



Original Article

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Rational Pharmacotherapy of Respiratory Diseases in the COVID-19 Pandemic

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ABSTRACT

The purpose of this article is to draw attention to the treatment of respiratory diseases in the COVID-19 pandemic. In addition, we want to address the issue of vaccination, to pay attention to the incidence of disease among children. The design of this study was longitudinal. For this purpose, we use articles and studies from English-language sources, such as UpToDate, as well as peer-reviewed scientific articles from medical journals and the results of surveys of outpatient medical practitioners. There were no particular changes in the pharmacotherapy of respiratory diseases during the COVID-19 pandemic. Changes occurred in the recommendations for aerosol delivery of the drug, and it was recommended that the use of targeted therapy and the use of antileukotriene drugs for bronchial asthma with positive COVID be delayed until recovery. Covid is changing the doctor-patient communication system today, giving rise to telemedicine. He reminds us of the importance of vaccination in pandemics if it is possible, and it is already possible, and of the importance of population immunity. And also, we should not forget about the therapy of other diseases and consider the conditions of a pandemic when making treatment decisions.

Key words: COVID-19, Treatment, Respiratory diseases, Cystic fibrosis, Bronchial asthma

INTRODUCTION

Coronaviruses were first discovered back in 1966 but first came to public attention in 2019, causing a prolonged pandemic. Before that, in 2002, the SARS-CoV coronavirus caused severe acute respiratory distress syndrome in China, but then the infection was contained. The virus later returned as MERS-CoV in 2012 causing Middle East respiratory syndrome. So, the virus itself is far from new. All of these viruses are zoonoses, but they have their characteristics. Humans are highly sensitive and susceptible to it. If at first it was thought that COVID-19 affects the respiratory system, leading to pneumonia, or runs in a mild form, as an ordinary acute respiratory disease, today the world knows that almost all body systems are affected by SARS-CoV-2. The acute illness is followed by a difficult recovery period and long-term sequelae of the infection. This article does

not address the treatment of COVID-19. Today we are reminded that no one has canceled other respiratory diseases. There is still a high incidence of rhinopharyngitis, otitis media, sinusitis, influenza, and other infections. It is also worth touching on the issue of comorbidity with non-infectious pathologies such as cystic fibrosis, bronchial asthma, and chronic obstructive pulmonary disease [1]. So how do we behave appropriately when choosing treatment tactics for these diseases in the face of the COVID-19 pandemic? We will recall the situations when we should suspect infection with coronavirus, how and when to test and determine further management tactics. How coronavirus vaccination is affected and how to combine it with other vaccines [2]. In our work, we use resources from UpToDate, PubMed, and peer-reviewed articles, references to which will be given in the list of references. The article has a description of the experiences of respiratory diseases in adolescents and children, peculiarities of the course, and impact on later life, taken from interviews with local pediatricians. The validity and significance of the latter are not as high as the information from peer-reviewed sources but may be of value in the work of practicing family physicians and pediatricians.

MATERIALS AND METHODS

Although the focus is now on the timely detection and treatment of patients with Covid-19, we must remember that the other infectious diseases of the respiratory system have not disappeared. On the contrary, it is worth looking at them from a slightly different angle. First, how have changes in social life affected the incidence of the disease, and second, has something changed in treatment? Of course, the number of cases of pneumonia has increased. And, if earlier among out-of-hospital cases of pneumonia (cases of pneumonia that developed outside the conditions of the hospital or not later than 48 hours of stay in it), mainly influenza viruses, parainfluenza, respiratory syncytial virus were distinguished, as well as bacteria - *Streptococcus pneumoniae* and more rarely *Mycoplasma pneumoniae*, *Haemophilus influenzae* and *Legionella* spp and CA-MRSA, today all types of pneumonia should be considered as cases of pneumonia, caused by Sars-Cov-2 virus until it is proved otherwise [2].

Infectious pathology of the respiratory system

If it is found that the pneumonia is not caused by Sars-Cov-2, we stick to the usual treatment regimen, determine the severity of the condition, find out whether the patient will be treated as an outpatient or requires inpatient care.

The empirical therapy still depends on the possible pathogen, the risk of infection with a resistant pathogen, the severity of the condition, as well as on the individual characteristics of the patient and existing allergic reactions in the anamnesis [2].

And here it is worth mentioning the risk of irrational use of antibiotic therapy. Even in the absence of a Covid-19 pandemic, this leads to bacterial resistance and resistance to the therapy used. And in the setting of Covid-19, this entails additional risks. We're not talking about outpatients; we're talking about patients who are hospitalized, particularly those in the ICU. People who are admitted to these units have, for the most part, reduced immunity and additional risk factors for lethal outcomes. Add to this the accession of bacterial infection; we get a reduced chance of survival. And now add a drug-resistant bacterial infection. And many antibiotics are already difficult to prescribe in the ICU because many patients may have contraindications or restrictions on their use due to the severity of their condition [3].

