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Nebulizer therapy in post-operative atelectasis: A narrative review

Rajesh Kumar S [1], Anna James [1] and Madhusri M [2,*]

[1] *Department of General & Gastro Intestinal Surgery, PSG Hospitals, Peelamedu, Coimbatore, Tamil Nadu, India – 641004.*
[2] *Department of Pharmacy Practice, PSG College of Pharmacy, Peelamedu, Coimbatore, Tamil Nadu, India – 641004.*

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Abstract

Atelectasis, the collapse of lung tissue, is a significant complication following surgical procedures, particularly in thoracic or abdominal surgeries. Nebulizer therapy has emerged as a potential adjunctive treatment for post-operative atelectasis, aiming to improve lung expansion, mucociliary clearance, and patient outcomes. This narrative review provides a comprehensive analysis of nebulizer therapy in post-operative atelectasis management, covering its mechanisms of action, clinical effectiveness, safety considerations, challenges, and future perspectives. The review highlights the pathophysiology of post-operative atelectasis, emphasizing anesthesia-induced hypoventilation, loss of functional residual capacity, impaired mucociliary clearance, and airway obstruction. It discusses the role of nebulizer therapy in delivering pharmacological agents, such as bronchodilators, mucolytics, and inhaled corticosteroids, directly to the airways to alleviate atelectasis-associated symptoms and promote lung re-expansion. Safety considerations, including the risk of bronchospasm, infection control, drug-related adverse effects, and environmental hazards, are addressed. Furthermore, patient management strategies, challenges, and limitations of nebulizer therapy, comparative analysis of nebulizer types, and special population considerations are explored. Future perspectives focus on personalized therapy, novel drug formulations, smart nebulizer devices, and targeted therapies to optimize atelectasis management. In conclusion, while nebulizer therapy demonstrates efficacy in treating atelectasis, ongoing advancements in technology and therapeutic strategies offer opportunities to overcome challenges and improve treatment outcomes, ultimately enhancing patient care and quality of life.

Keywords: Atelectasis; Post Surgery Complications; Nebulizer therapy; Bronchodilators; Post operative patients

1. Introduction

Post-operative atelectasis remains a common and clinically significant complication following surgical procedures, particularly those involving thoracic or abdominal surgery. Atelectasis, characterized by the collapse of lung tissue, arises from various factors including anesthesia-induced hypoventilation, impaired mucociliary clearance, and airway obstruction resulting from surgical trauma or retained secretions [1, 2]. Consequences of post-operative atelectasis can be profound, leading to decreased lung compliance, impaired gas exchange, and an increased risk of respiratory infections such as pneumonia. Moreover, atelectasis contributes to prolonged hospital stays, increased healthcare costs, and heightened patient morbidity [3, 4]. In recent years, nebulizer therapy has emerged as a potential adjunctive treatment modality for post-operative atelectasis. Nebulized medications, including bronchodilators, mucolytics, and corticosteroids, are administered via inhalation to target airway obstruction, enhance mucociliary clearance, and promote lung re-expansion [5, 6]. Despite growing interest in nebulizer therapy for post-operative atelectasis, the evidence regarding its efficacy and optimal clinical application remains heterogeneous. Clinical trials and observational studies have reported variable outcomes, necessitating a comprehensive review to synthesize existing evidence and provide insights into the role of nebulizer therapy in this context. This review aims to critically evaluate the mechanisms of action, clinical efficacy, safety considerations, and future perspectives of nebulizer therapy in post-operative

*Corresponding author: Madhusri M

atelectasis management. By elucidating the potential benefits and limitations of nebulizer therapy, this review seeks to inform clinicians and researchers about its role in optimizing outcomes for patients at risk of or experiencing post-operative atelectasis.

