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Use of aerosol therapy in patients undergoing mechanical ventilation in the ICU

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Abstract

Aerosol therapy is a form of medication administration that favors a quick and easy absorption of them in the respiratory tract; thus favoring great advantages in improving the health status of patients who are undergoing mechanical ventilation in the ICU. The most commonly used medications are bronchodilators, beta-agonists and anticholinergics. The use of this therapy should be used more frequently in these patients, but factors specific to the individual and the medication should be considered for its application; its use in patients with COVID-19 should also be considered.

Keywords: Aerosol therapy; Mechanical ventilation; COVID-19; Bronchodilators

1. Introduction

Aerosol therapy is a method of treatment that enables the delivery of medications in aerosolized form via inhalation using a nebulizer [1]. This approach allows for higher concentrations of the administered drug to reach the bronchial tree while minimizing systemic side effects [1]. Several factors influence its effectiveness, including particle size, the patient's age, inhalation pattern, and the underlying condition of the lungs [1,2].

Nebulizers generate aerosol particles approximately 15 µm in size, which can serve as carriers for bacteria and viruses [1]. During nebulization, the production of large volumes of respiratory aerosols can increase the risk of infection transmission via droplets and aerosolized nuclei, especially as these particles may travel further than usual [1,2].

When nebulized medication is required in patients under invasive mechanical ventilation, the use of vibrating mesh nebulizers is recommended. This type of device allows drug delivery within the closed ventilator circuit, avoiding circuit disconnection and thereby reducing contamination risk [1,2].

This study is based on a literature review focused on the application of aerosol therapy in mechanically ventilated patients [1].

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2. Results

An aerosol refers to the suspension of liquid or solid particles within a gas medium [3]. Aerosol or inhalation therapy involves delivering medications in aerosol form to patients for therapeutic purposes [3]. Specifically, it refers to administering drugs through the endotracheal route using aerosolized formulations [3], a practice commonly employed in intensive care units for mechanically ventilated patients [3].

This method enhances drug deposition in the lower respiratory tract, allowing for local action and subsequent absorption by the body [3]. However, effective delivery to the targeted area within the airways (VA) depends largely on the technique used [3,4]. As such, several variables must be considered when selecting the most suitable device, including the patient's age, clinical condition, ventilatory mode, and available resources [3,4].

Aerosol therapy is widely used in ICUs due to its clear advantages over other administration routes [5]. It allows for a faster therapeutic onset compared to oral or intravenous delivery [5], and reduces the risk of systemic side effects often associated with anti-inflammatory agents or antibiotics [5]. Additionally, the required aerosol doses are generally lower than those needed for systemic administration [5].

This therapy enables direct drug delivery to the lungs, offering faster effects and improved safety profiles relative to systemic treatments [5]. Among its most frequent applications is the use of bronchodilators, which help to enhance airway patency and improve the patient's respiratory status [5].

Aerosol therapy lies at the intersection of ease of administration and complexity in preparation. For a visual reference of its positioning within therapeutic modalities, see Figure 1 [6].

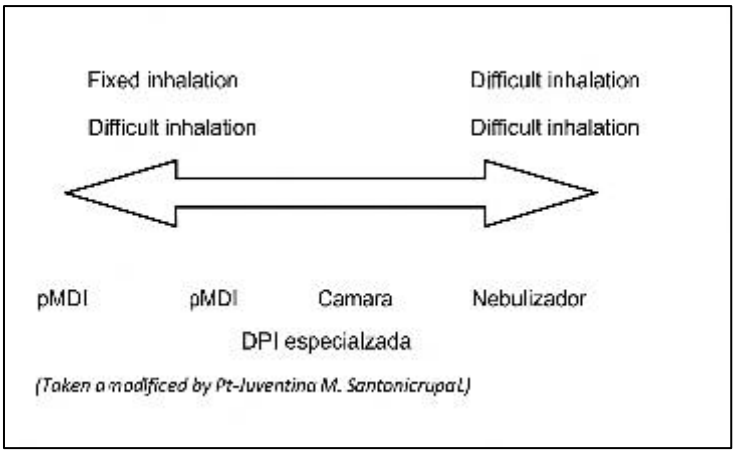

Figure 1 Graphic scale that places each device according to the ease of preparation and use. Taken and modified from Newman SP. Taken from: Cuneo B, Lopez-pineda A, Soler-catalu JJ. Open Respiratory Archives. 2019; 1(2):7–