In addition, we still have high rates of influenza, and despite awareness, annual vaccination coverage leaves much to be desired. We continue to be sensitive to this infection and even if a patient is vaccinated, it is worth remembering the risk of illness and the severity of influenza pneumonia. Fortunately, there are effective flu medications available today, namely Oseltamivir. So, the same scheme: rule out Covid-19, test for influenza, and decide on the patient's treatment tactics.

No data is indicating the need to delay or cancel flu vaccination after having had Covid-19 or after having been vaccinated against it. If there is no reaction to Covid-19 vaccination, there is no need to delay vaccination for other infections, including pneumococcal disease.

We should not forget the importance of non-pharmacological methods of improving the condition of the disease. With the Covid-19 pandemic, we still walk outdoors, ventilate the room, and keep the humidity at about 45%. But, at the same time, avoid crowded places, keep the necessary distance between people, use personal protective equipment, and see your family doctor if you have symptoms.

Acute otitis media has a specific clinic and, although quite common, still tends to decrease in frequency due to pneumococcal vaccination. Since pneumococcus is the most common cause of the disease, the treatment is an antibiotic. It is amoxicillin clavulanate: amoxicillin 875 mg with clavulanate 125 mg orally twice daily for adults [1] and 90 mg per kg of weight per day for children. There are no specifics about pandemic-related therapy other than general recommendations about individual protective equipment and avoiding going to crowded places.

Acute respiratory diseases remain. Let's combine them into one group, taking into account the viral nature of the disease and considering the drugs prescribed and their appropriateness.

The first one is antivirals. If it's not the flu, humanity has nothing to boast about. There is not a single drug to date that has proven to be effective in treating respiratory viral infections.

Second, local antiseptics. This is simple - if there is no sore throat, they should not be used, even if the mucous membrane is hyperemic. I like the expression of pediatrician Lidia Babich: "We do not treat the color of the throat.

Third, vasoconstrictors in the treatment of nasal congestion. They are available. But remember that they are not used in young children, are not used more than 3 times a day for more than 3-5 days, as they can be addictive, and also have a systemic effect on the body. But nasal cleansing, that is, flushing is a very useful recommendation.

The fourth, often prescribed remedy is multivitamins. There is no evidence of their usefulness, but there is data on the risk of allergic reactions. In addition, we do not know how they are absorbed by the human body, whether there is no competing action between them. Vitamins should be prescribed if they are deficient, which must be confirmed by laboratory tests. But, there is evidence of the benefits of prescribing zinc, omega-3 when insufficient intake with food and separately distinguish vitamin D. Vitamin D-3 should be prescribed either in a prophylactic dosage of 1000 international units per day for patients after 1 year of life and 400-600 units before one year of age. In the case of disease, the dosage is increased to 2000-4000 thousand. This is the drug that is effective in prescribing, by affecting the human immune system during the Covid-19 pandemic [3].

In general, the therapy of this group of diseases has not undergone significant changes, except for a change in the dose of vitamin D-3 in some cases, as well as the prescription of zinc preparations.

To replenish the amount of information we turned to the district pediatricians. In the course of the conversation, the following information was obtained. On average, there were 5-7 Covid-19 cases in a district of about 900 children from 0 to 18 years old during the pandemic period. A possible reason for this data, in our opinion, is the frequent asymptomatic or little symptomatic course in children and adolescents. This in turn leads to the fact that many children were not specifically diagnosed. In addition, when asked if the therapy of acute viral infectious diseases is different now and before, we received the following answer. Regarding pharmacotherapy, treatment tactics have not changed, but more attention has been given to symptoms such as general weakness, which is often the only sign to help suspect Covid-19 in adolescents. Also, with the pandemic, the benefits of telemedicine, i.e., telephone and video consultations, have become more common, reducing the frequency of human contact. It was noted that, due to the strengthening of anti-epidemic safety measures, cases of airborne diseases, which include the diseases of interest to us, became much less frequent.

In order not to waste time at appointments and not to miss a possible case of Covid-19 disease, let us remember the criteria for diagnosing this infection. You should be alert to the following:

- confirmed contact with a patient with coronavirus
- Recent travel or trips
- loss of taste and/or smell
- increased fatigue
- myalgia
- diarrhea
- fever
- cough
- shortness of breath

There may also be sore throat, rhinorrhea, and even physical signs of lower respiratory tract inflammation.

