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Rational Approach to Pharmacotherapy in Respiratory Diseases during the COVID-19 Pandemic

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Abstract

This article aims to highlight the treatment of respiratory diseases during the COVID-19 pandemic, with a focus on vaccination and the impact of the disease on children. The study uses a longitudinal design, referencing English-language resources such as UpToDate, peer-reviewed journals, and surveys from outpatient healthcare practitioners. While there were no major changes to the treatment of respiratory diseases during the pandemic, there were updates to the recommendations for aerosolized drug delivery. It was recommended that the use of targeted therapies and antileukotriene medications for patients with bronchial asthma and confirmed COVID-19 be delayed until recovery. COVID-19 has also changed the doctor-patient relationship, leading to an increase in telemedicine. This pandemic highlights the importance of vaccination and population immunity, which is now achievable. In addition, the treatment of other conditions must continue to be considered, with treatment decisions made in light of the ongoing pandemic.

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

Introduction

Coronaviruses were first identified in 1966, but it was in 2019 that they gained widespread global attention due to the onset of the COVID-19 pandemic. Before this, the SARS-CoV virus triggered an outbreak of severe acute respiratory distress syndrome in 2002 in China, but the situation was controlled. In 2012, a different strain, MERS-CoV, emerged, causing the Middle East respiratory syndrome. Although coronaviruses have been around for a while, they remain zoonotic diseases with distinct features, and humans are particularly vulnerable. Initially, it was believed that COVID-19 primarily caused respiratory issues, leading to pneumonia or mild flu-like symptoms, but it has become clear that SARS-CoV-2 impacts nearly all organ systems. The acute phase of the illness is often followed by a challenging recovery period and long-lasting consequences. This article does not focus on COVID-19 treatment; instead, it highlights the ongoing prevalence of other respiratory illnesses.

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Diseases like rhinopharyngitis, otitis media, sinusitis, and influenza continue to be common. Additionally, comorbidities such as cystic fibrosis, bronchial asthma, and chronic obstructive pulmonary disease remain relevant [1, 2]. This article discusses how to approach treatment for these conditions during the COVID-19 pandemic, considering when to suspect COVID-19, how and when to test for it, and how to manage the situation. It also addresses the interaction between COVID-19 vaccination and other vaccines.

Materials and Methods

The article is based on resources from UpToDate, PubMed, and peer-reviewed articles, with all references listed at the end. Additionally, insights from local pediatricians regarding respiratory diseases in children and adolescents, their progression, and long-term effects are included. While these insights may not carry the same weight as peer-reviewed sources, they offer valuable information for family doctors and pediatricians in everyday practice.

Results and Discussion

While attention is currently focused on the swift identification and management of COVID-19 patients, it is crucial to remember that other respiratory infections continue to pose a threat. It is important to reassess these conditions in light of the pandemic. First, one must consider how changes in societal behavior have impacted the frequency of these illnesses, and second, whether treatment approaches have evolved. Undoubtedly, the incidence of pneumonia has risen. In the past, among cases of community-acquired pneumonia (those developed outside of a hospital setting or within 48 hours of hospital admission), the primary pathogens were influenza viruses, parainfluenza, respiratory syncytial virus, as well as bacteria such as *Streptococcus pneumoniae*, and less frequently *Mycoplasma pneumoniae*, *Haemophilus influenzae*, *Legionella* spp., and CA-MRSA. However, now, until proven otherwise, all cases of pneumonia should be considered as potentially caused by the SARS-CoV-2 virus [2].

Infectious pathology of the respiratory system

In cases where pneumonia is not attributed to SARS-CoV-2, treatment follows standard protocols, with a focus on assessing the patient's condition severity and determining whether outpatient care is appropriate or if hospitalization is required. The choice of empirical therapy is influenced by factors such as the suspected pathogen, the risk of resistant infections, the patient's overall health, and any known allergies [2]. It is crucial to highlight the risks associated with improper antibiotic use, which can lead to bacterial resistance even outside the context of the COVID-19 pandemic, with additional complications in the pandemic setting. This is especially concerning for hospitalized patients, particularly those in intensive care units (ICUs), who are often immunocompromised and face increased risks of poor outcomes. The introduction of bacterial infections, particularly antibiotic-resistant ones, further reduces survival chances, as many antibiotics are contraindicated or limited in ICU settings due to the severity of patients' conditions [3].

