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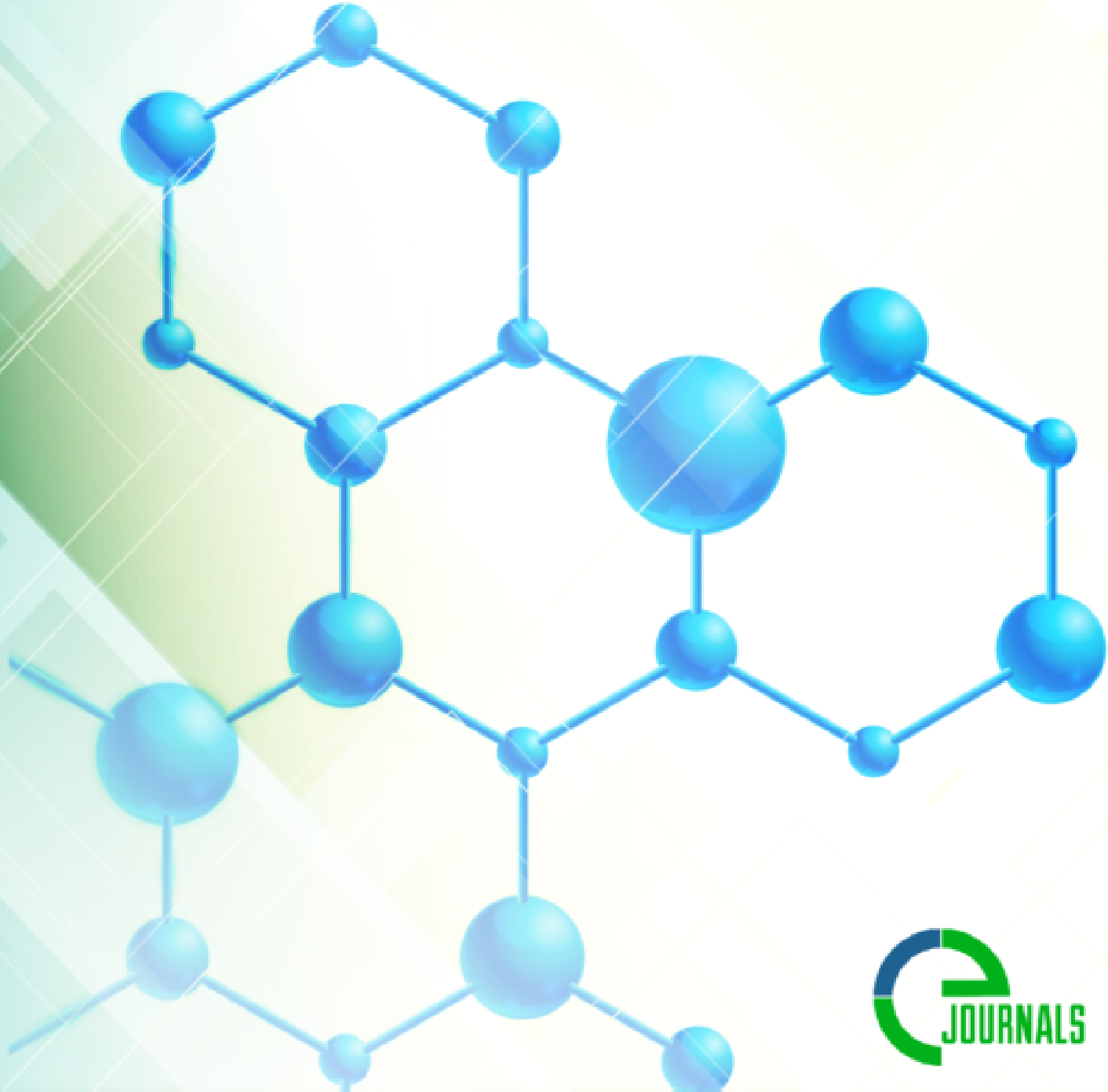

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BRONCHIAL ASTHMA AND ALLERGIC RHINITIS IN THE ERA OF COVID-19: DATA FROM PUBLICATIONS OF THE FIRST SPRING OF THE PANDEMIC AND EXPERT RECOMMENDATIONS

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Abstract. The onset of asthma and its exacerbation in some cases is associated with respiratory viruses. The emergence of a new type of coronavirus infection has raised these issues again, including predicting the risk of COVID-19 in asthma patients. The article describes the data on the association of asthma with respiratory viral infections, including COVID-19, approaches to the differential diagnosis in asthma and allergic rhinitis, expert recommendations on the prevention and treatment of diseases during an epidemic.

Keywords: asthma, respiratory viruses, novel coronavirus infection (COVID-19), asthma exacerbation, asthma treatment, COVID-19 prevention, allergic rhinitis.