As we can see, there are not many specific signs to rely on. The only loss of taste and/or sense of smell, fever, shortness of breath, and a corresponding history (travel, contact with an infectious patient) cause increased alertness.

Here is an example showing the symptoms by their approximate frequency of occurrence in the population (Table 1).

Table 1. Symptoms by their approximate frequency of occurrence in the population

Symptom	%
Cough	80
Fever	>90
Anosmia	50
Ageusia	50
Dyspnea	55
Diarrhea	3
Vomiting	5
Headache	8
Myalgia	11
Sore throat	14
Rhinorrhea	7
Fatigue	44

Therefore, in a pandemic, we must suspect Covid-19 until proven absent.

For early diagnosis, we use a nucleic acid amplification test (NAMA), most commonly with reverse transcription-polymerase chain reaction (RT-PCR) analysis, to detect SARS-CoV-2 RNA in the upper respiratory tract or an antigen test, although the latter is considered less informative and still requires confirmation [4-7].

If the diagnosis of Covid-19 is not confirmed, we assume a different diagnosis and apply the treatment methods and tactics already known to us, depending on the pathology.

Non-infectious pathology of the respiratory system

What about noninfectious pathology? Consider what we have learned about the comorbidity of coronavirus and other diseases affecting the respiratory system.

What has changed in the lives of patients with chronic obstructive pulmonary disease? Concerning therapy, the changes consist of the recommendation to reduce the use of aerosol drug delivery whenever possible. The reason is that there is a risk of aerosol spraying of the virus, especially in health care facilities and nursing homes. If the patient can do so, it is advisable to use another device that allows you to receive the drug in the right dosage but does not create an aerosol.

But patients with this disease are at increased risk for Covid-19 infection and its severe course because of pre-existing pathological changes in the lungs, a history of smoking, and an initially increased risk of developing pneumonia. For these reasons, it is recommended that this group of patients, if possible, reduce the frequency of social contact during the pandemic [8-10].

The next group of patients are patients with bronchial asthma. To date, it has not been established whether these patients are more susceptible to Covid-19 infection. There is controversy on this point, so research is ongoing.

The treatment recommendations are as follows: baseline therapy should continue with the same regimen. But, similarly to patients with COPD, it is recommended that nebulizer use be avoided if possible. If a patient has a confirmed Covid-19 infection, he should take a break from antileukotriene drugs and targeted therapy for a while until the symptoms disappear and the laboratory result is negative [11, 12].

The third group is patients with cystic fibrosis. Although both diseases develop neutrophilic inflammation and release cytokines, to date there is no evidence of a more severe course of Covid-19 in patients with cystic fibrosis. This may be due to the use of therapy for the underlying disease, as well as the ongoing prevention of infection and isolation of patients. In addition, they are more often young patients. Research is ongoing [12].

RESULTS AND DISCUSSION

To summarize, Covid-19 does not have highly specific symptoms, but there are still certain signs that make it possible to suspect this infection.

If we can rule out SARS-Cov-2 infection after examining the patient, we treat the patient according to his or her other diagnosis.

Once again, we emphasize the importance of a reasonable prescription of antibiotics, as only a rational approach will avoid a possible tragedy in the future. The adherence of a bacterial infection in the inpatient treatment of a patient with covid, especially in the intensive care unit, can have fatal consequences. The responsibility for antibiotic resistance begins in the outpatient setting.

In children, the incidence is not much different from that in adults, but children are more often asymptomatic or asymptomatic, which may be the reason for the lack of frequency of diagnostic tests. In a meta-analysis that included more than 9,000 children, 13% were asymptomatic carriers of the infection [6, 13-18]. Most often, children had a mild form of the disease. The severity and frequency of the disease increase with the age of the patient. Generally, the duration of the disease is about 2 weeks [5, 19-21].

The only way to fight the infection, its severe course, and its consequences is by vaccination. It is no longer only possible to vaccinate adults, but also children after the age of 12. Today, we are already talking about younger children and it has good prospects. The FDA reports that it is reasonable to vaccinate children 5-11 years old with the Pfizer vaccine, but while the dose for children from 12 years old is 30 mcg, the dose for children 5 to 11 years old is 10 mcg. Don't forget the vaccination calendar, as well as the annual influenza virus vaccination. Patients with chronic pulmonary pathology should be vaccinated with the recommended vaccines during the non-acute period.

CONCLUSION

The first group of the study included patients with infectious diseases of the respiratory system and according to their results, the methods and schemes of treatment did not change. The second group consisted of patients with chronic non-infectious diseases. Bronchial asthma was an exception here, as it was not recommended to use targeted and anti-leukotriene drugs until recovery. Aerosol routes of administration are not recommended for all patients during the pandemic.

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