

Aerosol Delivery to a Critically Ill Patient: A Big Issue Easily Solved by Developing Guidelines

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ABSTRACT

Nowadays, therapeutic aerosols are commonly delivered to mechanically ventilated patients by nebulizers and pressurized metered dose inhaler attached to an adapter or a spacer. Studies with asthmatics and chronic obstructive pulmonary disease patients have confirmed that aerosol delivery during mechanical ventilation is feasible. They have also reported that the inhaled drugs administered during mechanical ventilation provide greater and faster clinical outcomes than when delivering during spontaneous unassisted breathing. Researchers studied factors that would affect aerosol delivery during mechanical ventilation. Even with the tremendous amount of publications in this area, there have still been no recommendations or guidelines released to help respiratory therapists in their decision as to when to deliver aerosol to ventilated patients. Mostly,

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respiratory therapists read the literature and decide accordingly what to do and which device to use for their patients. This puts the patients at risk of receiving a sub-therapeutic or toxic dose of the inhaled aerosol. Some studies raise an alarm of physician decision upon reading any released publication related to aerosol delivery in mechanical ventilation without a trusted recommendation and guidelines. This increases the need for the development of recommendations and guidelines, by a trusted board or society, for aerosol delivery to such critically ill patients. To summarize, inhaled drugs administered to critically ill patients is of benefit compared to taking the patient off the ventilator and delivering during spontaneous unassisted breathing. However, dependable guidelines are needed to optimize aerosol delivery.

Keywords: Fill volume; HFNC; Humidification; Non-invasive ventilation; pMDI; Spacer; Ventilator setting; Vibrating mesh nebulizers

INTRODUCTION

Therapeutic aerosols are commonly administered to mechanically ventilated patients [1–4]. These agents are delivered by nebulizers [5–8] and a pressurized metered-dose inhaler (pMDI)

attached to an adapter or spacer through ventilator circuits [6, 9–11].

Studies in patients with stable asthma [12] and chronic obstructive lung disease (COPD) [13] have confirmed that aerosol delivery during mechanical ventilation is feasible and provides great and fast clinical outcomes [7, 14].

Researchers have studied factors that would affect aerosol delivery during mechanical ventilation, e.g., aerosol generators, add-on devices, patient interfaces, patient-related factors, ventilator-related factors, and circuit-related factors [9, 10, 13, 15–26]. They even studied the effect of the design of the nebulizer reservoir chamber on aerosol delivery [27] and fugitive aerosol effect on surrounding healthcare provider [25, 28].

Most of these studies concluded that aerosol delivery is much better when using a vibrating mesh nebulizer (VMN) in a dry non-humidified circuit [18, 19, 29]. The position of the nebulizer in the ventilation circuit varied according to the ventilation setting, type of ventilator, and ventilation circuit used.

When using a single-limb ventilation circuit, it is better to place the aerosol generator between the patients and the leak port as shown in Fig. 1 [13, 17], but when using a dual-limb ventilation circuit, it is better to place the aerosol generator in the inspiratory limb, as shown in Fig. 2 [24, 30] for better aerosol delivery.

Even with the tremendous amount of publications in this area, still no recommendations or guidelines have been released to help respiratory therapists in their decisions when delivering aerosol to ventilated patients.

Mostly, respiratory therapists read the literature and decide accordingly what to do and which device to use for their patients. This puts the patients at risk of receiving a sub-therapeutic or toxic dose of inhaled aerosol. The aim of the present mini-review is to show how important the development of guidelines for aerosol delivery to cortically ill patients is.

EFFECT OF FILL VOLUME AND HUMIDITY ON AEROSOL DELIVERY

An example of the need of such important guidelines is our last finding regarding the effect of fill volume of respiratory solution, placed in the nebulizer reservoir chamber, on delivered aerosol [25, 31, 32].

Similar to what has been found by many studies, we reported that increasing fill volume of respiratory solution placed in the nebulizer reservoir chamber by normal saline resulted in much higher aerosol when using a jet nebulizer, as shown in Fig. 3. However, increasing the fill volume had no significant effect when using VMN, as shown in Fig. 3. It even increased the nebulization time with no significant benefit [25, 31, 32]. So increasing the fill volume with saline is not beneficial for all types of nebulizers.

