



CURRENT ASPECTS OF TREATMENT AND COMPLICATIONS OF COVID-19 IN CHILDREN WITH ALLERGIC DISEASES (LITERARY REVIEW)

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Abstract:

Children with comorbidities such as developmental disorders, endocrine system problems, allergic diseases, cancer pathology, immunodeficiency, the disease is more severe than in healthy children. Children have similar symptoms of coronavirus to adults - fever, conjunctivitis, muscle pain, gastrointestinal disorders. Scientists believe, she added, that one complication of coronavirus in children is multiviral syndrome. It's a delayed immunologic response to COVID 19. It's a condition that can occur in a child whether the disease is symptomatic or asymptomatic

Keywords: COVID-19, children, SARS-CoV-2, allergy, new coronavirus infection, bronchial asthma, atopic dermatitis, contact dermatitis, allergic rhinitis, chronic urticaria.

INTRODUCTION: Coronavirus infection - COVID-19 (Corona Virus Disease - 2019), caused by SARS-CoV-2 (Severe Acute Respiratory Syndrome Corona Virus 2), has become a real disaster for all mankind. Today, the issues concerning diagnosis, clinic, complications control, therapy, prevention, including vaccination for the new coronavirus infection are relevant. It is also important to identify risk factors of severe course, peculiarities of infection development against the background of comorbid conditions and different immunological reactivity of human organism. The comorbidity of allergic and infectious diseases is based on common humoral and cellular immune response mechanisms. Measles and varicella viruses, influenza, parainfluenza, rhinoviruses, enteroviruses, respiratory syncytial viruses, coronaviruses and others often serve as triggers for allergic diseases. Coronavirus epidemic came in the spring, which is associated with a revival in nature - everything around is green, the plants are in bloom. The latter, in turn, unfortunately, cause the development or exacerbation of allergies, that is, the season of exacerbation of diseases associated with pollen allergy comes. In children with allergic rhinitis (AR) or bronchial asthma (BA), maintaining and, more often, increasing the dosages of allergy-related baseline therapy is essential for effective therapy and reducing the risk of complications, including bacterial complications. In some patients, in the case of bacterial complications of primary viral infection, a combination of antibiotic therapy with continued use of topical glucocorticosteroid hormones (GCS) will be rational. In patients who have not previously received GCS, an infection in the respiratory organs may warrant their prescription. For example, the use of the "nebulized",

otherwise inhaled drug budesonide in patients younger than 3 years of age for exacerbations of bronchial asthma caused by acute respiratory infections significantly reduces the risk of antibiotics and the duration of the exacerbation episode. Also the use of combined formoterol with inhaled GCS (iGCS), in particular formoterol/budesonide, has shown to be effective in relieving various exacerbations of bronchial asthma, including those caused by acute respiratory infections. In severe cases, systemic (tablets/injections) GCS are prescribed. Therapy with GCS should be started as early as possible, without waiting for wheezing in the lungs. It was shown that patients were less likely to seek emergency care and to be hospitalized when using iHCS. Cancellation of anti-inflammatory therapy for BA or AR will necessarily lead to hypersecretion of mucus by epithelial cells, an increase in edema of the airway wall and difficulty in breathing. Thus, exacerbation of allergic inflammation will exacerbate the manifestations of the infectious process. Together with other factors, airflow restriction will significantly increase the risk of bacterial complications joining the primary viral infection. Besides anti-inflammatory therapy, patients with allergies against the background of acute respiratory infections may also need emergency therapy for the underlying disease: beta-sympathomimetics for bronchial asthma and antiallergic drugs for allergic rhinitis. Note that the presence of concomitant AD is a direct contraindication to the use of "old", sedative (sleeping pills) antiallergic drugs due to their potential bronchoconstrictor and sputum thickening action; AD is explicitly listed as a contraindication in the instructions of chlorpirine, dimethindene and clemastine. General principles of therapy of exacerbations are used: short-



