute for Health and Care Excellence (NICE) [6, 13].

GOLD recognizes that patients with COPD are at risk for complications from COVID-19 and strongly recommends that people with COPD follow hygiene measures to reduce the risk of infection. Patients with COPD should continue their usual treatment according to national COVID-19 guidelines and use information provided by WHO. If necessary, oxygen therapy should be administered according to standard recommendations. It is also necessary to ensure that each patient is given at

least a 30-day supply of medication. Pulmonary function tests should not be performed unnecessarily [12]. During the pandemic, the use of a nebulizer is not recommended; metered-dose inhalers with spacers are preferred [4]. Patients are advised to wash their hands, use spacers and mouthpieces and wash them with soapy water before and after using inhalers [6].

To date, recommendations have been published by the Chinese Thoracic Society/Chinese Association of Internal Medicine [8] and the Canadian Thoracic Society [14] on optimizing the care of patients with COPD during the COVID-19 pandemic.

Practical recommendations and summary information on the management of patients with COPD are presented in the National Consensus

"Features of managing comorbid patients during the pandemic of a new coronavirus infection (COVID-19)" [2].

Currently, the international medical community is actively discussing the effects of glucocorticosteroids (GCS) (inhaled and systemic) on the course of COVID-19. It is known that respiratory viral infections are among the significant triggers of COPD exacerbation, which is associated with their ability to increase the synthesis of proinflammatory cytokines (interleukins (IL) 1, 6 and 11) in the epithelial cells of the respiratory tract [11]. Therefore, from a pharmacodynamic point of view, the benefits of topical GCS in COVID-19 (with similar induction of IL-1 and IL-6) seem obvious. Moreover, there are data on the suppression of SARS-CoV-2 virus replication when using budesonide in combination with formoterol and glycopyrronium in vitro, possibly due to a decrease in the expression of ACE2 and TMPRSS2 receptors, which are necessary for the penetration of the virus into the cell, during their use [17]. Concerns about continuing ICS therapy in COPD are associated with an increased risk of respiratory tract infection, including pneumonia [16], possibly due to a decrease in the natural antiviral immune response, reduced neutrophil migration, delayed viral clearance [3,4,9] and an increased risk of COVID-19-associated death.

British scientists Schultze A., Walker AJ, MacKenna B. et al. in a nationwide population-based study based on the analysis of de-identified records for individuals with COPD and bronchial asthma, with and without COVID-19, from the Korean Health Insurance Review and Assessment (HIRA) database, found that the use of inhaled corticosteroids was associated with a significantly higher risk of mortality in an unadjusted analysis (OR 3.11; 95% CI 1.60-6.03; $P < 0.001$), although the association was not significant after adjusting for age, gender, region, TPP SystmOne software data (coded diagnoses, medications, physiological parameters) and hospital type (adjusted OR 0.94; 95% CI 0.43-2.07; $P = 0.88$).

In an observational cohort study from March 1 to May 6, 2020, researchers from the UK also assessed the impact of ICS on COVID-19 outcome in patients with COPD. The study included 148,557 patients with COPD aged ≥35 years, current or

former smokers, who were receiving ICS or a long-acting β-agonist + long-acting muscarinic antagonist for 4 months before the start of the study [32]. Results of this study: patients with COPD receiving ICS had an increased risk of COVID-19-associated death compared with patients receiving combination therapy (long-acting β-agonist + long-acting muscarinic antagonist) by 39% (hazard ratio, 1.39 [95% CI, 1.10–1.76]).

At the same time, there are research results indicating the absence of a relationship between the use of inhaled corticosteroids by COPD patients and clinical outcomes [11].

To date, the issue related to the use of systemic GCS by patients remains unclear. A meta-analysis has shown that their use as indicated for a short course (5-10 days) can reduce the patient's need for emergency care, which compensates for the low risk that systemic GCS can prolong viral replication [16].

It should be noted that GOLD does not have scientific evidence to avoid the use of inhaled or oral GCS in patients with COPD against the background of SARS-CoV-2 infection [13]. At the same time, the European Respiratory Society recommends to refrain from using inhaled GCS in patients with COPD during COVID-19 if the eosinophil level in 1 μl of blood is <150 cells and exacerbations occur less than 2 times a year [5].

Conclusions. Thus, all of the above shows the relevance of the problem of comorbid COPD and COVID-19. Given that COPD is a multifactorial disease with many clinical phenotypes, studies are needed on the impact of COVID-19 on the course and further prognosis in patients with COPD depending on the phenotype and risk category of exacerbations, which will allow for a personalized approach to managing such patients.

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