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Aerosol Therapy for Ventilator-Dependent Patients: Devices, Issues, Selection & Technique

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Aerosol devices have been used to administer inhaled medications since the invention of modern mechanical ventilators. Although many new aerosol devices are available for ventilator-dependent patients, successful aerosol therapy still depends on thorough clinician knowledge of aerosol devices and their proper use. This paper explains the types of aerosol devices available on the market and provides strategies for choosing the right device for optimal treatment of mechanically-ventilated patients.

Description of Aerosol Delivery Devices

Nebulizers: Jet, ultrasonic and mesh nebulizers are used for aerosol drug delivery by converting liquid medications into small droplets that can be inhaled into the lower respiratory tract of ventilator-dependent patients.

To aerosolize liquid medications, jet nebulizers use a jet of compressed air or oxygen to draw on a reservoir and shear the liquid into particles. Jet nebulizers are widely used for ventilator-dependent patients because they are inexpensive and easy to use.

Ultrasonic nebulizers are powered by electricity or battery to generate high frequency vibrations with a piezo, thus creating a standing wave in the medication and aerosols at the crest of the wave.[1,2] Unlike jet nebulizers, they do not add gas to the ventilator circuit, rather, aerosol particle size and drug output are affected by the frequency and amplitude of vibration of the piezoelectric crystal. Aerosol particle size is inversely related to the vibration frequency of the piezo-electric crystal, while drug output is directly related to the amplitude of crystal vibration.[3,4]

The mesh nebulizer, also operated by electricity or battery, vibrates a piezo that moves liquid formulations through a fine mesh to generate aerosol.[1,2,5] The mesh nebulizer is a single-use device with a vibrating aperture plate designed to deliver aerosolized medications to mechanically-ventilated patients. The nebulizer is compatible with conventional ventilators. Because the mesh nebulizer operates without compressed gas, it does not change ventilator parameters and the reservoir of the nebulizer can be re-filled without interrupting ventilation. Furthermore, mesh nebulizers are easy to use and have a higher rate of drug output than jet nebulizers. Unlike ultrasonic nebulizers, they do not affect the temperature or concentration of the solution being delivered.[6]

As with other new nebulizers, mesh nebulizer designs are portable, handheld, and highly efficient with low residual volume.[1,2,5] They also have a silent operation and rapid output. Also, solutions, proteins and liposomal formulations can be nebulized by mesh nebulizers. Because of these advantages, mesh nebulizers are likely become popular for delivering aerosols to ventilator-dependent patients. Whereas in vitro studies have shown mesh nebulizers to be efficient in aerosol delivery during mechanical ventilation,[7,8] more clinical information about them is needed.

Pressurized Metered-Dose Inhalers (pMDIs): The pMDI is the most commonly used aerosol device for inhalation therapy worldwide; it is a compact and portable device that is easy to operate with short treatment time, multi-dose convenience and good dose consistency.[9-11] The basic components of a pMDI include a canister, propellants, drug formulation, metering valve and actuator. A pressurized mixture of propellants, surfactants, preservatives and active drug is released from the metering valve of the canister, which fits into an actuator boot.

Two types of propellants are used with pMDIs: (1) chlorofluorocarbon (CFC) and (2) hydrofluoroalkane (HFA). HFA-pMDIs are different from CFC-pMDIs in terms of the formulation, metering-valve and actuator design.[54,9] For example, HFAs contain ethanolic solutions while CFCs use a surfactant for dispersion. HFAs have a softer and finer aerosol spray with greater lung deposition than CFCs.[12-14] However, despite differences in the pMDI formulations, HFA-pMDIs are similar to those of CFC pMDIs, in terms of bronchodilator response,[15,16] pulmonary function[17,18] and side effects.[19]

A variety of spacers are used for aerosol drug delivery in mechanically-ventilated patients. However, electrostatic charge and the type of spacer need to be considered. The electrostatic charge decreases aerosol delivery by drawing small particles to the walls of the chamber; therefore, clinicians need to review the electrostatic properties of the spacer before treatment. Spacers are made of metal, paper or plastic, each of which have different electrostatic properties. Electrostatic charge is not an issue with metal or paper spacers, but plastic spacers may have electrostatic or non-electrostatic properties. If a plastic spacer with electrostatic properties is used for aerosol therapy, clinicians should wash it with liquid detergent to reduce the electrostatic charge before treatment. Actuating the pMDI 12 or 20 times into a spacer also reduces the electrostatic charge. However, many pMDI doses are wasted with this technique, and it is less effective than washing.[20,21]

Types of spacers include unidirectional, bidirectional and cylindrical/reservoir adaptors. The spacer type influences the efficiency of aerosol delivery during mechanical ventilation.[9,22-24] While bidirectional spacers are superior to unidirectional spacers in dose delivery, cylindrical spacers have been shown to have 4-to-6 fold greater efficiency

on aerosol delivery than unidirectional and bidirectional spacers that attach directly to the endotracheal tube (ETT).[25-27]

