Humidification, Airway Secretion Management, and Aerosol Therapy

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Abbreviations

NIV/NIMV	Noninvasive mechanical ventilation
VT	Tidal volume
HME	Heat and moisture exchangers
HH	Active humidifiers
pMDI	Pressurized metered dose inhalers
VHC	Valved holding chambers
VMN	Vibrating network nebulizer
ICU	intensive care unit

28.1 Introduction

28.1.1 Concept Humidity and Physiology and Role of the Upper Airway

Humidity is the amount of water vapor contained in the gas and is usually defined as absolute or relative humidity. The gas temperature is critical because its water vapor content depends on the gas temperature. The corresponding humidity is the percentage (%) of water vapor in the gas near its maximum carrying capacity. Absolute humidity is the total amount of water vapor in the gas, expressed in milligrams of suspended water in liters of gas (mg/L). Absolute humidity is directly related to the gas temperature. It is necessary in terms of humidification as, at low temperatures, the relative humidity can be 100%, while the total humidity can be

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far below the recommended value [1]. Inspired air conditioning occurs when a gas is heated and hydrated as it passes through the airways to reach the alveolar level in optimal conditions. Although the gas acquires temperature and humidity during its path inside of the airways, the main area in which takes place the heating of the air breathed in is the nose. The temperature of the nasal mucosa is relatively 32 °C, and although the contact time between inspired air and nasal mucosa is short, this time it is sufficient to give heat. In extension, the nose has a high potential to control blood perfusion and thus balance the loss of heat during inspiration. The respiratory mucosa is lined by ciliated columnar epithelium and pseudostratified numerous goblet cells. These cells and submucosal glands support the mucosal layer that serves as a trap for the pathogens and as an interface for moisture exchange. At the level of the concluding bronchioles, the epithelium becomes a simple cubic type with minimum few goblet cells and submucosal glands. Therefore, the capacity of these pathways to perform the same level of humidification as the upper airway is limited. In addition, the air circulates through a narrow conduit by generating a turbulent flow that optimizes the heating, humidifying, and filtering. The exhaled air humidity is partially preserved by condensation on the mucosa during exhalation due to temperature differences approximately 25% of the heat, and humidity increases during exhalation [2]. The eyelash movement is called metachronal ciliary; the pulse frequency is directly proportional to the temperature (t °). It is expected that at 37°C the ciliary beat is 750 b/min and at 40°C it rises to 1100 b/min. Excessive moisture affects the ciliary function since it increases the volume of secretions due to its low viscosity and the risk of atelectasis obstructing the airway. This explains the motivation of gas condensation at a temperature higher than 37 °C and 100% of the gas saturation, thus causing a reduction in mucus viscosity and an increase in the pericellular liquid thickness, which may be too liquid to be adequately coupled to the tips of the eyelashes, thereby influencing the mucociliary transport. Considering the temperature of the inspired air rises throughout its passage through the airway, at the level of the alveolar-capillary interface, it is at body temperature (37 °C), with 100% relative humidity and 44 mg/L absolute humidity. The feature where the gas acquires these conditions is the isothermal saturation limit; this limit is ordinarily close to the fourth or fifth bronchial generation. It is crucial to reaching the isothermal saturation limit to bypass injury to the mucosa and the ciliary epithelium. An artificial airway prevents inspired air from contacting the mucosa of the upper airway affecting conditioning gas. The normal physiology of conditioning gas is altered when the patient requires an artificial airway; intubation eliminates the natural filtration mechanisms, humidification, and warming of inspired air. The humidification of inspired gas is necessary for all mechanically ventilated patients; however, the discussion about the fitting humidification continues today [3].

NIMV provides dry and cold gas through the upper airway, causing dryness of the mucosa and respiratory dysfunction. Leakage compensation used by NIMV creates high flow during the respiratory cycle, which leads to the lack of heat and humidity [4]. Although in NIMV the upper airway is saved, humidification during NIMV might not be optimal due to the higher flow delivered, thus producing

increased mucous viscosity and secretion recognition. These conditions improve the danger of obstruction of the upper airways.

28.2 Humidification Devices

Two prototypes of devices for conditioning inspired gases in the presence or inadequacy of an artificial airway are possible: heat and moisture exchangers (HME) and active humidifiers (HH) [5].