Bronchial asthma and COVID-19

Frequency, risk of death and pathogenetic mechanisms

There are currently few data on the incidence of COVID-19 among patients with asthma. A number of studies have not found a relationship between COVID-19 and asthma, but studies have been published that demonstrate that asthma is relatively common in patients with COVID-19. Several studies on COVID-19 only mentioned AD as a comorbidity, which is not enough to draw firm conclusions.

According to relatively early data from the Chinese Centers for Disease Control (CDC), only 2.4% of 44,672 patients with COVID-19 examined had CBOD, including AD [1]. Another study reported the absence of concomitant asthma in an evaluation of 1590 patients in China [2]. J. Zhang et al. [3] observed 140 patients with COVID-19 in Wuhan, China, among whom 11.4% had hypersensitivity to certain drugs, and 1.4% had urticaria, but none of them were diagnosed with AD or other allergic diseases. A study conducted in Lombardy (Italy), including 1591 patients with COVID-19, also showed a relatively low prevalence of obstructive pulmonary disease in 42 (4%) patients [4]. However, according to New York data (USA), the frequency of BA was 9% of 5700 examined with COVID-19 [5]. At the same time, it should be noted that the study does not clearly define the exact clinical phenotypes and methods of treatment of patients, and according to New York State mortality statistics, AD is not in the "top 10" comorbidities as of April 30, 2020 (New York State Department of Health COVID-19 Tracker-Fatality). These results generally give the impression that allergic diseases may not be a predisposing or aggravating factor for COVID-19. However, the interpretation of these data should be approached very carefully, as information about COVID-19 is only accumulating, will be further accumulated and analyzed more carefully.

Asthma data on the risk of death associated with COVID-19 also demonstrate a slightly lower significance of this pathology compared to other risk factors and comorbidities. For example, in an English population study by E. Williamson et al. [6] analyzed 5683 deaths of patients with COVID-19 who were treated from February 1 to April 25, 2020. Along with male gender (RR 1.99, 95% CI 1.88-2.10), advanced age, uncontrolled diabetes mellitus (RR 2.36, 95% CI 2.18-2.56) and other diseases/conditions, death from COVID-19 was also independently associated with severe AD treated with oral glucocorticosteroids (GCS) (RR 1 .25, 95% CI 1.08-1.44). At the same time, in the

preprint of the article with another study dated May 08, 2020, it was noted that BA is associated with longer intubation of patients in case of severe COVID-19 (1003 patients): 10.2ё6.9 days versus 5.3 ё5.9 days in patients without BA (p=0.002); but not with an increased risk of death [7]. In addition, this preprint, based on data from the American CDC, noted that 17% of those hospitalized with COVID-19 had asthma, and in the age group of 20-49 years, asthma was observed in 27% and was the second most common NCD after obesity (the prevalence of asthma in the United States - about 19 million among the adult population). Thus, the available evidence is somewhat conflicting and warrants further study of the characteristics of asthma in COVID-19.

The pathogenetic mechanisms of COVID-19 in AD are not well understood. It can be assumed that the course and outcome of COVID-19 in patients with BA, as well as in patients with other chronic NCDs, may be associated with the expression of ACE2 and TMPRSS2. Recently published preliminary data from an American study that examined the expression of the ACE2 and TMPRSS2 genes in 330 AD patients compared with 79 healthy patients. ACE2 gene expression was lower than that of TMPRSS2, and its levels were similar in AD patients and healthy controls. However, among AD patients, male, African American, and diabetes mellitus were associated with higher expression of ACE2 and TMPRSS2. At the same time, the use of inhaled corticosteroids (IGCS), on the contrary, was associated with lower expression of ACE2 and TMPRSS2. Triamcinolone acetate treatment did not reduce the expression of both genes. Based on these data, the authors suggested that it would be reasonable to subgroup AD patients with a likely higher risk of poor outcomes from COVID-19 (men, African Americans, patients with diabetes mellitus). The lower expression of ACE2 and TMPRSS2 during treatment with ICS, according to the authors of the article, is the reason for a prospective assessment of the possible protective role of ICS in reducing susceptibility to SARSCoV-2 and the incidence of COVID-19 [8].

Differential diagnosis of asthma exacerbation and COVID-19

The association of COVID-19 directly with asthma exacerbations is also poorly understood. It is known that good control of asthma symptoms is always important to reduce the risk of exacerbation [6, 9, 10], including those induced by respiratory infection. It should also be taken into account that exacerbation of BA can be caused by other reasons: exposure to allergens (for example, seasonal), drugs, another respiratory infection (not SARSCoV-2), discontinuation of the regular use of ICS (pathogenetic therapy for BA), a complex of reasons.

