



Aerosol Medication Use in COVID-19 Pandemic

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ABSTRACT

Administration of aerolized drugs to patients diagnosed with COVID-19 leads to the risk of transmission of patient-generated infectious aerosols to healthcare providers. While the COVID-19 pandemic is ongoing, in order to provide the best treatment for patients and at the same time to protect healthcare providers at the highest level, it is necessary to increase access to information and pay maximum attention to preventive measures.

Keywords: Aerosolized medications, bioaerosols, COVID-19

To the Editor,

The coronavirus disease, namely COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), continues worldwide. The SARS-CoV-2 outbreak was first detected in Wuhan, China in December 2019 (1). COVID-19, recognized by the World Health Organization as an international public health emergency on January 30, 2020, was declared as a pandemic on March 11, 2020 (2). The main transmission pathway for COVID-19 disease is droplets from the respiratory system produced by sneezing, coughing, and even speech (2). There is an ongoing debate about inhaled medication use in pulmonary diseases. Unnecessary aerosol inhalation therapy should be avoided in patients with COVID-19. If COVID-19 patients have concomitant COPD or asthma, a dry powder inhaler and/or pressured metered dose inhaler (pMDI) plus a spacer should be used (3).

With the onset of the COVID-19 pandemic, concerns about the use of inhaled corticosteroids have begun in patients and physicians. It is crucial that asthmatic subjects should continue their controller medications as previously determined by their physicians. If not, the risk of exacerbations may increase and may lead to worse consequences. Physicians caring for asthmatic patients should instruct them fully that disease control may be impaired if they disrupt their inhaled medications (4,5).

It is also essential that each asthmatic patient has a comprehensive asthma action plan so that they can manage their disease at home. The asthma action plan should be considered to be even more important during the COVID-19 pandemic. Within the framework of the action plan, patients should continue their treatment and know that they should not hesitate to increase the treatment step and even to use systemic corticosteroids when necessary (4,6).

Another major concern regarding inhaled medications is the virus transmission risk during aerosol drug delivery, especially via a nebulizer. Exhalation of the patient diagnosed with COVID-19 while using an aerosol-forming device may increase the risk of spreading infectious droplets for several meters (4,6-8). Infection of many healthcare providers during the COVID-19 pandemic has raised concerns about implementing aerosol-producing procedures. The international authorities discourage drug delivery via nebulizers, unless unavoidable, for asthma management during the COVID-19 pandemic. A recently published article has provided a detailed view on the safety and efficiency of aerosolized medications in the treatment of patients with COVID-19 (9). Pressurised metered-dose inhalers and a spacer (with a tightly fitting face mask, if required) should be preferred for delivery of reliever medications in asthma exacerbations. Patients

should be cautious to use their own inhalers and spacers, and not to share inhalers or spacers with anyone else, including family members. Patients should take their own medications and spacers with them if they need to go to the hospital (4,6). The use of nebulizers in healthcare settings is not recommended and delivering short-acting bronchodilators via spacers is the preferred route of treatment. It is noteworthy that the spacers used must be sterilized according to the manufacturer's recommendations, or it may even be more appropriate to use a separate spacer for each patient (4).

If the use of a nebulizer is essential due to reasons such as unavailability of spacers, using a nebulizer with a mouthpiece instead of a facemask should be considered. A facemask is an unfavorable interface for aerosol therapy in the treatment of SARS-CoV-2-infected patients since the airflow of the nebulizer forces the aerosol into the ambient air during expiration (9,10). Some nebulizers have valves and expiratory filters. Filters attached to nebulizers may also reduce the risk of transmission of viral infections via the generation of aerosols that can spread infectious droplets. Therefore, the best method to prevent the spread of aerosols is to use a mouthpiece with a filter attached to the exhalation port. In any case, healthcare providers must take personal protective measures appropriately (10-12).