Despite of which device is chosen, it should infallibly coincide the minimum conditions to reinstate the role of the upper airway, which, according to the American Association for Respiratory Care, are [1]:

- 30 mg/L absolute humidity, 34 °C, and 100% related humidity for HME
- Within 33 and 44 mg/L absolute humidity, between 34 °C and 41 °C, 100% relative humidity for HH

28.3 Active Humidifiers

The active humidifiers are devices formed of an electric heater placed a plastic casing with a metal base in which is stored sterile water. When the base is heated, the water temperature rises by convection. Some active humidifiers are self-regulated by a mechanism consisting of a heating wire (a wire-heated breathing circuit) that keeps constant the temperature of the gas during its passage in the circuit and a wire with two temperature sensors connected to the output of the heater (distal) and to a part of the circuit (near the patient) to control the system temperature.

28.3.1 Assembly

Active humidifiers are positioned in line in the inspiratory leg of the respirator. The circuit leaving the inhalation valve is connected to the inlet hole of the plastic casing, which must always be filled to the level indicated by the manufacturer. Subsequently, a second section of the circuit (of standard length) is connected to the outlet hole of the casing and to the "Y" of the circuit responsible for supplying gas to the patient. With this type of humidification device, it is necessary to use siphons, tanks with unidirectional circulation systems that allow the excess condensate to be deposited without air leaks. Among other problems, excessive accumulation of water in the circuit can lead to self-activation, misreading of the ventilator monitor, or even the drainage of contaminated material into the patient's airways. The output circuit from the inhalation valve is connected to the casing inlet hole in plastic, which must always be filled to the level indicated by the manufacturer. Subsequently, a second section of the (standard length circuit) is connected to the casing output hole and the "Y" of the charge circuit to provide

gas to the patient. With this type of humidification device, it is required to use siphons, tanks with unidirectional circulation systems that deposit the excess condensate without air leakage. Among other problems, the excessive accumulation of water in the circuit can lead to autotrigger, the misreading of the fan, or even to monitor drainage of contaminated material in the patient's airway. These humidifier varieties are separated into several categories: bubble humidifiers, waterfall humidifiers, bypass humidifiers, and shirt humidifiers [6]. Of the active humidification systems, the bypass is the most generally used now in the ICU, and they are utilized in mechanical ventilation and noninvasive ventilation. The gas that goes to the patient moves across the heated water surface, which creates the humidification to come close to 100% RH and can deliver up to 44 mg/L of AH [7]. The water is heated via heating base, which transfers heat by convection from the metal of the bases. It is self-regulating by a servomechanism and consists of a heating cable (which controls the temperature of the gas in the circuit, thus limiting condensation in the piping and the possibility of bacterial colonization), a cable with two temperature sensors, which are secured at the output of the humidifier, and a Y-piece (near the patient) to servo-control the temperature of the system. In most current devices, the temperature is preset at 37 °C. This system manages control of the gas temperature to the patient, despite of differences in the gas flow or water level in the reservoir, notwithstanding having an average time of reaction. The water that condenses the pipes is supposed to be contaminated and should not be returned to the humidifier. The main obstacle with this device is that it does not filter particles [8].

28.3.2 Precautions and Monitoring for Active Humidifiers

- Recognize that the tubing drains the water downward and not near the artificial airway or the ventilator.
- Place the water traps accurately to receive drained water.
- Regularly monitor the active humidifier device (water level and temperature level indicate the presence of condensation).
- Never fill above the suggested level.
- Comply with the manufacturer's terms.
- Do not remove the condensation toward the humidifier chamber.

28.4 Passive Humidifiers

They are economical and simple to use with conventional connectors for IMV. They include a high communication surface of paper, with compressed metallic parts which attract particles of expired water vapor and heat, pressing and releasing it in the next inspiration. The dispositive without a particle filter is used only for disposable heat and moisture exchangers (HME). To fulfill this purpose, the HME can be