Exacerbation of asthma (like its onset) and the course of COVID-19 can be difficult to distinguish clinically. It is known that the most common symptoms of COVID-19 (dry cough and shortness of breath) are included in the criteria for exacerbation of asthma [9]. When collecting complaints, differentiating BA and a new coronavirus infection, it is advisable to pay attention to anosmia, febrile fever, severe weakness, characteristic of COVID-19 and epidemiological history. If COVID-19 is suspected in a patient with asthma, as in any other patient, it is necessary to perform PCR diagnostics (smears from the nose and oropharynx), a quantitative study of IgM and IgG antibodies to SARSCoV-2, as well as computed tomography of the chest, based on current recommendations.

Long-term outcomes of COVID-19

There is currently no information on long-term outcomes in patients with asthma after COVID-19. A very cautious suggestion has been made that the SARS-CoV-2 virus may be a trigger in the development of AD in patients who have not previously had it. However, this assumption requires long-term prospective follow-up of patients without a diagnosis of AD who have experienced COVID-19.

Treatment of asthma and allergic rhinitis during the period of risk of respiratory viral

infection

In March and April 2020, experts from the GINA international committee published a number of recommendations for the management of patients with asthma during the COVID-19 pandemic [11]. Experts from the Russian Federation also joined them [29]. The following main conclusions were formulated:

1.Patients with asthma should continue to take prescribed asthma medications, in particular ICS and oral corticosteroids, if prescribed:

Patients with asthma should adhere to the regular treatment of the disease prescribed by the doctor. Discontinuation of ICS therapy often leads to a potentially dangerous worsening of asthma;

- patients with severe asthma should continue biological therapy (additional treatment with injectable genetically engineered drugs) and not stop taking oral corticosteroids, if they are prescribed.

2.All patients should have a written asthma management plan with instructions to:

- about increasing the basic therapy and therapy to relieve symptoms (therapy on demand) with an increase in asthma symptoms;
- on the appointment of a short course of oral corticosteroids for severe exacerbations of asthma (indicating the dose of the drug and the duration of administration);
- about when and where to seek medical help;
- additional individual recommendations for the treatment and prevention of asthma.

It is important to note that it is advisable to prefer remote control [12].

Allergic rhinitis (AR) is common in patients with asthma. Considering the global threat of COVID-19 and the fact that about 44% of all infections occur from asymptomatic carriers [13], experts believe that it is necessary to keep AR under the maximum possible control in order to reduce its symptoms (sneezing, rhinorrhea and cough), which contribute to the spread virus, if present. Patients with AR are strongly advised to maintain social distancing, wear a mask to avoid exposure to the aerosol generated by sneezing or talking, carry an adequate supply of masks, and dispose of them safely after use. There are suggestions that it is advisable to screen patients with AR for the presence of SARS-CoV-2, since they can be powerful distributors of this infectious agent [14].

The differential diagnostic search for COVID-19 in a patient with AR can be facilitated by sudden and complete anosmia, one of the early signs of infection caused by SARS-CoV-2.

According to experts, seasonal AR therapy is best started as early as possible and carried out regularly during the appropriate period of pollination of the allergen plant [15, 16] for optimal prevention of AR symptoms. None of the recommended treatments for AR is considered contraindicated. There are no contraindications to the use of intranasal corticosteroids during the epidemic of a new respiratory infection - this is the agreed opinion of more than 90% of experts [15]. Patients with AR should continue to take intranasal corticosteroids as directed by their doctor. It has been confirmed that intranasal corticosteroids do not reduce immune protection, normalize the structure and function of the nasal mucosa [16]. Preliminary data have been published indicating that some topical corticosteroids, such as ciclesonide and mometasone, can inhibit coronavirus replication [17].

Experts suggest continuing the current allergen-specific immunotherapy (ASIT) during the epidemic of a respiratory infection. However, starting a new course of ASIT or injecting ASIT is not recommended due to the need for repeated visits to the doctor and medical facility. Sublingual immunotherapy (SLIT) is considered preferable, in which only the initial dose of the drug should be taken under the supervision of a doctor, as well as the transition to SLIT from the injection method of drug administration [18].

Treatment of COVID-19 in patients with bronchial asthma

Treatment of COVID-19 in asthma is carried out in accordance with the current version of the guidelines "Prevention, diagnosis and treatment of a new coronavirus infection COVID-19" approved by the Russian Ministry of Health. Currently, there are no data on individual principles for the treatment of a new coronavirus infection in patients with asthma. However, taking into account the high frequency of atopy in patients with asthma, the likelihood of allergic reactions in some of them (including multiple ones), acareful collection of an allergic anamnesis and its strict consideration when prescribing any drugs with reliable monitoring of possible side effects is necessary. This also applies to the prescription of biological drugs to an asthmapatient with severe COVID-19.