Another example of the need of such important guidelines was our new finding, which opposes all the previously published literature. Previous literature has suggested switching off the humidifier while delivering aerosol to ventilated patients to increase lung deposition [18, 19, 29]. This would let the

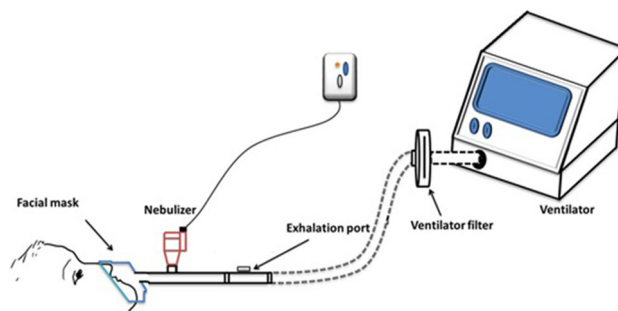


Fig. 1 Position of aerosol generator in the single-limb ventilation circuit [47]

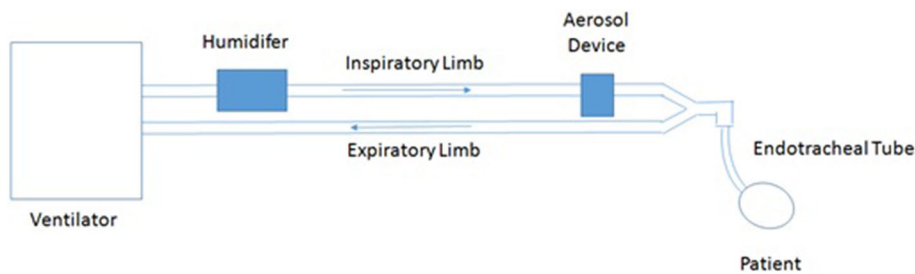


Fig. 2 Position of aerosol generator in dual-limb ventilation circuit [24]

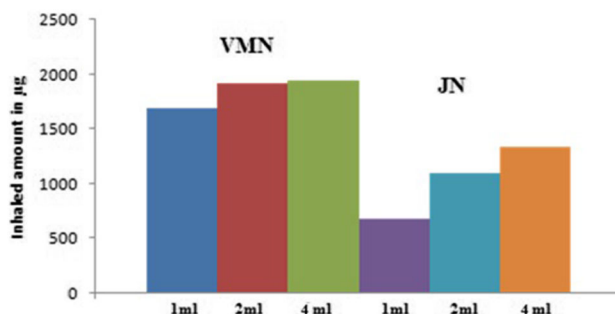


Fig. 3 Total aerosolized salbutamol in µg, presented as mean, from 5000 µg in 1, 2, and 4 ml fill volumes ($n = 10$) [25]

patient face the risk of inhaling dry gas, which has a harmful effect on the lungs [33]. These risks are even greater if the clinician fails to turn on the humidifier upon conclusion of aerosol administration.

We reported that there was no need to switch off the humidifier while delivering aerosol to the ventilated patient, as shown in Fig. 4 [25]. We verified our finding by studies using automatic continuous positive airway

pressure (auto-CPAP) [26] and non-invasive single-limb [31, 32] and invasive dual-limb [30] ventilations and still found no significance between delivering aerosol in humid or dry circuits. Furthermore, we found no significant effect of switching off or on the humidifier on the clinical status of ventilated patients [24]. So, why put the patient at risk of receiving dry gas, while delivering aerosol, which might harm his or her lungs? In addition, it was previously