hydrophobic (HMEF, heat and moisture exchanger filter), hygroscopic (HHME, hygroscopy heat and moisture exchanger), or both with filter (HHMEF, hygroscopy heat and moisture exchanger and filter). Hygroscopic is an attribute of a compound chemical material, which absorbs condensation from the air. The aluminum element of this device immediately exchanges temperatures during expiration condensation created between the layers of this material. The preserved heat and moisture are replaced during inspiration. Adding a fibrous component helps retain moisture and decreases the accumulation of condensation in the secondary position of the device. Hydrophobic is an adjunct for those substances or elements that resist water and cannot combine or absorb. They utilize a paper or polypropylene treated with calcium or lithium chloride, to improve moisture maintenance and repel water that is not absorbed. It is essential to consider that these devices additionally perform as a bacterial filter. The HME are situated between the Y-piece of the patient, which can increase the resistance to airflow, not only during inspiration but also when expiration. The minimum resistance to the flow is 0.5–3.6 $cmH_2O/L/s$. It is essential to record the dead space produced by these devices, which can be mutable. Among separate devices, according to some measurements, it can reach 95 mL. Passive humidifiers should never be used in conjunction with active humidifiers [9].

28.4.1 Dead Space

The working system of passive humidifiers means that a higher volume of condenser material will produce better device performance. For this reason, the "ideal" dead space for a humidifier is approximately 50 mL. This dead space does not describe a problem for patients with invasive mechanical ventilation (iMV) because the dead space can be counterbalanced for the ventilator's programming. However, in patients with artificial airways, without the necessity of iMV, the increase in the ventilatory minute volume as a compensatory mechanism for the dead space could generate a hard-to-tolerate load in patients with low ventilatory reserve. Consequently, passive humidifiers with a "small volume" were produced. Although they can be more "tolerable," they produce a low humidification capacity that worsens when the tidal volume (VT) increases and supplementary O_2 [10]. The necessary dead space added by the passive humidifiers during iMV becomes essential when the pathology requires strategies for lung protection (low VT). Studies conducted by Prat [11] and Hinkson [12] account for this, showing significant changes in arterial carbon dioxide partial pressure ($PaCO_2$) (and in pH) under these circumstances.

28.4.2 Resistance

Although the resistance of an additional device could be judged negligible (5 $cmH_2O/L/s$ assessed as "dry"), resistance can vary under differences in the

conditions (presence of condensation, impaction due to secretions, changes in ventilatory parameters, increases in the VT, and the flow). Although some studies [13] have registered that the presence of "humidity" in a device does not lead to essential changes in resistance, redundant condensation or impaction (due to secretions or blood) can alter it.

28.4.3 Active or Passive Humidification?

In utilizing NIMV, the type of ventilators assumes a vital role in the decision of the humidifier to be used. For a single-branch turbine ventilator and with leakage compensation, the use of HH in patients undergoing times more significant than 24 h of NIMV to enhance the feeling of oral dehydration and tolerance as recommended by Oto in 2014 would be recognized [4]. It is also essential to examine the testimonials of Esquinas et al. [14] in terms of the factors involved in choosing the type of humidification to use, such as air leakage, interface type, type of ventilator, ambient temperature, and inhaled gas temperature, among others. Considering when using HME in single-branch NIMV, there must be a description of where the exhalatory port is in the system. Current recommendations favor the use of heated humidifiers (HH) during NIMV [15], decreasing nasal resistance, helping expectoration, and increasing adhesion and comfort, especially in patients with bronchial secretions [15]. HME is not supported in NIMV because the dead space of the device harms CO_2 removal and minute ventilation in patients managed with NIMV in ICU; this is more evident in hypercapnic patients [15]. *Also*, it has been seen that it increases work in breathing. In Table 28.1 the main advantages and disadvantages on the use of HME and HH are reported.

Table 28.1 Advantages and disadvantages of HH and HME

Devices	Advantages	Disadvantages
Active	Universal application	Cost
	Reliability	Using water
	Alarms	Condensation
	Wide ranges of temperature and humidity	Risk of contamination
	Temperature monitoring	Low possibility of electrical shock and burns
	Reaches the maximum absolute humidity	No filter
Passive	Cost	Does not apply all patients
	Passive operation	Increase dead space
	User-friendly	Increase resistance
	Removal of condensation	Potential occlusion
	Portable	Misting problems

28.4.4 Background of Aerosol Therapy

The drug concentrations in lung tissue are affected by the aerosol dose administered, patient factors, device factors, and drug formulation. The productiveness of the aerosolized drug depends on the dose accumulated at the target site of action and its distribution in the lungs.