Anti-asthma therapy for COVID-19 experts recommend continuing in full. In addition, with COVID-19 in a patient with asthma, the likelihood of an exacerbation of asthma itself should be taken into account and treated in this case according to the principles of exacerbation treatment [19]. At the same time, when conducting inhalation therapy in a patient, special approaches should be taken into account (reflected in the last section of this article before the conclusion).

Currently, the search for effective therapeutic agents for patients with COVID-19 with asthma or other diseases is ongoing. Preliminary data have appeared to assess the effect of IL-13 on the expression of ACE2 and TMPRSS2 in the epithelial cells of the respiratory tract of AD patients: ex vivo IL-13 suppresses the expression of ACE2 and increases the expression of TMPRSS2 [19]. These results, according to the authors, deserve attention and require further study in patients with asthma and atopy.

Special scientifically developed approaches to the rehabilitation treatment of patients with asthma during/after COVID-19 are not yet available, rehabilitation measures are carried out according to general rules.

Prevention of COVID-19 in patients with bronchial asthma

Prevention of COVID-19 in patients with asthmaincludes generally accepted principles developed by WHO experts and the national health system. In CVD, experts strongly advise following all recommendations for the prevention of respiratory infections, including COVID-19, to minimize the risk of infection [6, 9, 11, 20]. Doctors who have patients with CBOD are under dispensary observation are recommended to continue it, however, during the spread and epidemic of a respiratory infection, it is advisable to give preference to remote control [12, 20]. It is extremely important to inform patients with CBRD to seek immediate medical attention at the very first signs of a respiratory infection - early intervention can reduce the risk of severe COVID-19 and asthma exacerbation.

Some aspects of the organization of emergency and inpatient care for patients with bronchial asthma with COVID-19

The organization of emergency and inpatient care for patients with asthma who fell ill with COVID-19 is generally carried out according to general principles. However, it must necessarily take into account the likely need for appropriate inhalation therapy, as well as the possible, in severe COVID-19, the need for long-term respiratory support with simultaneous inhalation of drugs for the treatment of asthma or its exacerbation [9, 11].

We consider it important to reiterate that, in accordance with the current recommendations of domestic and international experts from the PPO and GINA, the results of studies currently do not have scientific data confirming that during the epidemic and during COVID-19, inhalation or oral administration of corticosteroids should be avoided in patients with asthma. if they are shown [9, 11]. In COVID-19, patients with asthma, as well as physicians managing patients with asthma, should continue to adhere

to the optimal daily basic therapy for asthma or treatment of its exacerbation in accordance with current approaches [6, 9, 11, 20]. Inhaled asthma therapy for COVID-19 should not be discontinued, including during hospitalization, without its replacement in accordance with the Federal Clinical Guidelines.

Recommended attitude to inhalation therapy and spirometry during the spread/ epidemic of a dangerous respiratory infection

Back in March 2020, experts from the GINA international committee formulated a number of recommendations regarding inhalation therapy during the COVID-19 epidemic [9, 11]. These fundamental aspects and all preventive measures when working with an infection of hazard class II must be observed to reduce the risk of infection of patients, medical and other employees of institutions.

1.Avoid using nebulizers where possible:

- nebulizers increase the risk of spreading the virus to other patients and healthcare workers;
- use of a metered-dose aerosol inhaler through a spacer is the preferred treatment for severe exacerbations, if necessary, use a mouthpiece or a tight-fitting mask.

2.Avoid spirometry in patients with confirmed/suspected COVID-19:

- spirometry can spread viral particles and expose staff and patients to the risk of infection;
- as long as there is a spread of a viral infection in your area, postpone spirometry and measurement of peak expiratory flow (peak flowmetry) in medical institutions, unless it is urgently necessary;
- Take precautions when coming into contact with respiratory secretions.

3.Follow strict infection control procedures if aerosol generating procedures are needed:

- inhalations, oxygen therapy (including through the nose), sputum induction, manual ventilation, non-invasive ventilation and intubation;
- it must be remembered that the use of nebulizer therapy, high-flow oxygen therapy and non-invasive lung ventilation (NIVL) increases the aerosolization of SARS-CoV-2, increasing the risk of infection of medical staff [12];
- when using nebulizer therapy, NIV, medical workers who are in the ward or in the patient's room must wear personal protective equipment. NIV should be carried out with viral filters. It should be noted that NIV is an important aspect of the treatment of acute respiratory failure and is associated with a decrease in mortality in COPD exacerbations [13].

Conclusion

During the COVID-19 pandemic, asthma patients need close medical attention, careful monitoring of symptoms of the disease, and prevention of a new coronavirus infection. Particular attention should be paid to patients with severe asthma who take oral corticosteroids as a baseline drug due to the risk of adverse outcomes in case of COVID-19. Patients with asthma who develop COVID-19 should continue to be treated with basic inhaled drugs or should be given optimal therapy for an asthma exacerbation if it occurs.

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