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COMMENTARY

Evidence-based treatment during the SARS-CoV-2 pandemic: Identifying the knowns and unknowns of nebulization

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ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus 19 (COVID-19), has resulted in a worldwide pandemic and currently represents a major public health issue. Among the considerations for patients with respiratory disease is the optimal delivery of inhaled bronchodilators to maximize patient care. Despite the lack of evidence, there is heightened concern about the potential risk for transmission of SARS-CoV-2 in the form of aerosolized respiratory droplets during the nebulized treatment of patients with COVID-19. In this commentary, the lack of evidence regarding nebulization and transmission of coronaviruses are discussed.

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), has resulted in a global pandemic with important associated considerations to public health. Among these considerations is the optimal delivery of inhaled bronchodilators to maximize patient care while minimizing SARS-CoV-2 transmission. The potential risk of SARS-CoV-2 transmission through aerosolized respiratory droplets during nebulized treatment of patients with COVID-19 is a currently unsubstantiated concern that has served as the primary driver of a steep increase in the dispensing of albuterol metered-dose inhalers (MDIs). This, in turn, has led to issues obtaining adequate supplies of albuterol MDIs in some parts of the United States.¹

To date, there is a lack of data available to determine whether nebulization may generate potentially infectious aerosols. As a result, evidence against the use of nebulization should be interpreted with caution. A recent publication in the *New England Journal of Medicine* has shown aerosol stability of SARS-CoV-2. However, aerosols in this study were generated under laboratory conditions and may not be applicable to a

clinical setting.² Studies in hospital settings in Singapore and Hong Kong did not provide any direct evidence that patients who were symptomatic with COVID-19 were the source of viral RNA in analyzed air samples.^{3,4} The first U.S. case of community-acquired COVID-19 was confirmed in a patient hospitalized in California. This patient was not suspected to have COVID-19 at the time of hospitalization and had several aerosol-generating procedures, including nebulization. Of the 121 health care providers (HCPs) exposed to the patient with COVID-19, 43 were symptomatic and were tested for SARS-CoV-2 and 3 tested positive for COVID-19. None of the 3 HCPs wore personal protective equipment when in contact with the patient; therefore, it is difficult to determine with certainty if viral transmission and nebulization were linked.⁵ A recent study in 4 Wuhan hospitals assessed the protective effects of personal protective equipment for 420 HCPs who provided care to patients with COVID-19 and were involved in aerosol-generating procedures. Despite a high risk of exposure, no HCPs contracted SARS-CoV-2.⁶

Regarding data relating to SARS-CoV transmission and nebulization, it was not possible to identify if the viral transmission came from the nebulizer itself or if the viral droplets were generated by the patient in one study investigating the temporal and spatial relationship of airborne droplets to patients with SARS-CoV.⁷ Furthermore, a 2004 study using polymerase chain reaction assessment of air samples around a patient with SARS-CoV undergoing nebulized treatment found no evidence of virus-specific nucleic acids.⁸ A 2012 review article on aerosol-generating procedures concluded that there was no evidence of SARS-CoV transmission risk related to

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Key Points**Background:**

- The potential risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission through aerosolized respiratory droplets during nebulized treatment of patients with coronavirus 19 is currently a reasonable yet unsubstantiated concern.

Findings:

- A review of the literature suggested that there is a lack of clear evidence to suggest that nebulized treatment transmits SARS-CoV-2 particles.
- Based on the lack of evidence, health care providers should critically evaluate the available data and exercise clinical judgment when considering treatment for patients.

nebulizers. However, other aerosol-generating procedures such as tracheal intubation, noninvasive ventilation, tracheotomy, and manual ventilation before intubation posed an increased risk of virus transmission to HCPs.⁹

Considering the lack of clear evidence of increased infection risk with nebulized therapy, the Centers for Disease Control and Prevention does not advise against the use of nebulizer treatments,¹⁰ but it does recommend isolating patients with possible infection and the use of personal protective equipment by HCPs.¹¹ In addition, other protective measures include stringent sanitization protocols, using negative-pressure rooms, disposing or disinfecting personal protective equipment after each use, and maintaining a distance of at least 6 feet or more from patients with infection or possible infection.¹² The National Institute for Health and Care Excellence recommends the continued use of nebulized treatment when applicable.¹³ They do not deem nebulization as a viral aerosol-generating procedure because the droplets are from the nebulizer chamber containing the liquid bronchodilator and not from the patient.

The limited availability of albuterol MDIs may result in many patients (with or without COVID-19) having varying degrees of respiratory distress with few if any treatment options to relieve their dyspnea. However, forgoing treatment is also not without risks, as aerosols caused by patients who are coughing can be a major source of aerosolized viral particles and an infection hazard for HCPs.¹⁴

In summary, at present there is a lack of clear evidence to suggest that nebulization can transmit viral particles. HCPs across all settings should critically evaluate the available data and exercise clinical judgment when considering treatment.

Furthermore, HCPs should take the necessary precautions to minimize the risk of infection.

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