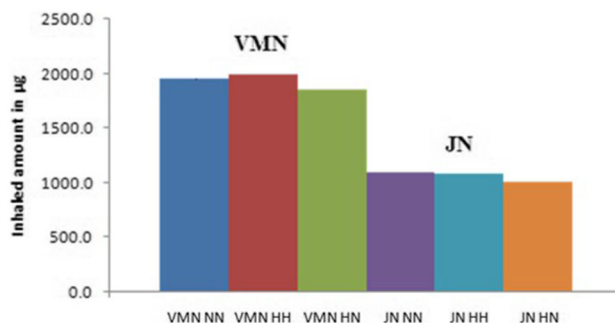


Fig. 4 Total aerosolized dose in µg, presented in mean, with ambient, humidified, and heated humidity with JN and VMN ($n = 10$), no heat and no humidification (NN),

humidification with no heat (HN), and heat with humidification (HH) [25]

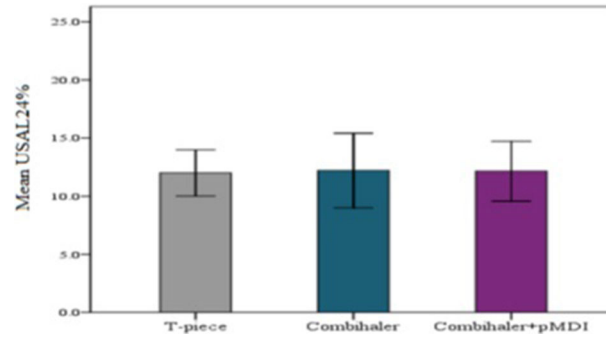


Fig. 5 Mean (SD) urinary excretion of salbutamol 24 h post inhalation of salbutamol respirable solution via vibrating mesh nebulizer through the three different connections expressed as percentage of nominal dose ($n = 12$) [48]

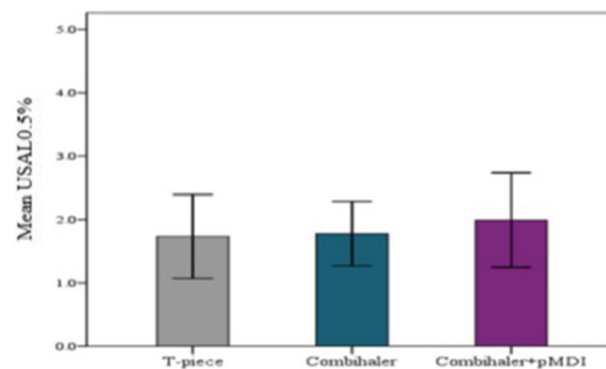


Fig. 6 Mean (SD) urinary excretion of salbutamol 30 min post inhalation of salbutamol respirable solution via vibrating mesh nebulizer through the three different connections expressed as percentage of nominal dose ($n = 12$) [48]

reported that the ventilation circuit will still contain humid air for more than 20 min after switching off the humidifier [34]. This was attributed to the patient exhaling humid air and the presence of condensation in the circuit that kept absolute humidity high despite reduced circuit temperature [34].

THE USE OF SPACER WITH NEBULIZER

A final example of the need for guidelines is a new add-on spacer called the Combihaler, which was designed for the use of a pMDI and nebulizer together in a ventilation circuit. The producer of this device claims that giving the patient one or two pMDI bronchodilator puffs before using the nebulizer increases aerosol delivery of the nebulized medication. They

validated this in a dual-limb ventilation circuit while placing the spacer in an inspiratory limb [35]. However, in a single limb, we did not find any significant effects on the systemically absorbed aerosol, as shown in Fig. 5, but just a slight insignificant increase in lung deposition, as shown in Fig. 6 [36]. Additionally, the large volume of the spacer increased the dead volume inspired by the patient in the single-limb ventilation circuit [36].

These studies and others raise an alarm of physician decision upon reading any released publication related to aerosol delivery in mechanical ventilation without good trusted recommendations and guidelines. These recommendations and guidelines need to be developed by a trusted board or society for aerosol delivery to such critically ill patients.