Apart from nebulizer treatments, high flow oxygen therapy and respiratory support are also problematic in asthmatic patients with COVID-19. There are no definitive suggestions from the asthma guidelines on this subject. In patients treated with high-flow oxygen therapy due to severe hypoxemic failure, it is possible to administer aerosolized therapy through the high-flow cannula. Unfortunately, a high-flow nasal cannula may also increase bioaerosol dispersion in the environment, favoring transmission of SARS-CoV-2, since it does not have a closed circuit, unlike ventilators. So it should be kept in mind that it is beneficial to wear a surgical mask over a high-flow nasal cannula in patients to reduce aerosol conduction. A high-flow nasal cannula with a surgical mask on the patient's face may be a reasonable application that can be useful in hypoxemic COVID-19 patients and prevent intubation (13).

Aerosol drug delivery in mechanically ventilated patients with COVID-19 is a challenging issue in terms of protection of both the other patients and healthcare providers. Keeping the ventilator circuit intact is crucial

to prevent increased transmission of SARS-CoV-2 to the healthcare providers. The use of pMDI should be preferred for routine bronchodilator therapy in mechanically-ventilated patients. Nebulizers lined up in the ventilator circuit can become contaminated with bacteria and increase the risk of ventilator-associated pneumonia. When using a pMDI for aerosol drug delivery in mechanically-ventilated patients, an actuator is needed in line with the ventilator circuit. If a non-collapsible chamber spacer is used, it must be removed from the ventilator circuit between treatments. Preferring a collapsible chamber spacer enables the spacer to remain in the ventilator circuit and the circuit does not need to be disconnected for each bronchodilator treatment. Since leaving the foldable spacer in the ventilator circuit between treatments causes condensate to accumulate in it, care should be taken not to let the condensate move into the patient's respiratory tract (14,15).

Using a mesh nebulizer overcomes many problems in aerosol drug delivery in mechanically ventilated patients with COVID-19. Mesh nebulizers are devices that use a vibrating mesh or plate with multiple apertures to generate fine-particle, low-velocity aerosols. These devices have a high efficiency of delivering aerosol to the lung. Unlike jet nebulizers, mesh nebulizers do not add gas flow to the circuit and aerosol delivery is more efficient than when a jet nebulizer is used. Moreover, mesh nebulizers can remain on the line for up to 28 days, and thanks to their reservoir design, bronchodilator drugs can be administered without any need to break the ventilator circuit. It is recommended to place the mesh nebulizer at the intake end of the humidifier tank of the ventilator (3,9,14-17). It is also advantageous to use HEPA filters in the expiratory limb of the circuit to reduce the risk of transmission of COVID-19 to healthcare professionals (18).

In patients with COVID-19, noninvasive ventilation (NIV) can effectively improve respiratory failure and eliminate the need for mechanical ventilation while inadvertently creating a high risk of virus transmission to healthcare workers. Aerosol therapy during NIV can be applied by pMDI plus a spacer or a nebulizer. Alternatively, the patient can be removed from ventilation and inhaled medication can be given as usual, but this approach has the disadvantage of interrupting ventilation. Since it has dual limb circuits with inspiratory and expiratory valves, a critical maintenance ventilator for NIV has the same factors affecting aerosol delivery as those affecting aerosol delivery with invasive ventilation. If NIV is employed with a single

limb circuit with a leak port serving as the exhalation port, the nebulizer can be placed in three different locations: 1) to the vented mask with a leak port, 2) between the leak port and the ventilator on the NIV circuit, 3) between the leak port on the circuit and the unvented mask. Efficiency of aerosol drug delivery differs according to the position of the nebulizer. The best performance for the drug to reach the patient is when it is placed between the nebulizer leak port and the mask using an unventilated mask (19,20). A metered dose inhaler should be used with a spacer. A mesh nebulizer can also be directly included in the mask for NIV (15). A novel method has been developed to reduce the increased transmission risk for healthcare workers during NIV, in the existence of COVID-19. This is a fixed flow canopy surrounding the patient and creating a closed area where noninvasive respiratory support can be used safely. Currently, this newly developed method is the best way to reduce the exposure of hospital staff to infectious aerosols while applying NIV in patients with COVID (21).

To conclude, while the COVID-19 pandemic is continuing, it is necessary to increase the access to information and pay maximum attention to preventive measures in order to ensure the best treatment of patients and to simultaneously protect the healthcare professionals and the patients at the highest level.