Issues with Aerosol Delivery Devices

Problems with Nebulizers: Jet nebulizers are bulky. They require a compressor or pressurized gas to operate, and are labor-intensive.[20,28,29] They are also less efficient than other aerosol devices and retain a lot of the medication in the nebulizer cup, limiting the drug available to the patient. They require more preparation to setup, and more time for cleaning and maintenance than pMDIs. Further, the additional gas flow delivered into the ventilator circuit may change the set flow and delivered volume and require adjustments of alarm settings both during and after nebulization if the ventilator does not compensate for nebulizer gas flow entering the circuit. This is especially important in ventilator-dependent children because they are affected to a greater extent when extra flow is added to the ventilator circuit. Clinicians should exercise caution when changing ventilator parameters and return to them to pretreatment levels after the treatment is completed. Since jet nebulizers are attached to the ventilator circuit with a standard T adaptor, attaching or removing the nebulizer from the ventilator circuit may interrupt ventilation. Therefore, valved T adaptors should be used in order to allow placement and removal of the jet nebulizer without loss of pressure in the ventilator circuit.

Ultrasonic nebulizers also have several problems. They are bulky and more expensive than jet nebulizers. Their particle size is larger than with jet nebulizers, and drug solutions used with ultrasonic nebulizers become more concentrated during operation. There is an increase in solution temperature after a few minutes of operation, and as a result, ultrasonic nebulizers may denature some drug formulations. Although smaller ultrasonic nebulizers are used to deliver aerosolized drugs to mechanically-ventilated patients,[30] the cost and size of these nebulizers make them less desirable, in addition to their inefficiency in nebulizing drug suspensions and more viscous solutions.[31,32] Therefore, ultrasonic nebulizers are not widely used for aerosol delivery during mechanical ventilation.

Mesh nebulizers are more expensive than jet nebulizers. Suspension or viscous drugs may clog the pores of the mesh nebulizer which may not be easily detectible by the output of the nebulizer.[33] Cleaning of mesh nebulizers should be gentle in order to prevent damage to the mesh.

When a nebulizer is used with mechanically-ventilated patients, escape of aerosol to the environment creates health risks to healthcare providers and bystanders.[34] Other problems associated with nebulizers are infection due to contamination (jet nebulizer) and increases in drug concentration in the nebulizer cup when using jet and ultrasonic nebulizers.

Problems with pMDIs: If a dose counter is not used with a pMDI, it is difficult to determine the dose left in the pMDI. Thus, pMDIs may be used beyond their capacity or remaining doses may be wasted. The dose counters, which are attached to the top or boot of the pMDI, are manufactured by different companies. Although use of dose counters is recommended with all pMDIs, it should be noted that newer pMDIs with dose counters may not permit removal of the canister from the actuator. In this case, the actuator itself must fit an adapter to be connected to the ventilator circuit, but the efficiency of such systems is not known. Integrating dose counters into new pMDIs is required by the FDA in order to determine the total number of doses available in the device.[35]

Selection of an Aerosol Device for Mechanically-Ventilated Patients

Nebulizers or pMDIs with in-line spacers are used to administer inhaled medications during mechanical ventilation. Both nebulizers and pMDIs produce similar therapeutic effects in mechanically-ventilated patients.[4,22,36-38] The therapeutic aim and availability of the drug generally determine which aerosol device to use. pMDIs are preferred for inhalation therapy in ventilator-dependent patients because of problems associated with use of nebulizers and the advantages of pMDI, such as convenience, lower cost and decreased risk of damaging the flow sensor.[4,39] However, only a few drug formulations are available as pMDIs. Therefore, they are mainly used to deliver bronchodilators and corticosteroids

for ventilator-supported patients with airway obstruction,[22,23,40] while nebulizers are used to deliver a variety of drugs such as bronchodilators, corticosteroids, antibiotics, prostaglandins, surfactant, mucolytic agents and other formulations that are not available as pMDIs. A few studies have shown that use of pMDIs with ventilator-dependent patients has increased significantly over the years [41,42] because of their convenience, more consistent dosing and reduced chances of bacterial contamination.[43,44]

Factors Affecting Aerosol Drug Delivery During Mechanical Ventilation

Aerosol delivery during mechanical ventilation depends on several factors. These can be divided into three categories: (1) ventilator-related factors, (2) circuit-related factors and (3) device-related factors.[45]

Ventilator-related Factors: Ventilator-related factors such as inspiratory flow rate, ventilator mode, inspiratory time, tidal volume, bias flow and wave patterns make a significant difference in aerosol drug delivery to ventilator-dependent patients. The lower the flow, the greater the amount of aerosol delivered to the patient. Since high inspiratory flow rates increase turbulent flow and inertial impaction of aerosol particles, aerosol deposition with high inspiratory flow rates is less than with lower flow rates. Peak flow rates of 40-50 L/min may be used to improve drug delivery during mechanical ventilation as long as this is tolerated by the patient.[46,47]