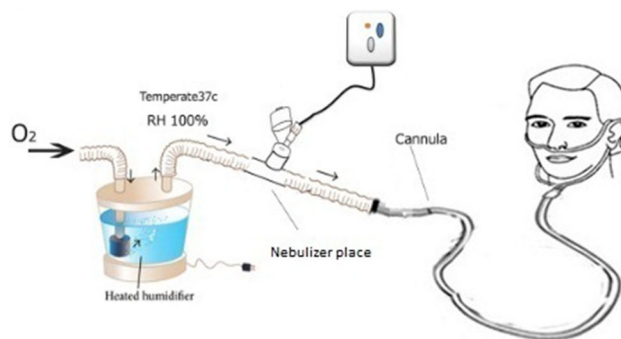


Fig. 7 Position of aerosol generators after the humidification chamber within high-flow nasal cannula oxygen therapy (HFNC) [46]

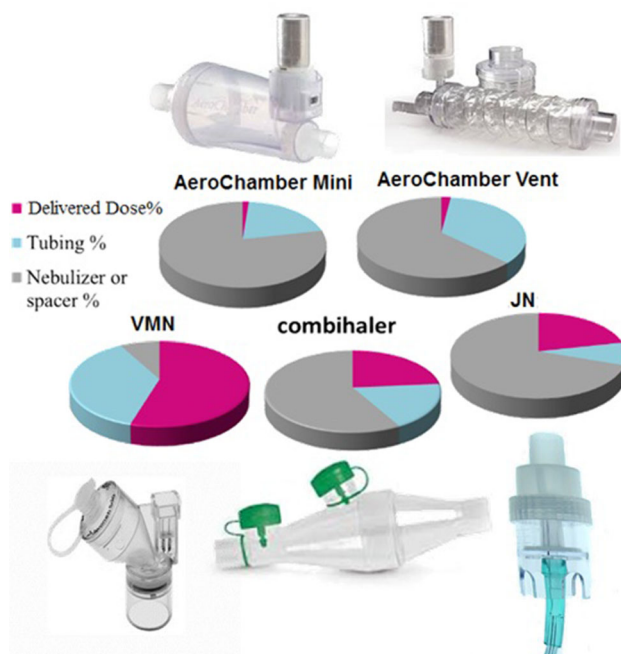


Fig. 8 Mean fate, in percentage, of the dose delivered using five different inhalation methods ($n = 5$) [46]

AEROSOL DELIVERY TO PATIENTS USING HIGH-FLOW NASAL CANNULA (HFNC)

Another critically ill patient who would benefit from the delivery of aerosol is the patient using a high-flow nasal cannula (HFNC). In practice, the nasal cannula is the most popular tool used for providing critically ill patients with supplemental oxygen [37–40].

HFNC is better tolerated than the non-invasive ventilation with a mask and can provide a wide extent of oxygen concentrations as needed [41].

Recently, there has been a growing trend towards delivering aerosol medications using HFNC. The possibility of such therapeutic combination in a clinical setting is still argued.

Aerosol delivery through the nose is advantageous over oral inhalation, as it can improve both patient comfort and compliance by simply

using a cannula to administer frequently dosing drugs and also drugs nebulized over long times [42].

The question arising here was how to combine aerosol delivery with the HFNC system and at the same time maximize aerosol delivery to the lungs. Previous bench studies, which evaluated combining aerosol delivery with an HFNC system, spotted that delivered dose was found to increase with decreasing gas flow rates and with wider-sized cannulas [43–45]. They also recommended placement of aerosol generators immediately after the humidification chamber within the circuit for better aerosol delivery, as shown in Fig. 7 [43–45].

We validated this by delivering aerosol to COPD patients using oxygen flow rate (5 l/min) in adult nasal-cannula to compare both the pulmonary and systemic bioavailability of different aerosol generators. Aerosol generators were placed immediately after the humidification chamber within the circuit [46].

We found that inhaled aerosols can be delivered efficiently at low oxygen flow using VMN and jet nebulizer in an HFNC system, while pMDIs with spacers deliver negligible amounts of drug below that expected for clinical response at this flow, as shown in Fig. 8 [46].

CONCLUSIONS

To summarize, inhaled drugs administered to critically ill patients during mechanical ventilation or HFNC is of benefit compared to taking the patient off the ventilator and delivering during spontaneous unassisted breathing. However, dependable guidelines are needed to optimize aerosol delivery.

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Data Availability. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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