



# Pros and Cons of Nebulizer Treatment in Asthma Exacerbation During the COVID-19 Pandemic

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## ABSTRACT

Nebulizers generate aerosols and may potentially transmit respiratory viral particles including SARS-CoV-2. There is a great concern about the use of a nebulizer in the treatment of asthma exacerbations in the hospital or home setting during the COVID-19 pandemic and its use is not recommended unless essential. However, aerosol therapy should not be avoided in obligatory indications. Therefore, indications of nebulizer use during the pandemic should be evaluated on an individual basis in case of a severe asthma attack, and infection control recommendations should be followed by clinicians while using nebulizers. In this article, we aimed to assess the safety in addition to the “pro” and “con” sides of nebulizer treatment in asthma exacerbation during the COVID-19 pandemic.

**Keywords:** Asthma, coronavirus disease 2019, COVID-19, SARS-CoV-2, nebulizers

## INTRODUCTION

Asthma is one of the most common respiratory diseases worldwide and exacerbations of the disease in both children and adults are the main cause of the disease morbidity, lung function loss and lower health related quality of life (1). The main goals of the asthma management recommended by evidence-based asthma guidelines are to achieve good control of symptoms and maintain normal physical activity by minimizing asthma-related exacerbations by using appropriate regular therapy and treating asthma flare-ups effectively (1,2).

Despite an increased number of controllers in asthma treatment and the use of asthma action plans, an acute asthma attack is still one of the most common causes of emergency visits (1). Inhaled  $\beta_2$  agonists are the first line drugs for acute asthma attacks and the Global Initiative

for Asthma (GINA) and the Turkish National Asthma Guidelines recommend the use of inhaled  $\beta_2$  agonists by metered dose inhalers (MDIs) via a spacer or nebulizer in both adults and children according to the level of severity of the asthma attack (1, 2).

In patients who are unable to use other aerosol devices such as MDIs or dry powder inhalers (DPIs) properly because of the dyspnea associated with the disease or attack severity, nebulizer treatment is a good option to improve drug delivery. Nebulizers generate aerosols by vaporizing the drug solution placed in a small reservoir, and use a stream of compressed air or oxygen to produce continuous aerosols (3). However, nebulizers can disseminate aerosols and potentially transmit respiratory viral particles for approximately 1 meter (3) and this is the reason for the great concern about the use of nebulizers

in the treatment of asthma exacerbations in the hospital or home setting during the new coronavirus (SARS-CoV-2) disease (COVID-19) pandemic. In our recent study, ninety-two percent of the clinicians including 183 Turkish National Society of Allergy and Clinical Immunology (TNSACI) members reported preferring inhalers, chambers, or spacers instead of nebulizers in case of emergency management of asthma attacks (4). As a result of this concern about nebulizer use, the necessary aerosol therapy might be avoided in patients with asthma who cannot use MDIs or DPIs properly. Therefore, in this article, we aimed to assess the safety in addition to “pro” and “con” sides of nebulizer treatment in asthma exacerbation during the COVID-19 pandemic.

### **Known Advantages & Disadvantages of Nebulizer Treatment**

SARS-CoV-2 is transmitted through droplets (5). Although whether nebulizer therapy in COVID-19 patients will increase the spread of infection is not clearly determined, its use is not recommended during the SARS-CoV-2 pandemic (1,2). However, delivery of drugs using a nebulizer has advantages such as being easy to use with minimal cooperation, being cheap, and providing an opportunity to mix and use high doses of drugs (3). On the other hand, there are also disadvantages such as continuous handling, electricity consumption, bacterial contamination, and spread of infections (3). The patient must hold the reservoir for at least 10 minutes for a jet nebulizer, which is longer than hand-halers (3). Newer nebulizers such as the ultrasonic and mesh types are faster and more efficient to deliver the aerosols to the patient (3). However, traditional jet nebulizers are still commonly used in many hospitals, since newer devices are more expensive and do not provide bronchodilatation like jet nebulizers (6).

Even though each patient uses his own delivery mask and reservoir, the nebulizer device that may be used in common by many patients in hospitals or even by the same patient may become contaminated with bacteria or viruses in time (7). This could be solved by regular cleaning of the nebulizer system. Coronavirus may be released into the environment during patient expiration, and the virus may remain viable in aerosols for hours (5). The dispersion of aerosols has been reported to be dependent on the distance to the aerosol source, and a distance of approximately 90 cm from the nebulizer system is defined as the radius of risk for a safe zone (7).