For critically ill patients with low compliance and low resistance, aerosol delivery through a nebulizer is more efficient with volume-controlled ventilation than pressure-controlled ventilation.[48] This is not the case with pMDIs. Also, it has been shown that spontaneous ventilation modes such as continuous positive airway pressure (CPAP) increase aerosol delivery by 30% compared to controlled breaths of equivalent tidal volume.[49] Nebulizers generate aerosol over time; therefore, using a longer inspiratory time increases the efficiency of nebulizers, in contrast, pMDIs, which have a short aerosol generation time, are not influenced by the duration of inspiratory time.

Tidal volume (Vt) is directly related to aerosol deposition. Although setting Vt

greater than 500 ml in an adult improves aerosol drug delivery during mechanical ventilation,[47,49] larger Vt can damage the lungs of mechanically-ventilated patients. Vt may be a problem when it is not adequate to move the aerosol from the generator to the end of the patient airway in a single breath; therefore, it is important to set the Vt larger than the volume of the ventilator circuit and artificial airway in order to increase aerosol delivery.

Although descending ramp wave patterns provide higher efficiency than square wave patterns at the same peak flow, the effect of inspiratory waveform is much less in pMDIs than in nebulizers.[48] Bias flow, also known as trigger sensitivity, affects the efficiency of nebulizers during mechanical ventilation. Increasing bias flow from 2 to 5 L/min decreases aerosol deposition in ventilator-dependent patients by diluting aerosols and increasing the washout into the expiratory limb between breaths.[8]

Circuit-related Factors: Using heat-moisture exchangers (HMEs) or heated humidifiers, the gas in the ventilator circuit is heated and humidified in order to avoid drying the airway mucosa. Since the filter in the HME is considered a barrier to aerosol delivery, it should not be placed between the aerosol device and the patient. Also, if a dry circuit is used, aerosol therapy should be completed in 15 minutes to minimize the effects of dry gas on the airway mucosa.[40]

As shown in Figure 1, some HMEs designed for aerosol delivery (HME-AD) allow inhalation therapy without removing the HME-AD from the circuit during mechanical ventilation. Although the designs of these HME-ADs are different, each HME-AD has two configurations: (1) an HME configuration that functions like a regular HME, and (2) an aerosol configuration in which inspiratory gas bypasses the HME to deliver inhaled medications to ventilator-dependent patients. It has been reported that drug delivery varies with HME-ADs because of the design and composition of the HME-ADs,[50] but clinical research is needed to determine the in-vivo efficiency of aerosol delivery by different HME-ADs and the effectiveness of HME-ADs with different aerosol devices.

Several in-vitro studies have shown up to 50% reduction in aerosol delivery with heated/humidified ventilator circuits.[7,22,49,51-54] However, bypassing the humidifier and exposing a ventilator-dependent patient to dry and cold gas just to increase aerosol deposition is not recommended. Clinicians can increase the efficiency of aerosol therapy by paying attention to the technique of administration and increasing the dose when a heated humidifier is used.

The density of gas used with the ventilator has been shown to make a substantial difference in aerosol delivery. For instance, helium-oxygen mixtures greater than 50% increase aerosol delivery with nebulizers and pMDIs more than air or air-oxygen mixtures used to ventilate the patient.[55]

Aerosol deposition with artificial airways such as an endotracheal tube (ETT) or tracheostomy tube (TT) has not been studied much. Also, research on the efficiency of aerosol delivery in intubated patients has focused largely on ETT, with little analysis of effect of TT on aerosol delivery during mechanical ventilation. Since ETTs are narrower than the internal diameter of the trachea, they are associated with increased airway resistance and losses in aerosol delivery.[56,57] Previous in-vitro studies indicate that there is no difference in aerosol deposition between ETT with 9.0 -7.0 mmID, but aerosol delivery to ventilator-dependent patients is reduced as the inner diameter of ETT decreases from 6.0 mmID to 3.0 mmID.[52,56]

Device-related Factors: The nebulizer type and its position in the ventilator circuit have all been shown to impact the efficiency of aerosol delivery. Previous research reported variations in dose efficiency in different brands of nebulizers, and different units of the same brand.[58,59] Since fill volume and nebulizer type affect drug delivery,[57,60] following instructions in the drug/device label is critical.