Additionally, the persistence of influenza and the insufficient vaccination coverage remain a concern, with the virus continuing to pose a threat despite general awareness. Even vaccinated individuals are not immune to influenza, and the risk of severe influenza pneumonia remains. Fortunately, effective antiviral treatments, such as oseltamivir, are available. As with pneumonia, the approach to treatment should involve ruling out COVID-19, testing for influenza, and determining the appropriate course of action. There is no evidence suggesting the need to delay or cancel flu vaccinations following COVID-19 vaccination, nor is there any requirement to postpone other vaccinations, such as for pneumococcal disease, if no reaction to the COVID-19 vaccine is observed.

Non-pharmacological measures for improving patient outcomes should not be overlooked. During the pandemic, practices such as outdoor walks, room ventilation, and maintaining indoor humidity around 45% remain vital. At the same time, avoiding crowded areas, maintaining physical distance, wearing personal protective equipment, and consulting a family doctor when symptoms arise are essential preventive strategies. Acute otitis media remains a common condition but has decreased in frequency due to pneumococcal vaccination. Since *Streptococcus pneumoniae* is the most frequent cause, amoxicillin-clavulanate remains the first-line treatment, with adults receiving 875 mg of amoxicillin and 125 mg of clavulanate orally twice a day, while children should receive 90 mg/kg/day. There are no specific changes to pandemic-related treatments

beyond the standard recommendations for personal protective equipment and avoiding crowded places.

Acute respiratory diseases can be grouped based on their viral etiology, with treatments tailored to the specific type of infection. First, antivirals remain largely ineffective against most respiratory viruses except for influenza. Second, local antiseptics should only be used in the presence of a sore throat and are unnecessary if the mucous membrane is simply red. Pediatrician Lidia Babich's saying, "We do not treat the color of the throat," aptly reflects this. Third, nasal decongestants, while widely available, must be used cautiously, particularly in young children, and should not exceed three applications per day for more than 3-5 days due to the risk of dependence and systemic side effects. Nasal irrigation, however, is highly recommended. Fourth, while multivitamins are commonly prescribed, there is little evidence supporting their efficacy in treating viral infections, and they may cause allergic reactions. Vitamins should only be prescribed when deficiencies are confirmed through laboratory tests. Nonetheless, supplementation with zinc, omega-3 fatty acids, and vitamin D-3, especially in cases of deficiency, has shown benefits. Vitamin D-3 should be given at a prophylactic dose of 1000 IU daily for individuals over one year old, and 400-600 IU for those under one year. In the case of illness, the dosage can be increased to 2000-4000 IU. Vitamin D-3 has proven beneficial in modulating the immune system during the COVID-19 pandemic [3].

Overall, treatment strategies for these diseases have not changed significantly, aside from adjustments in vitamin D-3 and zinc dosages. To further supplement our knowledge, district pediatricians provided valuable insights. In one district with approximately 900 children aged 0-18, an average of 5-7 COVID-19 cases were reported during the pandemic, likely due to the frequent asymptomatic or minimally symptomatic course in children and adolescents, which often led to underdiagnosis. When asked whether the management of acute viral infections has changed, pediatricians noted that while pharmacological treatments remained consistent, there was an increased focus on symptoms like general fatigue, which often signaled COVID-19 in adolescents. Additionally, the pandemic has highlighted the benefits of telemedicine, allowing for consultations via phone or video, which reduced the frequency of in-person contact. The implementation of stricter anti-epidemic measures also contributed to a decline in airborne diseases, including those relevant to our discussion.

To ensure efficient use of appointment time and prevent missing a potential case of COVID-19, it's important to be aware of the key diagnostic criteria for this infection. Healthcare providers should stay vigilant for the following signs:

- Confirmed exposure to a person diagnosed with coronavirus
- Recent travel or trips
- Loss of taste and/or smell
- Increased fatigue
- Muscle aches (myalgia)
- Diarrhea
- Fever
- Cough
- Difficulty breathing (shortness of breath)

Additional symptoms such as sore throat, runny nose (rhinorrhea), and even physical evidence of lower respiratory tract inflammation may also be present.