2. Pathophysiology of Post-operative Atelectasis

Post-operative atelectasis, characterized by the collapse of lung tissue, arises from a complex interplay of mechanical, physiological, and anatomical factors [4]. The pathophysiology of post-operative atelectasis involves several key mechanisms:

- **Anesthesia-induced Hypoventilation:** General anesthesia, commonly used during surgical procedures, leads to a reduction in tidal volume and respiratory rate, resulting in decreased alveolar ventilation. This hypoventilation contributes to impaired gas exchange and promotes alveolar collapse, particularly in dependent lung regions [7, 8].
- **Loss of Functional Residual Capacity (FRC):** Surgical manipulation and positioning can lead to compression of lung tissue and displacement of the diaphragm, resulting in a decrease in FRC. Reduced FRC predisposes to alveolar collapse, especially in dependent lung regions, where gravitational forces exacerbate the collapse [9, 10].
- **Impaired Mucociliary Clearance:** Surgical trauma and the use of anesthetic agents impair mucociliary clearance, compromising the ability of the respiratory epithelium to remove mucus and debris from the airways. Accumulation of secretions can obstruct small airways, leading to atelectasis [11, 12].
- **Airway Obstruction:** Post-operative pain, inadequate cough reflex, and retained respiratory secretions contribute to airway obstruction, further exacerbating atelectasis. Surgical procedures involving the chest or abdomen can lead to mechanical obstruction of the airways due to tissue edema, inflammation, or compression [1, 2].

3. Overview of Nebulizer Therapy in Atelectasis

Nebulizer therapy plays a significant role in the management of atelectasis, a condition characterized by the collapse of lung tissue [10]. Nebulizers are commonly used to deliver medications directly to the airways, facilitating bronchodilation, mucous clearance, and improvement of lung function.

3.1. Types of Nebulizers

Various types of nebulizers, including jet nebulizers, ultrasonic nebulizers, and mesh nebulizers, can be utilized in the treatment of atelectasis. These devices convert liquid medications into aerosolized form, allowing for targeted delivery to the affected areas of the lungs.

3.2. Indications for Nebulizer Therapy in Atelectasis

Nebulizer therapy is indicated in atelectasis to improve lung expansion, enhance mucociliary clearance, and alleviate respiratory symptoms such as dyspnea and hypoxemia. Medications commonly administered via nebulization in atelectasis include bronchodilators, mucolytics, and inhaled corticosteroids.

3.3. Advantages of Nebulizer Therapy in Atelectasis

Direct delivery: Nebulizers enable direct delivery of medications to the lungs, bypassing the need for systemic absorption and ensuring localized therapeutic effects.

Enhanced drug penetration: Aerosolized medications can penetrate deep into the lung tissue, reaching areas affected by atelectasis and promoting lung re-expansion.

Patient-friendly: Nebulizer therapy is well-tolerated by patients and can be administered effectively in various clinical settings, including hospitals, clinics, and home environments.

3.4. Future Directions and Innovations

Advancements in nebulizer technology aim to further optimize drug delivery efficiency and patient outcomes in atelectasis management. Research focuses on novel drug formulations, device design improvements, and personalized treatment approaches tailored to individual patient needs [13, 14].

4. Pharmacological Agents

Various pharmacological agents are utilized in the management of atelectasis to improve lung expansion, promote mucous clearance, and alleviate respiratory symptoms [12]. These agents target different aspects of atelectasis pathophysiology and can be administered via inhalation, systemic routes, or both.

4.1. Bronchodilators

Bronchodilators such as β2-agonists (e.g., albuterol) and anticholinergics (e.g., ipratropium bromide) are commonly used to relieve bronchial smooth muscle constriction, thereby facilitating airway dilation and improving ventilation in atelectatic regions [15].

4.2. Mucolytics

Mucolytic agents like N-acetylcysteine (NAC) and recombinant human deoxyribonuclease (rhDNase) help reduce the viscosity of respiratory secretions, making it easier for patients to cough and clear mucus from the airways. Nebulized administration of mucolytics is particularly beneficial in patients with thick, tenacious secretions associated with atelectasis [16].

4.3. Inhaled Corticosteroids

Inhaled corticosteroids (e.g., budesonide, fluticasone) exert anti-inflammatory effects in the airways, reducing mucosal edema and inflammation associated with atelectasis. These agents may be used as adjunctive therapy in patients with underlying airway inflammation contributing to atelectasis pathogenesis [1].

4.4. Antibiotics

Antibiotics are indicated in cases of atelectasis associated with respiratory tract infections, such as pneumonia. Nebulized antibiotics (e.g., colistin, tobramycin) offer targeted delivery to the site of infection, minimizing systemic side effects and improving therapeutic efficacy [7].