A large proportion of patients in intensive care units (ICUs) rely on mechanical ventilation, which introduces multiple variables that can affect the effectiveness of aerosol drug delivery. These include the type and position of the aerosol generator within the ventilatory circuit, ventilator settings, the presence of humidification, synchronization with inspiratory flow, and sites of potential deposition within the system [6,7]. Significant research efforts have been dedicated to understanding and controlling these factors to enhance pulmonary drug deposition and minimize loss due to accumulation in ventilator components or artificial airways [6,7].

The complexity of delivering aerosols in ventilator-dependent patients stems from the interaction of several technical and physiological parameters that influence the amount of medication reaching the lungs [6,7]. Technological advancements such as vibrating mesh nebulizers and pressurized metered-dose inhalers (pMDIs) using hydrofluoroalkane (HFA) propellants have improved the reliability of aerosol therapy in this context [6,7]. However, the successful use of pMDIs in mechanically ventilated patients requires the integration of specialized adaptors that can function within closed-circuit systems, ranging from basic single-port connectors to more advanced spacer chambers [6,7].

Several critical aspects determine the efficiency of pMDI-based aerosol delivery in mechanically ventilated patients [6,7], including:

- **Synchronization with Inspiration:** The timing of pMDI actuation relative to the inspiratory phase significantly impacts the dose delivered to the lungs.
- **Shaking and Priming:** Manufacturers universally recommend that pMDIs be shaken and primed with several puffs into the air before first use and after long intervals of inactivity.
- **Actuator Types:** A variety of commercially available actuators, differing in shape and dimensions, may influence aerosol deposition outcomes.
- **Placement in the Circuit:** Positioning the spacer chamber within the inspiratory limb of the ventilator circuit has been shown to enhance lung delivery and clinical effectiveness.
- **Humidity and Temperature:** Studies using mechanical models have shown that aerosol delivery is reduced by up to 40% in circuits with active humidification compared to dry circuits.
- **Flow and Gas Density:** High inspiratory flows can lead to turbulent airflow within narrow artificial airways, increasing the likelihood of aerosol impaction before reaching the target site.

When appropriately used, pMDIs provide a safe and effective route for delivering inhaled medications to intubated patients. If the prescribed drug is available in this formulation and produces the desired clinical effects at standard doses, pMDIs are a practical and advantageous option [6,7]. To ensure optimal therapeutic outcomes, meticulous attention must be given to timing, actuator choice, and device positioning within the ventilator circuit [6,7].

2.1 Commonly Administered Medications in Aerosol Therapy

Bronchodilators remain the cornerstone of aerosol therapy, primarily due to their ability to relax smooth muscle and improve airway patency [8]. Among the most frequently used agents in this category are salbutamol, albuterol, ipratropium, and combination formulations such as albuterol/ipratropium or long-acting beta-agonists paired with corticosteroids, like salmeterol/fluticasone [8]. A key advantage of aerosolized bronchodilators lies in their rapid onset of action and lower incidence of systemic side effects, given that therapeutic doses are effective even in small quantities directly at the airway surface [8].

Inhaled corticosteroids, including dexamethasone and fluticasone, are often employed to mitigate airway inflammation [8]. These are typically indicated in chronic inflammatory airway conditions. In addition to steroids, certain anti-inflammatories and antimicrobial agents have also been adapted for aerosol delivery, helping manage infection and inflammation more locally [8].

Antibiotics such as amikacin, gentamicin, vancomycin, fosfomycin, and colistin can be administered via inhalation, particularly in critically ill patients or those with difficult-to-treat pulmonary infections [8]. A detailed list of medications commonly used during mechanical ventilation is summarized in Table 1, which includes bronchodilators, anti-inflammatories, mucolytics, surfactants, antimicrobials, corticosteroids, and anticoagulants [8].