The overall efficiency of the aerosol system is a compound of the emitted dose (ED), the dose delivered to the lung (PSF as a surrogate marker), and lung bioavailability. The ED and the PSF are generally determined in vitro and are regulated by the characteristics of the particles and the composition of the device. The bioavailability of the drug is influenced by patient factors, such as the anatomy of the airways and lungs, the permeability of the drug through the membranes, the drug metabolism, and the clearance of phagocytes in the lung [16]. We know that the airflow is not homogeneous in all lungs, even in health. The apical portions of the lungs receive a lung deposition of the order of a 2:1 ratio higher than the basal regions. This difference is significantly decreased in the supine position. Among the factors that affect the administration of aerosolized drugs in critically ill patients include the position of the patient, the formulation, the temperature, the size of the endotracheal tube, the obstruction of the airways or the ventilatory asynchrony, the flow pattern, the respiratory rate, the dose, and the applied frequency or the nebulizer position in the circuit.

28.4.5 Fundamentals of Aerosol Therapy

The size of the drug particles (measured in microns) used in an aerosol for respiratory diseases determines in which the airways will be deposited. The ideal size of the particles for respiratory drugs is from 1 to 8 microns. At these dimensions, the particles can reach the walls of the distal airways via sedimentation and diffusion. In contrast, the microscopic particles of the drug (<1 micron) have a poor transportability and high probability of being exhale. In contrast, very large particles (> 8 microns) tend to agglomerate and settle rapidly in the upper airways (oropharynx and language), from where they can be swallowed and absorbed, finally causing systemic side effects. It should be noted that the nebulizers, devices that generate aerosols of drugs, do not allow a uniform particle size; instead, they produce a wide range of particle sizes.

The pressurized metered dose inhalers (pMDIs) with valved holding chambers (VHC) have demonstrated efficacy superior deposition compared to nebulizers in various studies. However, VHC cannot be used for mechanical ventilators due to the inability to synchronize with the inspiratory delivery. The DPI (Dry-Powder Inhalers) have no fuel; they are inherently synchronized/activated with the breath and produce small variations in particle size. The deposition in the airways may occur by inertial impaction, gravitational settling, or diffusion (Brownian motion). Due to the

turbulence and high air velocities associated with aerosol, the inertial impact method is predominant in the first ten ramifications of the airways. However, in five to six generations, distal airway predominates sedimentation due to the lower air velocity [16]. At the alveolar level, a minimum air velocity means that there will be no effect of impact. A combination of sedimentation and diffusion will affect the deposition of the drug. The inspiratory flow of the patient influences the amount and type of deposited particles and the deposition mechanism. The scope of preferred aerosol is from 30 to 60 L/min. Elevated inspiratory flow (>100 L/min) favors the deposition to provide high impact and penetration speed. On the contrary, low inspiratory flow (<30 L/min) favored the sedimentation but involved the risk that the patient inhales only a tiny amount of the drug. The deposition of particles in the lower airways of children is hampered by the combination of high flow rates and decreasing diameter (from top to bottom) of the airways. The affinity of the particles for the water determines the extent to which they can change the size. For the aerosol successfully you must consider the aerosol system. The aerosol system includes the drug, the aerosol device, the disease (which is the target site), and the patient's respiratory system. The ventilator is an additional factor in mechanically ventilated patients.

28.4.6 Device Effects

Nebulizers are several devices that are used to transform liquid formulations and suspensions in the form of aerosols. These devices can be used to produce larger volumes of a drug in aerosol form, intermittently or continuously, to the purpose of prevention or treatment. Depending on their development mechanism, there are three types of nebulizers: jet, ultrasonic, and SMN. The subsequent development of "new-generation" devices such as the ultrasonic nebulizer and vibrating network nebulizer (VMN) has encouraged further studies and applications of aerosol therapy in the ICU because of the ability of these devices to constantly generate the particle size of aerosol desired, which considered to be optimal for deep lung penetration. The jet nebulizers are the cheapest and simple, although they are inefficient in administering drugs. Their disadvantages are the noise, the lack of control of the dosage, and the need to modify the ventilator settings such as the airflow and the tidal volume. The ultrasonic nebulizers are rarely used and also have limitations. They are expensive and large in size, increase the concentration of the drug during nebulization, and can cause thermal inactivation of the nebulized drug. A significant fraction of the aerosolized drug is trapped in the mucous membranes of the conducting airways. Conditions such as pneumonia and other inflammatory lung diseases cause lung surfactant deficiencies in both content and effect. Drugs with high solubility are likely to have a uniform dispersion than insoluble drugs. Inferential, soluble drugs are likely to have longer and more effective lung residence times, thereby improving drug potency. Surfactant deficiency is associated with atelectasis, which in turn reduces drug deposition [17]. Where possible, pMDI with spacers should be used. The use of PPE is likely to be limited in the ICU. The device should be selected for nebulizers based on the formulation used and the desired deposition site and

effect. The rate and extent of absorption of aerosolized substances depend on molecular weight, pH, electric charge, solubility, and stability.