Optimum Technique for Drug Delivery in Ventilator-Dependent Patients

Aerosol drug delivery to ventilator-dependent patients is affected by many factors. Understanding these factors has helped us to develop optimal techniques for using pMDIs and nebulizers. When proper administration technique is used, aerosol therapy in mechanically-ventilated patients is safe, convenient and effective. Figure 2 outlines the optimum administration technique with nebulizers and pMDIs.
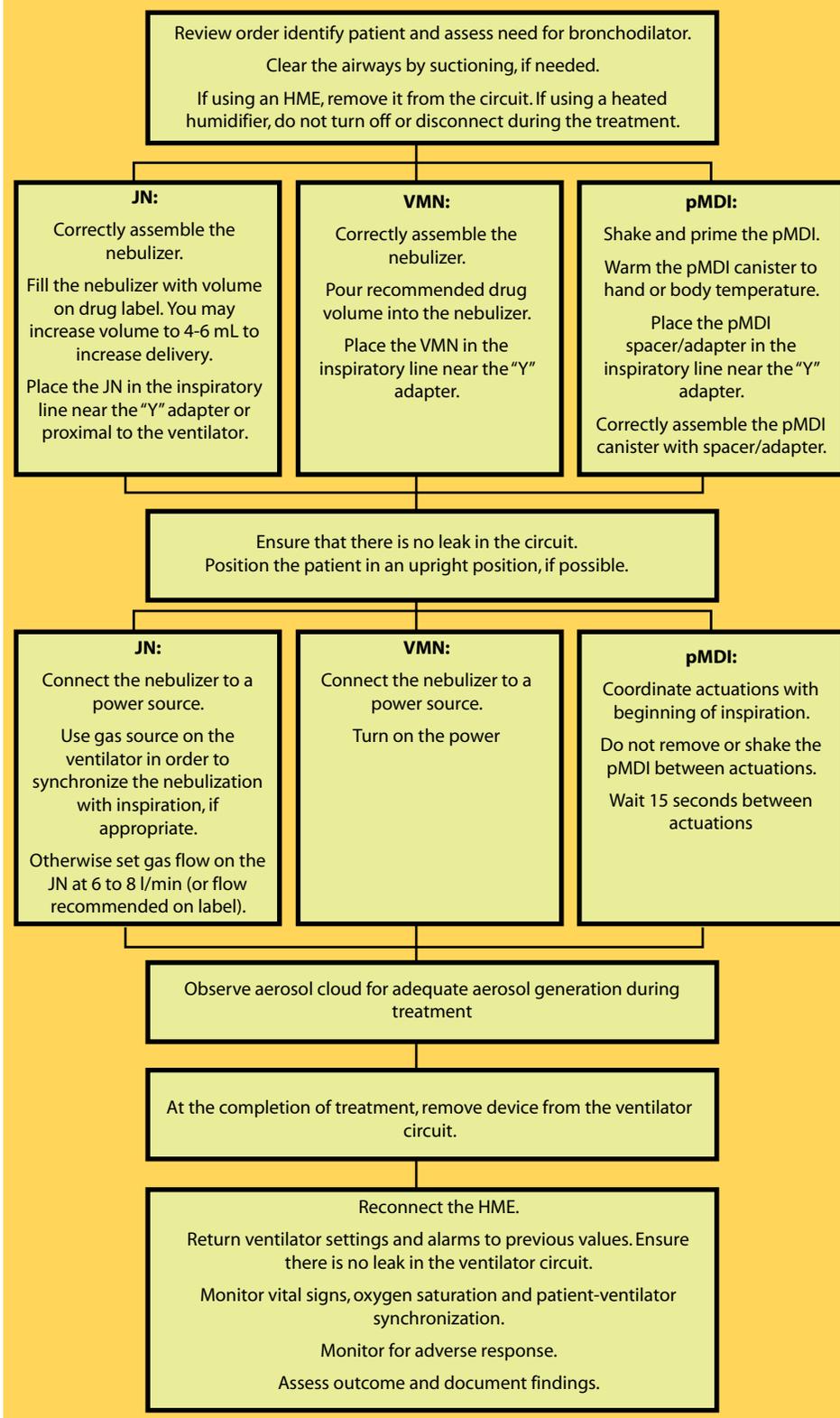
Patient position: Studies have shown that drug delivery to patients in a semi-fowler and sitting position produces a significant response.[61-65] Therefore, if the patient cannot sit in the bed during inhalation therapy, a semi-fowler position with the head of the bed elevated to 20° to 30° above the horizontal should be used for aerosol administration during mechanical ventilation.