REFERENCES

- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395(10223):497-506.
- <https://www.who.int/news-room/q-a-detail/q-a-coronaviruses>. (Accessed April 3, 2020.)
- Respiratory Therapy Group, Respiratory Medicine Branch, Chinese Medical Association. Expert consensus on protective measures related to respiratory therapy in patients with severe and critical coronavirus infection. *Chinese Journal of Tuberculosis and Respiratory Diseases*, 2020,17(00):E020 -E020. DOI: 10.3760 / cma.j.issn.1001-0939.2020.0020
- www.ginasthma.org. (Accessed April 23, 2020.)
- Asthma and Allergy Foundation of America- www.aafa.org (Accessed May 17, 2020.)
- <https://www.nationalasthma.org.au/news/2020/covid-19-and-your-asthma-patients>. (Accessed May 29, 2020.)
- Tran K, Cimon K, Severn M, Pessoa-Silva CL, Conly J. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: A systematic review. *PLoS One* 2012;7(4):e35797.
- Rau JL, Ari A, Restrepo RD. Performance comparison of nebulizer designs: Constant-output, breath-enhanced, and dosimetric. *Respir Care* 2004;49(2):174-9.
- Ari A. Practical strategies for a safe and effective delivery of aerosolized medications to patients with COVID-19. *Respiratory Medicine* 2020;167:105987.
- McGrath J, O'Toole C, GB, Joyce M, Byrne M, MacLoughlin R. Investigation of fugitive aerosols released into the environment during high-flow therapy. *Pharmaceutics* 2019;11:254.
- Wittgen BP, Kunst PW, Perkins WR, Lee JK, Postmus PE. Assessing a system to capture stray aerosol during inhalation of nebulized liposomal cisplatin. *J Aerosol Med* 2006;19(3):385-391.
- Ari A, Fink JB, Pilbeam S. Secondhand aerosol exposure during mechanical ventilation with and without expiratory filters: An in-vitro study. *Ind J Resp Care* 2016; 5(1): 677-82.
- Li J, Fink JB, Ehrmann S. High-flow nasal cannula for COVID-19 patients: Low risk of bio-aerosol dispersion. *Eur Respir J* 2020;55(5):2000892.
- Hess DR. Medicated Aerosol Delivery Devices. In: Volsko TA, Chatburn RL, El-Khatib MF (eds). *Equipment for Respiratory Care*. Burlington, Massachusetts: Jones & Bartlett Learning; 2014:527-552.
- Hess DR. Humidity and aerosol therapy. In: Hess DR, MacIntyre NR, Galvin WF, Mishoe SC. (eds). *Respiratory Care Principles and Practice*, 4th ed. Burlington: Jones and Bartlett Learning, 2020: 321-65.
- Dhand R. Nebulizers that use a vibrating mesh or plate with multiple apertures to generate aerosol. *Respir Care* 2002;47(12):1406-18.
- Miller A, Epstein D. Safe bronchodilator treatment in mechanically ventilated COVID-19 patients: A single center experience. *J Crit Care* 2020;58:56-7.
- Ari A, Fink J, Harwood R, Pilbeam S. Secondhand aerosol exposure during mechanical ventilation with and without expiratory filters: An in-vitro study. *Indian Journal of Respiratory Care* 2016;5:677-82.
- Sutherasan Y, Ball L, Raimondo P, Caratto V, Sanguineti E, Costantino F, et al. Effects of ventilator settings, nebulizer and exhalation port position on albuterol delivery during non-invasive ventilation: An in-vitro study. *BMC Pulm Med* 2017;17(1):9.
- Ari A. How to optimize aerosol drug delivery during noninvasive ventilation: What to use, how to use it, and why?. *Eurasian J Pulmonol* 2019;21:1-8.
- Adir Y, Segol O, Kompaniets D, Ziso H, Yaffe Y, Bergman I, et al. COVID-19: Minimising risk to healthcare workers during aerosol-producing respiratory therapy using an innovative constant flow canopy. *Eur Respir J* 2020; 55: 2001017.