acting bronchodilators (β 2-agonists) are prescribed (fenoterol + ipratropium bromide, salbutamol, salbutamol + ipratropium bromide in nebulized children). According to the international consensus document - GINA-2019, β 2-agonists are not prescribed as monotherapy in patients with AD; they must be administered together with ICS! The antipyretics used in patients with AR or BA during acute respiratory infections are the same as those used in children without allergies. Ibuprofen and paracetamol remain the main drugs of pediatric practice; there is currently no evidence that any of these molecules is preferred in patients with AD or AR. Note, however, that any drugs in the form of syrups or flavored suspensions for the allergic patient may be associated with a higher risk of complications in the form of exacerbation of atopic dermatitis or acute urticaria. The risk of such complications does not negate the need for their use when indicated, to reduce high hyperthermia. Traditionally prescribed for acute respiratory infections, "decongestants" (e.g., naphthizin) should be used with greater caution in patients with AR because of the increased risk of "drug-induced", vasoparetic rhinitis; they should not be used longer than 3-5 days. As an alternative to "intranasal" (nasal passages) vasoconstrictors, hypertonic saline solutions with moderate vasoconstrictor effect can be used. In patients with AR and AD the use of some, especially combined, herbal preparations is limited. Both direct allergic reactions to individual plant allergens and intensified response to habitual allergens are possible. Use of adaptogens in acute infections is unreasonable, and among expectorants in patients with AR or AD, preference should be given to the more predictable ambroxol, carbocysteine, in single cases and with known precautions (restriction on use in the evening) acetylcysteine may be appointed. Antibiotics. If an antibacterial drug is reasonably prescribed to a patient with concomitant allergic disease, the physician may be faced with the risk of a drug allergic reaction. A personal history of atopic disease is not considered a risk factor for drug allergy. Among patients who have previously reported "allergic" reactions to antibiotic use, the incidence of confirmed drug allergy is between 6 and 10%. In general, with the exception of a documented history of drug allergy, patients with respiratory AZ do not require special approaches to antibiotic selection and are prescribed the same drugs as other patients, based on the clinical picture of the disease and empirically suspected pathogen. The main group of antibiotics used remain semisynthetic penicillins, namely various preparations of amoxicillin. Starting with an inhibitor-protected drug (amoxicillin clavulanate) may be justified if the antibiotic is prescribed repeatedly during one cold season or if the aggressiveness of the pathogen is suspected (data of a flora culture with

sensitivity to antibiotics, anamnestic - infection in a medical facility, etc.). Immunomodulators. Of the immunomodulatory drugs, bacterial lysates are the safest and most effective group for patients with allergic respiratory diseases. Under the action of bacterial derivatives, the cytotoxic activity of natural killer (NK) increases and, therefore, the excretion of infected cells of the body. A young child with allergies (eczema, rhinitis) can be considered as a candidate for extended routine vaccination with mandatory inoculation against CIB and pneumococcus, since colonization of the nasopharynx with these microbes, according to cohort studies, is an independent risk factor for formation and aggravation of AD. In general, patients with AF need to avoid polypragmasy - simultaneous prescription of several drugs for acute respiratory infections and to maintain, and sometimes intensify, baseline (formoterol/IGCS) therapy for AD or AR. Most patients with allergies are predisposed to acute respiratory viral infection. SOVID-19 occurs in 0.39-12.3% of children. Children, as a rule, have a milder course of the disease than adults; their mortality rates are low. At the same time, adequate support of patients with chronic diseases, a special cohort among which are children with allergic diseases, should not be forgotten. Viruses and pandemic-related preventive hygienic measures often act as triggers for exacerbation of bronchial asthma, atopic dermatitis. The issues of timely diagnosis, adequate therapy of allergic diseases in children and information and methodological support of doctors are also problematic. It is important to understand which patients with bronchial asthma are particularly at risk, and how inhaled glucocorticosteroids may affect the course and outcome of COVID-19. International associations, societies have developed recommendations for the management of children with allergies during the COVID-19 pandemic. Inhaled glucocorticosteroids in bronchial asthma reduce the expression of the main target receptor genes for SARS-CoV-2. Anti-inflammatory therapy for bronchial asthma, primarily IGCS, should be continued until control of AD is achieved, which would help reduce the risk of adverse course of COVID-19. A systematic review combining all data on COVID-19 in the pediatric population indicates that children account for 1-6% of all cases diagnosed, the disease usually has a milder course with extremely low mortality rates compared to the adult population. A subgroup of patients with the severe form of COVID-19 develops an acute systemic inflammatory reaction, a so-called "cytokine storm" requiring intensive therapy. At the same time, among patients with comorbidities, the rate of hospitalizations and the need for intensive therapy is significantly higher. The true causes and mechanisms of a milder course of COVID-19 infection in children are not yet known. Perhaps a special role can be played by the features of cytokine response due to



immaturity of the immune system, as well as low expression of angiotensin-converting enzyme 2 (angiotensin-converting enzyme 2, ACE2) and other causes. Patients with concomitant chronic diseases such as diabetes mellitus, renal failure, hypertension and other cardiovascular pathology, and clotting disorders are a special risk group for the severe course of COVID-19. Currently, more than 339 million people worldwide suffer from asthma, at least 14% of whom are children. The pathogenetic mechanisms of how chronic inflammatory airway diseases such as asthma affect SARS-CoV-2 risk and the development of COVID-19 are being carefully studied. It is critical to understand which patients with asthma are particularly at risk and how inhaled glucocorticosteroids (IGCS) may influence the course and outcome of COVID-19.