Optimum Technique with Nebulizers: Jet nebulizers are operated continuously by pressurized gas or intermittently by a separate line connected to the ventilator which provides driving pressure and flow to the nebulizer. During intermittent operation (aka nebulizer function on the ventilator), the ventilator operates the nebulizer only in inspiration, thus reducing aerosol loss during expiration. When nebulizer function is used for aerosol therapy during mechanical ventilation, the ventilator compensates for the flow to the nebulizer to maintain constant tidal volume and minute ventilation. Although jet nebulizers are often operated continuously, it has been shown that intermittent nebulization increases aerosol deposition more than continuous nebulization during mechanical ventilation.[51,66] However, it must be noted that the lower pressure of the driving gas may affect the aerosol characteristics and delivery efficiency of a nebulizer operated through the ventilator. For instance, operating a nebulizer with a lower driving pressure (<15 psi) through a ventilator instead of using pressurized gas (≥50 psi) may generate larger particles and decrease the efficiency of the nebulizer.[40] However, it has been reported that the newer

Figure 1. HMEs designed for aerosol delivery during mechanical ventilation. A: Circuvent HME/HCH bypass (Smiths-Medical Keene, NH)with Gibeck Humidvent Filter Light S inline (Hudson RCI, Arlington Heights, IL). B: Humid-Flo HME (Hudson RCI, Arlington Heights, IL). C: Airlife bypass HME (Carefusion, San Diego, California). (Reproduced with permission, from Reference 70)

Figure 2. An algorithm describing steps for optimal drug administration technique by each aerosol generator (Reproduced with permission from Reference 45).

Review order identify patient and assess need for bronchodilator.

Clear the airways by suctioning, if needed.

If using an HME, remove it from the circuit. If using a heated humidifier, do not turn off or disconnect during the treatment.

JN:
Correctly assemble the nebulizer.
Fill the nebulizer with volume on drug label. You may increase volume to 4-6 mL to increase delivery.
Place the JN in the inspiratory line near the "Y" adapter or proximal to the ventilator.

VMN:
Correctly assemble the nebulizer.
Pour recommended drug volume into the nebulizer.
Place the VMN in the inspiratory line near the "Y" adapter.

pMDI:
Shake and prime the pMDI.
Warm the pMDI canister to hand or body temperature.
Place the pMDI spacer/adapter in the inspiratory line near the "Y" adapter.
Correctly assemble the pMDI canister with spacer/adapter.

Ensure that there is no leak in the circuit.
Position the patient in an upright position, if possible.

JN:
Connect the nebulizer to a power source.
Use gas source on the ventilator in order to synchronize the nebulization with inspiration, if appropriate.
Otherwise set gas flow on the JN at 6 to 8 l/min (or flow recommended on label).

VMN:
Connect the nebulizer to a power source.
Turn on the power

pMDI:
Coordinate actuations with beginning of inspiration.
Do not remove or shake the pMDI between actuations.
Wait 15 seconds between actuations

Observe aerosol cloud for adequate aerosol generation during treatment

At the completion of treatment, remove device from the ventilator circuit.

Reconnect the HME.
Return ventilator settings and alarms to previous values. Ensure there is no leak in the ventilator circuit.
Monitor vital signs, oxygen saturation and patient-ventilator synchronization.
Monitor for adverse response.
Assess outcome and document findings.

aerosol loss during the expiratory phase of the breathing cycle.[7] pMDIs, mesh and ultrasonic nebulizers that do not add gas flow to the ventilator circuit appear to be most efficient when placed in the inspiratory limb, 6 inches from the Y adaptor.[7] With the addition of continuous bias flow in the ventilator circuit, placement of aerosol generators near the ventilator may be more efficient.[8]

Optimum Technique with pMDIs: Priming and shaking the canister before treatment is important, especially prior to first use and when the canister has not been used for more than 24 hours. Otherwise, the drug in the pMDI formulation may separate from the propellants, which reduces aerosol delivery.[68] Also, synchronizing pMDI actuation with the beginning of inspiration is required for effective aerosol therapy during mechanical ventilation. Aerosol drug delivery to ventilator-dependent patients is maximized by synchronizing the actuation of pMDI with the beginning of inspiration.[69] When a spacer is used with a ventilator-dependent patient, it should be placed at approximately 15 cm from the ETT in order to achieve a significant bronchodilator response.[24,61]

Patient Monitoring: In order to eliminate the complications caused by aerosol treatment, some institutions require respiratory therapists to stay in the room when administering aerosol therapy through nebulizers. Although this increases respiratory therapist time spent with patients, such practice assures not only patient safety but also effective aerosol therapy for critically-ill patients.

Conclusion

In conclusion, there have been dramatic advances in aerosol drug delivery for ventilator-dependent patients over the years. However, aerosol therapy during mechanical ventilation is still complex because of challenges associated with the aerosol devices, inhaled medications, device selection and administration technique. Therefore, understanding aerosol delivery devices, potential problems and factors influencing drug delivery to mechanically-ventilated patients is crucial for the safety and effectiveness of aerosol therapy for patients in the ICU.

ventilators with built-in nebulizer function deliver reproducible and consistent doses to ventilator-dependent patients.[51,67]

When the jet nebulizer is placed closer to the ventilator and operated continuously under heated/humidified conditions, the aerosol tubing acts as a reservoir because continuous output of the jet nebulizer charges the inspiratory limb of the ventilator circuit between inspiration and minimizes

References

1. Ari A, Hess D, Myers TR, Rau JL. A Guide to Aerosol Delivery Devices for Respiratory Therapists. Dallas, Texas: American Association for Respiratory Care; 2009.