Table 1 Inhaled Medications Utilized During Mechanical Ventilation

Inhaled Medications Utilized During Mechanical Ventilation
Bronchodilators Beta-agonists: albuterol, terbutaline, metaproterenol, fenoterol Anticholinergics: ipratropium bromide Combinations: albuterol sulfate + ipratropium bromide; salmeterol + fluticasone; formoterol + budesonide Prostaglandins

Mucoactive agents
Dornase alfa
Surfactants
Antibiotics Antibacterial, Antiviral, Antifungal
Corticosteroids beclomethasone, budesonide, fluticasone
Anticoagulants heparin

Adapted from Ari A, Fink JB, Dhand R. Inhalation therapy in patients receiving mechanical ventilation: An update. J Aerosol Med Pulm Drug Deliv. 2012; 25(6):319–32

2.2 Clinical Indications for Aerosolized Medications

Aerosol therapy plays an essential role in both treatment and diagnostic strategies across various respiratory conditions. It is frequently prescribed in cases of asthma, chronic obstructive pulmonary disease (COPD), cystic fibrosis, lung infections, and malignancies affecting the pulmonary system or upper airways [9]. These infections may be of viral, bacterial, fungal, or toxic origin [9].

Among the agents with specialized indications is **Dornase alfa**, often administered to patients with cystic fibrosis to help break down thick mucus secretions [9]. Additionally, surfactant therapy is commonly used in neonates with hyaline membrane disease and in adults experiencing acute respiratory distress syndrome (ARDS) [9].

2.3 Aerosol Therapy Considerations in COVID-19 Patients

The COVID-19 pandemic has heightened the need for strict infection control, especially in critically ill patients requiring mechanical ventilation [10]. In this context, aerosolized medication delivery presents a particular risk, as it often involves manipulation or temporary disconnection of the ventilator circuit. Such actions can lead to environmental aerosol dispersion, thereby increasing exposure risk for healthcare workers [10].

Nebulizers typically produce particles in the 1–5 μm range, which are capable of harboring pathogens such as viruses and bacteria. The concern arises from their potential to generate high volumes of fine aerosols that can travel farther than would occur through normal respiratory dispersion, thus raising the likelihood of cross-contamination [10].

To minimize the risk of transmission while maintaining therapeutic efficacy, several precautions are recommended during aerosol therapy in mechanically ventilated COVID-19 patients [10]:

- Avoid opening the ventilator circuit whenever possible when administering aerosolized drugs.
- Jet nebulizers are discouraged due to their limited drug retention, circuit exposure, and tendency to release large amounts of aerosol into the environment.
- Prefer the use of pressurized metered-dose inhalers (pMDIs) for administering inhaled medications.
- If any circuit disconnection is necessary for device placement (e.g., spacers, filters), it should be done using proper technique: clamp the endotracheal tube with Rochester forceps and place the ventilator on standby mode to reduce aerosol dispersion.
- Recommended devices include various forms of spacers and in-line adapters designed to maintain circuit integrity and minimize environmental contamination.

These measures aim to balance effective respiratory treatment with strict infection control protocols in the care of patients affected by airborne infectious diseases such as COVID-19.

3. Discussion

In earlier decades, there was a dominant belief that aerosol drug delivery in mechanically ventilated patients was largely ineffective due to minimal deposition of the medication in the lungs [12]. One of the primary concerns was the assumption that aerosol particles could not successfully navigate through the complexity of the ventilator circuit and endotracheal tube. This perspective was reinforced by pivotal studies demonstrating significantly lower pulmonary deposition in intubated patients compared to non-ventilated individuals receiving the same therapy [12]. At the time, several limitations contributed to this inefficiency: suboptimal performance of available aerosol devices within ventilator systems, limited knowledge about the dynamics of aerosol delivery during ventilation, and the use of older ventilators that were not compatible with aerosol administration techniques [12].

4. Conclusion

In conclusion, aerosol therapy has proven to be an efficient and rapid method for delivering medications to patients receiving mechanical ventilation in the ICU, with minimal risk of adverse effects. Its use facilitates targeted drug delivery via the inhaled route, making it a valuable tool in critical care. Nevertheless, the effectiveness of this approach depends on several variables, including patient-specific factors such as age and underlying health conditions, as well as technical elements like particle size, gas density, drug pharmacodynamics, and the type of delivery device employed.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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