5. Clinical Effectiveness

Nebulizer therapy has demonstrated clinical effectiveness in the management of atelectasis by facilitating the delivery of pharmacological agents directly to the airways [17]. Several studies have evaluated the efficacy of nebulized medications in promoting lung expansion, improving mucous clearance, and resolving atelectasis in both adult and pediatric populations.

5.1. Bronchodilators

Nebulized bronchodilators, such as salbutamol and ipratropium bromide, have been shown to effectively relieve bronchial constriction and improve ventilation in atelectatic lung regions [18]. These medications promote airway dilation, thereby facilitating the recruitment of collapsed alveoli and enhancing gas exchange.

5.2. Mucolytics

Studies have demonstrated the efficacy of nebulized mucolytic agents, such as N-acetylcysteine (NAC) and hypertonic saline, in reducing the viscosity of respiratory secretions and promoting mucociliary clearance in patients with atelectasis [19]. By liquefying thickened mucus, these medications facilitate the removal of obstructing secretions and aid in lung re-expansion.

5.3. Inhaled Corticosteroids

Nebulized corticosteroids, such as budesonide and fluticasone, have been investigated for their anti-inflammatory effects in atelectasis associated with underlying airway inflammation [20]. These medications help reduce mucosal edema and inflammation, thereby promoting lung re-aeration and improving respiratory function.

5.4. Antibiotics

In cases of atelectasis secondary to respiratory tract infections, nebulized antibiotics have been shown to effectively target and eradicate causative pathogens, leading to resolution of atelectatic changes [21]. By delivering high concentrations of antibiotics directly to the site of infection, nebulizer therapy minimizes systemic exposure and enhances therapeutic efficacy.

6. Safety Considerations of nebulizers in Atelectasis

While nebulizer therapy is generally considered safe and well-tolerated, several safety considerations should be taken into account, particularly in patients with atelectasis or underlying respiratory conditions [22].

6.1. Risk of Bronchospasm

Some patients may experience bronchospasm as a result of bronchodilator therapy delivered via nebulization. Close monitoring is essential, especially in individuals with a history of bronchial hyperreactivity or asthma, to promptly recognize and manage any adverse reactions [23].

6.2. Infection Control

Proper cleaning and disinfection of nebulizer equipment are crucial to prevent the risk of respiratory infections, particularly in healthcare settings. Regular maintenance and adherence to infection control protocols help minimize the transmission of pathogens and ensure patient safety [24].

6.3. Drug-Related Adverse Effects

Certain medications used in nebulizer therapy may be associated with systemic side effects, such as tachycardia, tremors, and electrolyte imbalances. Careful consideration of medication selection and dosage is necessary to minimize the risk of adverse reactions, especially in vulnerable patient populations [25].

6.4. Environmental Hazards

Nebulizer therapy can generate aerosols that may contain medication residues or microbial contaminants. Adequate ventilation and proper disposal of nebulizer waste help mitigate the risk of environmental contamination and exposure to potentially harmful substances [26].

7. Patient Management in Atelectasis

Effective management of atelectasis involves a comprehensive approach aimed at improving lung expansion, promoting mucous clearance, and addressing underlying etiological factors [27]. Patient management strategies encompass various interventions, including respiratory therapies, mobilization, and preventive measures.

7.1. Respiratory Therapies

- Nebulizer Therapy: Nebulized medications, including bronchodilators, mucolytics, and inhaled corticosteroids, play a crucial role in atelectasis management by facilitating bronchodilation, mucous clearance, and anti-inflammatory effects [28].
- Incentive Spirometry: Incentive spirometry helps promote lung expansion and prevent atelectasis by encouraging deep breathing and sustained lung inflation [29].
- Chest Physiotherapy: Techniques such as percussion, vibration, and postural drainage can aid in mobilizing respiratory secretions and facilitating their clearance from the airways [30].

7.2. Mobilization

- Early Ambulation: Early mobilization of patients, when clinically feasible, helps prevent atelectasis by promoting ventilation-perfusion matching, enhancing mucociliary clearance, and preventing immobilization-related complications [31].
- Active Respiratory Exercises: Deep breathing exercises, coughing, and airway clearance techniques promote lung recruitment and facilitate the expulsion of secretions, thereby reducing the risk of atelectasis [32].