2. Dolovich MB, Dhand R. Aerosol drug delivery: developments in device design and clinical use. Lancet. 2010;377(9770):1032-1045.

3. Rau JL. Design principles of liquid nebulization devices currently in use. Respir Care. Nov 2002;47(11):1257-1275; discussion 1275-1258.

4. Dhand R, Mercier E. Effective inhaled drug administration to mechanically ventilated patients. Expert Opin Drug Deliv. Jan 2007;4(1):47-61.

5. Dhand R. Nebulizers that use a vibrating mesh or plate with multiple apertures to generate aerosol. Respir Care. Dec 2002;47(12):1406-1416; discussion 1416-1408.

6. Dhand R. Aerosol delivery during mechanical ventilation: from basic techniques to new devices. J Aerosol Med Pulm Drug Deliv. Mar 2008;21(1):45-60.

7. Ari A, Areabi H, Fink JB. Evaluation of position of aerosol device in two different ventilator circuits during mechanical ventilation. Respir Care. 2010;55(7):837-844.

8. Ari A, Atalay OT, Harwood R, Sheard MM, Aljamhan EA, Fink JB. Influence of nebulizer type, position, and bias flow on aerosol drug delivery in simulated pediatric and adult lung models during mechanical ventilation. Respir Care. Jul 2010;55(7):845-851.

9. Rubin B, Fink J. Optimizing aerosol delivery by pressurized metered-dose inhalers. Respir Care. 2005;50:1191.

10. Rubin BK. Air and soul: the science and application of aerosol therapy. Respir Care. Jul 2010;55(7):911-921.

11. Fink J. Metered-dose inhalers, dry powder inhalers and transitions. Respir Care. 2000;45:623-635.

12. Leach C, Davidson P, Boudreau R. Improved airway targeting with the CFC-free HFA-beclomethasone metered-dose inhaler compared with CFC-beclomethasone. Eur Respir J. 1998;12:1346.

13. Ross D, Gabrio B. Advances in metered dose inhaler technology with the development of a chlorofluorocarbon-free drug delivery system. J Aerosol Med. 1999;12:151.

14. Gross G, Thompson P, Chervisky P. Hydroflouoroalkane-134a beclomethasone dipropionate, 400 microg, is as effective as chlorofluorocarbon beclomethasone dipropionate, 800 microg, for the treatment of moderate asthma. Chest. 1999;115:343-351.

15. Bleecker ER, Tinkelman DG, Ramsdell J, et al. Proventil HFA provides bronchodilation comparable to ventolin over 12 weeks of regular use in asthmatics. Chest. Feb 1998;113(2):283-289.

16. Shapiro GS, Klinger NM, Ekholm BP, Colice GL. Comparable bronchodilation with hydrofluoroalkane-134a (HFA) albuterol and chlorofluorocarbons-11/12 (CFC) albuterol in children with asthma. J Asthma. Dec 2000;37(8):667-675.

17. Bronsky E, Ekholm BP, Klinger NM, Colice GL. Switching patients with asthma from chlorofluorocarbon (CFC) albuterol to hydrofluoroalkane-134a (HFA) albuterol. J Asthma. 1999;36(1):107-114.

18. Lumry W, Noveck R, Weinstein S, et al. Switching from Ventolin CFC to Ventolin HFA is well tolerated and effective in patients with asthma. Ann Allergy Asthma Immunol. Mar 2001;86(3):297-303.

19. Hendeles L, Colice GL, Meyer RJ. Withdrawal of albuterol inhalers containing chlorofluorocarbon propellants. N Engl J Med. Mar 29 2007;356(13):1344-1351.

20. Rau JL. Practical problems with aerosol therapy in COPD. Respir Care. Feb 2006;51(2):158-172.

21. Kenyon C, Thorsson L, Borgström L, Newman S. The effects of static charge in spacer devices on glucocorticosteroid aerosol disposition in asthmatic patients. Eur Respir J. 1998;11:606-610.

22. Dhand R, Tobin MJ. Inhaled bronchodilator therapy in mechanically ventilated patients. Am J Respir Crit Care Med. Jul 1997;156(1):3-10.

23. Dhand R. Inhalation therapy with metered-dose inhalers and dry powder inhalers in mechanically ventilated patients. Respir Care. Oct 2005;50(10):1331-1334; discussion 1344-1335.

24. Dhand R, Tobin MJ. Bronchodilator delivery with metered-dose inhalers in mechanically-ventilated patients. Eur Respir J. Mar 1996;9(3):585-595.