28.4.7 The Heliox Effect

A mixture of helium and oxygen (heliox) reduces the density of the gas and increases the deposition of aerosols, in particular in the peripheral lung. With pMDI, it was reported that heliox administration of aerosolized medications during mechanical ventilation increases [18]. However, with the jet nebulizers, heliox also increases the nebulization time, requiring higher gas flows to compensate for the low-density gas.

28.4.8 Type of Aerosol Generator in the Circuit

Currently, nebulizers and pMDIs, with and without spacers, are two types of devices prepared for use in mechanically ventilated patients. Depending on the site of action, they should be used in devices that produce one of the appropriate particle sizes. Nebulizers take much longer to deliver a standard dose compared to other devices. There is also a variation of efficiency between the nebulizer types and between different batches in nebulizers. This effect is accentuated if associated with the impact of different modes of ventilation and pulmonary mechanics. Thorough cleaning and disinfection of the nebulizer inadequately increase the risk of nosocomial pneumonia. The pMDIs are easy to administer, require less time for staff, provide a reliable dosage, and have a minimum of bacterial contamination risk than nebulizers. When used with a collapsible spacer into the circuit, it is not necessary to disconnect the circuit. The pMDIs are also cheaper nebulizers. Furthermore, the optimal location for the aerosol source connection l is approximately 15 cm from the wye in the inspiratory line, although there are no in vivo studies to draw definitive conclusions [19].

Humidification is believed to have a significant effect on aerosol drug delivery. Due to the hygroscopic effects of humidification, there may be a two to three times growth in particle size as they pass through the airways. This increase in size can reduce drug deposition in the peripheral lungs and hence pharmacological efficacy. The particulate air filter in the expiratory tract protects the ventilator, and the flowmeter may become saturated, causing the airflow to be blocked. It is supported to replace the filter after each nebulization treatment.

28.4.9 Features of Breath

The aspects of the ventilator breath have an influential effect on the efficacy of the administration of aerosol. Slower inspiratory flows, inspiratory time consumption, and tidal volumes >500 ml (using a pMDI) correlate well with improved aerosol

dispensing. The common effective mixture of tidal volume, flow, and other parameters of the fan for the aerosol dispensing can be calibrated on the drug and on the dispensing device using in vitro models [20].

The positive end-expiratory pressure (PEEP) is a setting of usually used ventilation as part of the lung protective ventilation strategy in severe lung disease. PEEP has significant effects on regional ventilation and perfusion and may affect the pharmacokinetics of aerosolized medication. In an animal model that used radiotracers, it was discovered that the PEEP improves the aerosol removal [20]. This could be due to the alveolar epithelium stretching and improving the aerosol distribution in the bloodstream. Meaning: PEEP is potentially advantageous, although further data to quantify the effect on the administration of aerosolized medications are necessary.

Optimization of ventilator parameters required for antibiotic aerosol modified by Lu et al. [21] as as follows:

- Positioning of the nebulizer: in the inspiratory limb 10 cm proximal to the Y fitting.
- Diluted in 10 ml of physiological solution.
- Remove the HME filter.
- Ventilation mode—volume control.
- Airflow pattern: constant inspiratory flow.
- Ventilator settings: RR 12/minute, 50% I:E ratio, VT 8 ml/kg.
- End of inspiration pause, 20% duty cycle.
- Expired aerosol particles collected in a filter.

28.4.10 Dose Effect and the Time

Despite the administration of inhaled medicines, significant extrapulmonary drug losses can mean that the actual amount of drug delivered may be less than the set. The doses should be different in patients with colonization, tracheobronchitis, or pneumonia. Increasing doses require longer nebulization times that are not well tolerated by patients with ARDS or other serious lung diseases. Most of the loss of drug occurs in the expiratory phase of ventilation. To minimize this loss, the activation of the inhaler or nebulizer may be coupled to inhalation.