Systemic glucocorticosteroids, as immunosuppressants, in some nosologies may induce the risk of or influence the severity of viral infections (e.g., in post-transplant patients). However, lack of ICS therapy threatens patients with asthma with serious and sometimes life-threatening exacerbations. The results of a recent meta-analysis of COVID-19 outcomes in patients with chronic respiratory disease who received IGCS therapy showed that there is currently insufficient evidence for withdrawal of highly effective and well-established IGCS treatment in patients with asthma .

Presumably, it is the differences in ACE2 and transmembrane protease, serine 2 (TMPRSS2) expression in patients with severe asthma that may modulate the individual susceptibility and clinical course of SARS-CoV-2 infection and thus determine cluster patterns of different COVID-19 risk in patients with asthma . The SARS-CoV-2 protein-ship is known to bind to ACE2 as a receptor during virus attachment to host cells, virus entry is also facilitated by priming of the protein-ship by the membrane-bound pro-tease TMPRSS2 .

Studies on factors influencing ACE2 gene expression have shown that it is the correlation with smoking, diabetes, and hypertension that accounts for the severity of COVID-19 disease.

The most likely explanation for the unexpected fact that asthma and other allergic diseases may not act as a risk factor for severe COVID-19 is reduced ACE2 gene expression in airway cells and therefore reduced susceptibility to infection.

In a study of airway cells from three different groups of children and adults, ACE2 gene expression was shown to be significantly inversely associated with biomarkers of T2 inflammation (including the presence of allergen-specific antibodies to 1 β E, FeNO levels and nasal epithelial 11 β expression), which contrasts with the condition of increased expression of intercellular adhesion molecule 1 (ICAM-1) detected in sputum of asthmatics. ICAM-1 is a rhinovirus receptor that can

cause mild respiratory symptoms in healthy individuals, but can also cause prolonged manifestations and lower respiratory tract damage, causing severe exacerbations in asthmatics.

Male gender, African-American ethnicity, and a history of diabetes mellitus have previously been found to be associated with increased expression of ACE2 and TSMRSS2 mRNA in induced sputum. Therefore, asthmatics with one or more of these factors should be particularly monitored to prevent the severe course of COVID-19. The same factors should also be used for the pediatric patient cohort.

Published observational studies to date have not confirmed the presence of asthma and/or respiratory allergy as significant risk factors for the development of a severe course of COVID-19. This fact suggests that it is confirmed atopy and/or bronchial asthma that is a predictor of a mild course of infection.

The questions of how SARS-CoV-2-associated gene expression is modulated in different cells (airways in asthma, or other tissues in other chronic diseases), whether it affects virus penetration and infectivity, and what the role of T2 inflammation in the pathogenetic process is, require further investigation. Key factors and markers (demographic, clinical, laboratory) that will help to accurately predict the trajectory of COVID-19 should be elucidated. Although the main efforts of the medical and political community are currently focused on preventing the spread of the pandemic and organizing medical care for patients with moderate and severe COVID-19, we must not forget the implementation of adequate management of patients with chronic diseases. A special cohort among them are children with allergic diseases. The pandemic period coincided with the natural weathering of cause-significant plants, which caused an annual exacerbation of both allergic rhinitis and asthma in a group of patients with specific sensitization

to tree pollen. Adapting to modern conditions, we have made key recommendations for the management of children with allergies during this difficult period for both patients and specialists.

- Procedures for determining measures of external respiratory function (spirometry) should be postponed unless absolutely necessary. In this case, portable personal devices measuring peak expiratory velocity (peak flow meters) can be used to monitor asthma control, including remote monitoring of the patient's condition (telemonitoring).

- Baseline IGCS therapy should be continued according to GINA clinical guidelines and EAACI position): patients with asthma should continue on baseline therapy. Keep in mind the risks of adverse outcomes due to discontinuation of baseline therapy (both inhaled or systemic glucocorticosteroids and biologics).



- The use of nebulizers (which increase the risk of penetration of the virus into the lower respiratory tract) should be avoided and replaced by larger (increased) volume spacers.

If an exacerbation of asthma is relieved by oral glucocorticosteroids, the course should be continued until the symptoms disappear (for moderate to severe exacerbations). Treatment with biologics should be continued. If COVID-19 infection is detected (with typical or asymptomatic manifestations), therapy should be stopped until resolution of the disease is diagnosed (until a negative test for SARS-CoV-2). Thereafter, treatment with the biologic drug should be resumed.

CONCLUSIONS: Patients with allergies should receive therapy routinely in full according to available clinical guidelines. An exception is the recommendation for temporary withdrawal of biological treatment during acute COVID-19

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