25. Rau J, Dunlevy C, Hill R. A comparison of inline MDI actuators for delivery of a beta agonist and a corticosteroid with a mechanically-ventilated lung model. Respir Care. 1998;43:705-712.

26. Rau J, Harwood R, Groff J. Evaluation of a reservoir device for metered-dose bronchodilator delivery to intubated adults: an in-vitro study. Chest. 1992;102(3):924-930.

27. Fuller HD, Dolovich MB, Turpie FH, Newhouse MT. Efficiency of bronchodilator aerosol delivery to the lungs from the metered dose inhaler in mechanically ventilated patients. A study comparing four different actuator devices. Chest. Jan 1994;105(1):214-218.

28. Dhand R, Dolovich M, Chipps B, Myers T, Restrepo R, Farrar J. The role of nebulized therapy in the management of COPD: evidence and recommendations. COPD. 2012;9(1):58-72.

29. Rau JL. The inhalation of drugs: advantages and problems. Respir Care. Mar 2005;50(3):367-382.

30. Thomas SH, O'Doherty MJ, Page CJ, Treacher DF, Nunan TO. Delivery of ultrasonic nebulized aerosols to a lung model during mechanical ventilation. Am Rev Resp Dis. 1993;148(4):872-877.

31. Dhand R, Sohal H. Pulmonary Drug Delivery System for inhalation therapy in mechanically ventilated patients. Expert Review of Medical Devices. 2008;5(1):9-20.

32. Nikander K, Turpeinen M, Wollmer P. The conventional ultrasonic nebulizer proved inefficient in nebulizing a suspension. J Aerosol Med. Summer 1999;12(2):47-53.

33. Rubin B. Pediatric aerosol therapy: new devices and new drugs. Respir Care. 2011;56(9):1411-1421.

34. Ari A, Fink J, Harwood R, Pilbeam S. Secondhand Aerosol Exposure during Mechanical Ventilation with and without Expiratory Filters: An In-Vitro Study. Respiratory Care. 2010;55(11):1566.

35. Guidance for Industry: Integration of Dose-Counting Mechanisms into MDI Drug Products. 2003; http://www.fda.gov/cder/guidance/5308fnl.htm#top.

36. Duarte A, Momi K, Bidani A. Bronchodilator therapy with metered dose inhaler and spacer versus nebulizer in mechanically ventilated patients: comparison of magnitude and duration of response. Respir Care. 2000;45(7):817-823.

37. Gay PC, Patel HG, Nelson SB, Gilles B, Hubmayr RD. Metered dose inhalers for bronchodilator delivery in intubated, mechanically ventilated patients. Chest. Jan 1991;99(1):66-71.

38. Guerin C, Chevre A, Dessirier P, et al. Inhaled fenoterol-ipratropium bromide in mechanically ventilated patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med. Apr 1999;159(4 Pt 1):1036-1042.

39. Laube BL, Janssens HM, de Jongh FH, et al. What the pulmonary specialist should know about the new inhalation therapies. Eur Respir J. Jun 2011;37(6):1308-1331.

40. Dhand R, Guntur VP. How best to deliver aerosol medications to mechanically ventilated patients. Clin Chest Med. Jun 2008;29(2):277-296, vi.

41. Ballard J, Lugo RA, Salyer JW. A survey of albuterol administration practices in intubated patients in the neonatal intensive care unit. Respir Care. Jan 2002;47(1):31-38.

42. Chang L, Honiden S, Haithcock J. Utilization of bronchodilators in ventilated patients without obstructive airways disease. Respir Care. 2007;52:154-158.

43. Hamill R, Houston E, Georghiou P. An outbreak of Burkholderia cepacia respiratory tract colonization and infection associated with nebulized albuterol therapy. Ann Intern Med. 1995;122:762.

44. Craven D, Lichtenberg D, Goularte T. Contaminated medication nebulizers in mechanical ventilator circuits. Source of bacterial aerosols. Am J Med. 1984;77:834-838.

45. Ari A, Fink JB. Factors affecting bronchodilator delivery in mechanically ventilated adults. Nurs Crit Care. Jul 2010;15(4):192-203.

46. Manthous C, Hall C, Schmidt G, Wood L. Metered-dose inhaler versus nebulized salbutamol in mechanically ventilated patients. Am Rev Resp Dis. 1993;148(6):1567-1570.

47. Manthous CA, Hall JB. Administration of therapeutic aerosols to mechanically ventilated patients. Chest. Aug 1994;106(2):560-571.

48. Hess DR, Dillman C, Kacmarek RM. In vitro evaluation of aerosol bronchodilator delivery during mechanical ventilation: pressure-control vs. volume control ventilation. Intensive Care Med. Jul 2003;29(7):1145-1150.