As observed, there is a limited number of highly specific symptoms that can be directly attributed to COVID-19. The most telling indicators—loss of taste and/or smell, fever, shortness of breath, combined with relevant history such as travel or exposure to a confirmed case—should heighten suspicion of the disease.

An example illustrating the approximate frequency of these symptoms in the population is presented in **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

During a pandemic, it is crucial to consider COVID-19 as a potential diagnosis until it is definitively excluded. To facilitate early detection, a nucleic acid amplification test (NAAT) is commonly utilized, with reverse transcription-polymerase chain reaction (RT-PCR) being the preferred method to identify SARS-CoV-2 RNA in the upper respiratory tract. Alternatively, an antigen test may be used, though it is regarded as less reliable and necessitates further confirmation [4-7]. If COVID-19 is ruled out, the focus shifts to diagnosing other possible conditions, and treatment strategies are based on the identified pathology, employing familiar therapeutic approaches.

Non-infectious pathology of the respiratory system

What can be said about non-infectious respiratory conditions? Let's review what we've learned regarding the coexistence of COVID-19 and other respiratory diseases.

How has the management of chronic obstructive pulmonary disease (COPD) patients evolved? In terms of treatment, a key adjustment is the recommendation to minimize the use of aerosol-based drug delivery systems when possible. This is due to the risk of viral aerosol transmission, particularly in healthcare settings and nursing homes. When feasible, it is advised to use alternative devices that ensure the correct dosage without generating an aerosol.

However, patients with COPD face heightened vulnerability to severe COVID-19 infections due to pre-existing lung damage, smoking history, and an increased likelihood of developing pneumonia. Consequently, it is advised that these individuals reduce social contact whenever possible during the pandemic [8-10].

Next, we consider patients with bronchial asthma. Research has yet to determine whether these individuals are more prone to COVID-19 infection. Ongoing studies continue to explore this issue.

Treatment recommendations for asthma remain largely unchanged, with continued baseline therapy. Similar to COPD patients, it is suggested to avoid nebulizer use if possible. For patients diagnosed with COVID-19, it is advised to temporarily discontinue antileukotriene therapy and targeted treatments until symptoms resolve and laboratory tests return negative [11, 12].

Lastly, individuals with cystic fibrosis, who experience neutrophilic inflammation and cytokine release in both conditions, do not appear to face a more severe course of COVID-19. This may be attributed to their ongoing treatment for cystic fibrosis and infection prevention measures, along with their younger age. Ongoing research is continuing to monitor the situation [12].

In summary, while COVID-19 symptoms are not highly specific, certain indicators can raise suspicion for the infection. If SARS-CoV-2 infection is excluded following assessment, treatment is adjusted based on the confirmed diagnosis.

Once again, we stress the importance of prescribing antibiotics judiciously. A responsible approach is critical in preventing future antibiotic resistance. The development of a bacterial infection in COVID-19 patients, especially in intensive care units, can result in fatal outcomes. The responsibility for combating antibiotic resistance starts in outpatient settings.

In children, the incidence of COVID-19 is similar to that in adults, but children are more likely to be asymptomatic or show mild symptoms. This could explain the lower frequency of diagnostic testing. A meta-analysis of over 9,000 children revealed that 13% were asymptomatic carriers of the virus [6, 13-18]. Most children experience mild disease, with the severity and frequency of the illness increasing with age. On average, the duration of the illness is about two weeks [5, 19-21].

Vaccination remains the most effective way to combat the infection and its severe outcomes. Vaccination is now available not only for adults but also for children aged 12 years and older. The focus is now shifting to younger children, with promising prospects. The FDA has stated that vaccinating children aged 5-11 years with the Pfizer vaccine is advisable. While the dose for children 12 years and older is 30 mcg, the dose for children aged 5-11 years is 10 mcg. Don't forget to follow the vaccination schedule, including the annual flu shot. Patients with chronic pulmonary conditions need to receive the recommended vaccinations during periods when their condition is not acute.

Conclusion

The first cohort of the research included patients with respiratory infections, and for this group, the treatment approaches and protocols remained unchanged. The second cohort was composed of individuals with chronic non-infectious conditions. An exception was made for patients with bronchial asthma, where the use of targeted therapies and anti-leukotriene medications was advised to be withheld until recovery. Additionally, aerosol-based drug delivery was generally discouraged for all patients during the pandemic.

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