### **Advantages of Nebulizer Treatment During the COVID-19 Pandemic**

During the pandemic, no increase in coronavirus transmission due to nebulizer treatment was reported in national and international publications, which might be explained by healthcare professionals taking the necessary preventive measures and prohibiting patient visits to corona services. Publication results also support practical experiences that nebulizer therapy does not seem to significantly increase the risk of infection transmission (8, 9). Liu et al. investigated with the PCR-based detection method the presence of SARS-CoV-2 in the aerosol samples of two different COVID-19 hospitals in Wuhan (8). It was found that airborne SARS-CoV-2 transmission was very limited in patient clinics and intensive care units with negative pressure isolation and high air exchange, whereas a higher viral load was observed in patient toilets and staff rooms with inadequate ventilation (8). Wan et al. placed 3 cassettes containing 1- and 0.2- $\mu\text{m}$  polytetrafluoroethylene (PTFE) and a 0.2- $\mu\text{m}$  polycarbonate filter 30 cm away from a patient's head during oxygen and nebulizer treatment to investigate the contagious effect of nebulizer therapy (9). The samples were analyzed by real time-PCR by filtering the ambient air for 20 minutes at a flow rate of 4.5 L/min. While the spray in filters administered by a nebulizer used as a positive control which contains the SARS-CoV-2 virus resulted 100 % PCR positivity, 0% pathogens were detected in the room air obtained during the oxygen and nebulizer treatment of the SARS-CoV-2 patient (9). This result showed that there was an extremely low amount of airborne coronavirus in a negative pressure isolation room and staff room with full personal protective equipment and it may indicate that nebulizers may not be a risk of virus transmission.

### **Disadvantages of Nebulizer Treatment During the COVID-19 Pandemic**

Nebulizers generate aerosol particles in the size of 1–5  $\mu\text{m}$ , which may lead to the entrance of bacteria and viruses into the lower airways (3). A recent study has evaluated the stability of SARS-CoV-2 and SARS-CoV-1 in aerosols and on various surfaces such as plastic, stainless steel, copper and cardboard (9). The researchers used three-jet Collison nebulizers to generate aerosols containing SARS-CoV-1-2. They found that environmental SARS-CoV-2 generated through nebulization could remain viable in aerosols <5  $\mu\text{m}$  for 3 hours, and SARS-CoV-2 was more stable on plastic and stainless steel than on copper and cardboard

(10). The study results suggest that SARS-CoV-2 can be transmitted by small particle aerosols generated through nebulizers (10). On February 26, 2020, the first case of COVID-19 was confirmed in the USA and the patient underwent multiple aerosol-generating procedures including nebulizer treatments, bilevel positive airway pressure (BiPAP) ventilation, endotracheal intubation, and bronchoscopy during the hospitalization period (11). Among the 121 health care workers who were exposed to the patient, 43 (35.5%) developed COVID-19 symptoms during the 14 days after exposure (11). Laboratory-confirmed COVID-19 was found to be more common in health care personnel who performed physical examinations and were exposed to the patient during nebulizer treatments (11).

Nebulizers generate a high volume of respiratory aerosols that may scatter over a long distance, and treatment with nebulizers may stimulate cough in patients, resulting in an increased risk of spreading the disease (12). The use of a nebulizer can increase the risk of SARS-CoV-2 infection by 0.9 times (13). Two-thirds of the aerosols generated from jet nebulizers are released into the environment, which may increase the risk of infection for the people who have close contact with the patient during nebulization therapy (14). Patient secretions can fall into the nebulizer's reservoir, which may also contribute to an increased risk of contamination in jet nebulizers (14). A nebulizer may have high infection risk if it is contaminated (14). Inhalers generate a lower amount of aerosol, and spacers may also decrease the transmission of exhaled bioaerosol which may contain virus to the environment (14). Taking these into account, the use of nebulizers should be avoided and the use of MDIs via chambers or spacers should be encouraged in confirmed or suspected COVID patients (1). Metered-dose inhalers are recommended by the GINA guidelines as a first-line method at the hospital and at home during the COVID pandemic (1). Dry powdered inhalers are also

recommended as a substitute for nebulizers during the pandemic (1). Nebulizers are discouraged unless essential (1). The NICE guidelines recommend continuing the use of the patient's own nebulizer at home (15). If a nebulizer will be used, mesh nebulizers should be preferred over jet nebulizers, and a mouthpiece should be preferred over a face mask (14). Washing hands before and the after the use of a nebulizer, not sharing the device with the other patients, and cleaning the device according to the manufacturer's instructions are also important steps regarding the use of a nebulizer during the COVID pandemic (16). According to the guidelines of the Cystic Fibrosis Foundation, disposable nebulizers should be used and reusable jet nebulizers should be cleaned after each therapy. Nebulizers can transmit viral droplets for 1 meter (14, 16). Therefore, the WHO recommends isolating COVID patients in well-ventilated rooms with open windows and staying at least 1 meter away from the patient during nebulizer use to minimize the risk of infection (14).

### Indications for Nebulizer Therapy

Despite its infectious risk, there is a need to use nebulizers in clinical practice for patients with uncooperative consciousness, severe dyspnea, severe hypoxemia, and intubation, as well as severe COVID-19 (Table I) (5). Thus, in these patients there is a need for more effective drugs and delivery methods in respiratory management.