49. Fink J, Dhand R, Duarte A, Jenne J, Tobin M. Aerosol delivery from a metered-dose inhaler during mechanical ventilation. An in-vitro model. Am J Respir Crit Care Med. 1996;154(2):382-387.

50. Bowers W, Harwood R, Fink J, Sheard M, Zimmerman R, Ari A. Effects of heat and moisture exchangers designed to allow aerosol delivery on aerosol deposition in simulated mechanically ventilated adults. Respiratory Care. 2010;55(11):1576.

51. Miller DD, Amin MM, Palmer LB, Shah AR, Smaldone GC. Aerosol delivery and modern mechanical ventilation: in vitro/in vivo evaluation. Am J Respir Crit Care Med. Nov 15 2003;168(10):1205-1209.

52. O'Riordan TG, Greco MJ, Perry RJ, Smaldone GC. Nebulizer function during mechanical ventilation. Am Rev Respir Dis. May 1992;145(5):1117-1122.

53. Fuller H, Dolovich M, Chambers C, Newhouse M. Aerosol delivery during mechanical ventilation: a predictive in-vitro lung model. J Aerosol Med. 1992;5:251-259

54. Garner SS, Wiest DB, Bradley JW. Albuterol delivery by metered-dose inhaler with a pediatric mechanical ventilatory circuit model. Pharmacotherapy. Mar-Apr 1994;14(2):210-214.

55. Goode ML, Fink JB, Dhand R, Tobin MJ. Improvement in aerosol delivery with helium-oxygen mixtures during mechanical ventilation. Am J Respir Crit Care Med. Jan 2001;163(1):109-114.

56. Ahrens RC, Ries RA, Popendorf W, Wiese JA. The delivery of therapeutic aerosols through endotracheal tubes. Pediatr Pulmonol. Jan-Feb 1986;2(1):19-26.

57. Wright P, Marini J, Bernard G. In vitro versus in-vivo comparisons of endotracheal tube airflow resistance. Am Rev Respir Dis 1989;140(1):10-16.

58. Alvine GF, Rodgers P, Fitzsimmons KM, Ahrens RC. Disposable jet nebulizers. How reliable are they? Chest. Feb 1992;101(2):316-319.

59. Berg E, Picard R. In-vitro delivery of budesonide from 30 jet nebulizer/compressor combinations using infant and child breathing patterns Respir Care 2009;54(12):1671-1678.

60. Hess D, Fisher D, Williams P, Pooler S, Kacmarek RM. Medication nebulizer performance. Effects of diluent volume, nebulizer flow, and nebulizer brand. Chest. Aug 1996;110(2):498-505.

61. Dhand R, Jubran A, Tobin MJ. Bronchodilator delivery by metered-dose inhaler in ventilator-supported patients. Am J Respir Crit Care Med. Jun 1995;151(6):1827-1833.

62. Dhand R, Duarte A, Jubran A, et al. Dose response to bronchodilator delivered by metered-dose inhaler in ventilator supported patients. Am J Respir Crit Care Med. 1996;154(2):388-393.

63. Mouloudi E, Prinianakis G, Kondili E, Georgopoulos D. Bronchodilator delivery by metered-dose inhaler in mechanically ventilated COPD patients: influence of flow pattern. Eur Respir J. Aug 2000;16(2):263-268.

64. Tzoufi M, Mentzelopoulos SD, Roussos C, Armaganidis A. The effects of nebulized salbutamol, external positive end-expiratory pressure, and their combination on respiratory mechanics, hemodynamics, and gas exchange in mechanically ventilated chronic obstructive pulmonary disease patients. Anesth Analg. Sep 2005;101(3):843-850, table of contents.

65. Mouloudi E, Katsanoulas K, Anastasaki M, Askitopoulou E, Georgopoulos D. Bronchodilator delivery by metered-dose inhaler in mechanically ventilated COPD patients: influence of end-inspiratory pause. Eur Respir J. Jul 1998;12(1):165-169.

66. Hughes J, Saez J. Effects of nebulizer mode and position in a mechanical ventilator circuit on dose efficiency. . Respir Care. 1987;32(12):1131-1135.

67. Dhand R. Aerosol therapy during mechanical ventilation: getting ready for prime time. Am J Respir Crit Care Med. Nov 15 2003;168(10):1148-1149.

68. Fink J, Dhand R. Bronchodilator resuscitation in the emergency department, part 2: dosing. Respir Care. 2000;45(5):497.

69. Diot P, Morra L, Smaldone GC. Albuterol delivery in a model of mechanical ventilation. Comparison of metered-dose inhaler and nebulizer efficiency. Am J Respir Crit Care Med. Oct 1995;152(4 Pt 1):1391-1394.

70. Bowers W. Effects of heat and moisture exchangers designed to allow aerosol delivery on airway resistance and aerosol deposition. Atlanta, GA: Georgia State University, 2010.

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