28.5 High-Flow Nasal Cannula Effect

High-flow nasal oxygen therapy is growing in use in various care settings including in intensive care units (ICU). A number of factors influence nebulization therapy in patients using high flow, which has recently been studied in an in vitro model [22].

1. Nebulizer location: A location away from the humidifier (closer to the patient) improves drug delivery upstream.

2. Nebulizer type: VMNs have demonstrated better delivery than jet nebulizers, although the choice of nebulizer depends on the formulation and desired site of action.
3. Airflow: Breathing mass delivery is lower with higher airflow and improves with lower airflow.
4. Patient efforts: Talking about the effect of airflow with a high-flow oxygen system, in situations mimicking respiratory distress (i.e., an increase in the patient's inspiratory airflow), delivery was indeed best. An open mouth, in contrast, had no significant differences from a closed mouth with respect to drug administration.

28.5.1 Contemporary Applications of Aerosol Therapy in Critical Care: Focus on Antibiotics

Despite these developments, the best evidence for the administration is not enforced, particularly for aerosolized antibiotics. Data from clinical and experimental studies to aminoglycosides and colistin are perhaps the most numerous to antibiotics in intensive care. The aminoglycosides are concentration-dependent antibiotics for which the Cmax/MIC ratio describes the most of the bactericidal effect. Studies have shown that aminoglycosides intravenously penetrate evil in the epithelial lining fluid [23].

In a model of pneumonia inoculation of *Escherichia coli*, it was observed that the aerosolized amikacin lung reaches significant concentrations.

On the other hand, there was no accumulation effect with repeated administration and therefore no toxicity problem with the aerosolized amikacin. In experimental studies, serum concentrations of amikacin were higher when the aerosolized amikacin was used in a pneumonia model compared to healthy lungs. In addition, a combination of intravenous aminoglycosides and aerosols has not been shown to increase cure rates compared to only aerosol antibiotics [24]. Therefore, for the treatment of ventilator-associated pneumonia, aerosol therapy alone may be adequate without the need for an intravenous therapy, decreasing the risk of systemic toxicity.

28.5.2 Limits of Aerosol Therapy in Intensive Care

In fact, there is a possibility of causing systemic toxicity (e.g., aminoglycoside nephrotoxicity) or local toxicity in the form of irritation of the airways, cough, and often bronchospasm, worsening hypoxemia (and secondary arrhythmias) and lung lesions during the use of aerosol therapy [25]. There have been reports of the fan malfunctions and obstruction of expiratory filters, contraindicated for the use of drugs with lipid components or sugar lactose in the formulation (such as zanamivir or formulations of lipid-based amphotericin). You need close monitoring of the potential increase in airway pressure and oxygen saturation to anticipate serious adverse events. Tolerance aerosol is different when medications are nebulized for

various periods of time. This may limit the use of the aerosol in patients with ARDS or severe hypoxemia, such as severe pneumonia (in contrast with the ventilator-associated tracheobronchitis), which often have poor tolerance [26]. The environmental contamination caused by aerosols of drugs in an open-loop system represents a small but significant risk to healthcare workers. The use of expiratory filters with valves in the aerosol dispensing devices could minimize this problem. This exposure to the occupational hazard should be evaluated, and interventions should be implemented to mitigate the risks. When using aerosolized antibiotics, it is recommended to change the filter after each therapy.

28.6 Conclusion

During the use of NIMV, inadequate air humidification is related to structural and functional impairment of the nasal mucosa. It suggests the use of active humidification (evidence 2B), while it is not recommended to use passive humidification (evidence 2C). However, recent publications using ICU ventilators disagree with these recommendations. We believe that to choose the type of humidifier for use during NIMV, there are certain aspects that must be taken into consideration as the fan type, the type of interface, and losses, among others, which could favor the use of HH compared to HME to improve tolerance and patient comfort. Aerosol drug delivery in NIV is affected by several factors, including the type of ventilator, mode of ventilation, circuit conditions, type of interface, type of aerosol generator, breathing parameters, drug-related factors, and patient-related factors. Aerosol drug delivery during NIV has gained popularity over the years. Due to many factors that impact drug delivery to patients receiving NIV, aerosol therapy in this patient population can be extremely complex. However, if clinicians know what to use, how to use it, and why, aerosol therapy can be feasible and effective during NIV.

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