The use of breath-actuated MDIs and DPIs with mechanical ventilation is not appropriate because of dry powder clumping during humidification (17). Additionally, patients with acute respiratory failure or severe cough, or patients who are non-cooperative may not be able to use MDIs or DPIs due to the lack of adequate inspiratory flow (7). The delivery of beta-agonists via an MDI or a DPI or intermittent and continuous nebulization

**Table I: Indications of nebulizer therapy during the COVID-19 pandemic.**

1. Patients with severe, life-threatening respiratory conditions (moderate-severe hypoxemia, hypo or hyperventilation)
2. Uncooperative patients finding it difficult to follow the usage instructions of MDIs or DPIs,
3. Patients with a poor response to MDIs or DPIs.
4. Intubated patients under mechanical ventilation
5. Patients with cystic fibrosis, pulmonary hypertension, Pneumocystis carinii pneumonia, or cancer who need to use specialized drugs that were developed to be used only with a nebulizer (dornase alfa, aerosolized tobramycin, aztreonam, pentamidine, ribavirin, and iloprost, etc.)

**MDIs:** Metered-dose inhalers, **DPIs:** Dry powdered inhalers

is based on the patient’s asthma status: stable or acute severe or non-severe asthma (9). Furthermore, there are some drugs that are developed to be used only in jet nebulizers such as dornase alfa, aerosolized tobramycin, aztreonam, pentamidine, ribavirin, and iloprost (7). Diluted acetylcysteine is also used with a nebulizer device for sputum induction. Therefore, in some patients such as cystic fibrosis, pulmonary hypertension, or *Pneumocystis carinii* pneumonia, nebulizer use seems to be essential for special drug delivery. As a result, using nebulizers should be considered in the above cases.

**Preventive Measures when Using Nebulizers**

Even though there is a concern regarding the use of nebulizers, there is also a need for them in some situations. In order to increase the safety of nebulizers, some measures can be taken;

1. If nebulizer therapy is needed in patients with COVID-19 who have an asthma attack, nebulizer therapy should be given in an airborne infection isolation room or negative pressure room (17). Healthcare professionals should also obey COVID-19 protection rules by using personal equipment and cleaning tools. Restriction of entering the patient’s room or ensuring only staying there for a short time during nebulization is another preventive method against infection transmission (17).

2. Using a filter is more than 90% effective in avoiding exhaled virus droplet spread (17). Furthermore, using a high-efficiency particulate air (HEPA) or a bacterial filter with a nebulizer might be more protective against the coronavirus (18). Using a face mask with a nebulizer is not effective in avoiding aerosol spread; moreover, it has a higher risk of disseminating aerosols by scattering faster from the small hole in the mask (18). However, placing a filter on the exhalation port of the mouthpiece may decrease the concentration of spreading droplets (19). Therefore, it

will be safer to use nebulizers with a filter or one-way valve fitted to the mouthpiece, to prevent spreading bioaerosol to the room air. Another option would be to use a mesh nebulizer combined with the mouthpiece in patients with COVID-19 (19).

3. There may be a need for bronchodilatation in critically ill asthmatic COVID-19 patients who are receiving ventilatory support. Exhaled particles from intubated patients during nebulization can stay in the air and can result in the transmission of coronavirus to medical staff (9). Therefore, it is essential to use HEPA filters through the ventilators. However, using a jet nebulizer or an MDI will not keep the ventilator circuit intact and will permit transmission of the virus. Mesh nebulizer use is recommended in such patients who are receiving ventilatory support. A mesh nebulizer can be added to the inspiration path of the ventilator circuit, and can stay in-line for up to 28 days (19). The main advantage of a mesh nebulizer is the possibility of drug administration into the mesh nebulizer reservoir without opening the ventilator circuit (19). Another point is that nebulizers should be placed in the inspiration circuit prior to the humidifier to reduce retrograde contamination from the patient (8).

Overall, nebulizer aerosol treatment has significant advantages and disadvantages, and physicians should make a decision on continuing or stopping the use of aerosol delivery treatment by considering both the patient’s condition and safety of medical staff. Turkish National Society of Allergy and Clinical Immunology Section recommendations for nebulizer treatment during the COVID-19 pandemic is given in Table II. It would be safer to use MDIs for bronchodilation therapy in COVID-19 positive asthma patients. However, delivering aerosol therapy through a nebulizer may be an option in some critically ill asthma patients by modifying the device and obeying strict protection rules against COVID-19.

**Table II: Turkish National Society of Allergy and Clinical Immunology Asthma Section Recommendations for Nebulizer treatment during the COVID-19 Pandemic**

1. Use of nebulizers should be avoided in confirmed or suspected COVID patients
2. MDIs and DPIs are recommended as a substitute for nebulizers in the hospital and at home during the COVID pandemic.
3. Patients can continue to use their own nebulizer at their home if they do not have COVID-19 infection. In COVID-19 positive patients, isolating the patient in well-ventilated rooms with open windows and staying at least 1 meter away from the patient during nebulizer treatment is needed.
4. If nebulizer therapy is essential and indicated, it can be used by following the infection control recommendations.

**MDIs:** Metered-dose inhalers, **DPIs:** Dry powdered inhalers

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