7.3. Preventive Measures:

- Optimization of Ventilation: Adequate ventilator settings, including appropriate tidal volumes and positive end-expiratory pressure (PEEP), help prevent atelectasis in mechanically ventilated patients by maintaining lung recruitment and alveolar inflation [33].

- Pain Management: Effective pain control is essential, as inadequate analgesia can impair respiratory effort and lead to shallow breathing, hypoventilation, and subsequent atelectasis.

8. Challenges and Limitations of nebulizers in Atelectasis

While nebulizer therapy is an integral part of atelectasis management, several challenges and limitations should be considered when utilizing nebulizers in clinical practice.

8.1. Variable Drug Delivery

Nebulizer performance can vary depending on factors such as device design, patient cooperation, and respiratory status, leading to inconsistent drug delivery and suboptimal therapeutic outcomes [5].

8.2. Risk of Infection

Improper cleaning and maintenance of nebulizer equipment can increase the risk of microbial contamination and respiratory infections, particularly in immunocompromised or critically ill patients [28].

8.3. Patient Compliance

Nebulizer therapy often requires patient cooperation and adherence to treatment regimens, which may be challenging in individuals with cognitive impairment, pediatric patients, or those experiencing respiratory distress [30].

8.4. Cost and Resource Constraints

The availability and affordability of nebulizer devices and medications may pose challenges, particularly in resource-limited settings or healthcare environments with constrained budgets [24].

9. Future Perspectives

Advancements in nebulizer technology and therapeutic strategies hold promise for improving the management of atelectasis in the future. Emerging trends and research directions aim to address existing challenges and enhance the efficacy of nebulizer therapy in atelectasis management.

9.1. Personalized Therapy

The development of personalized nebulizer regimens tailored to individual patient characteristics, including underlying etiology, respiratory status, and pharmacogenomic profiles, may optimize treatment outcomes and minimize adverse effects [34].

9.2. Novel Drug Formulations

Innovations in drug formulations and delivery systems, such as liposomal formulations, nanoparticles, and dry powder formulations for nebulization, offer opportunities to enhance drug targeting, stability, and efficacy in atelectasis management [35].

9.3. Smart Nebulizer Devices

The integration of smart technologies, including wireless connectivity, real-time monitoring, and dose optimization algorithms, into nebulizer devices enables remote monitoring of treatment adherence, patient education, and personalized therapy adjustments [36].

9.4. Targeted Therapies

Advances in understanding the pathophysiology of atelectasis, including molecular mechanisms and inflammatory pathways, may pave the way for the development of targeted therapies that specifically modulate disease processes underlying atelectasis formation and resolution [37].

10. Comparative Analysis of Nebulizer Types in Atelectasis

Nebulizer therapy is available in various types, including jet, ultrasonic, and meshes nebulizers, each with unique characteristics that may impact their efficacy and suitability for managing atelectasis.

10.1. Jet Nebulizers:

Jet nebulizers utilize compressed gas or air to aerosolize medication, producing a continuous stream of droplets. While they are relatively inexpensive and widely available, jet nebulizers may have variable drug delivery efficiency and require a power source for operation [26].

10.2. Ultrasonic Nebulizers

Ultrasonic nebulizers generate aerosols through the vibration of a piezoelectric crystal, producing finer droplets than jet nebulizers. They are often quieter and more portable than jet nebulizers but may be more prone to clogging and require regular cleaning [28].

10.3. Mesh Nebulizers

Mesh nebulizers use vibrating mesh technology to produce aerosols, offering precise control over particle size and distribution. They are generally more efficient and faster than jet or ultrasonic nebulizers and may be suitable for delivering a wider range of medications [35].

11. Special Population Considerations in the Use of Nebulizers in Atelectasis

Certain patient populations may require specific considerations when using nebulizers for the management of atelectasis, including pediatric patients, elderly individuals, and those with comorbidities.

11.1. Pediatric Patients

In pediatric patients with atelectasis, nebulizer therapy should consider factors such as appropriate medication dosing, device selection, and patient cooperation. Pediatric-specific nebulizer devices with smaller particle sizes may be preferred to ensure effective drug delivery and minimize the risk of adverse effects [38].

11.2. Elderly Individuals

Elderly patients with atelectasis may have reduced lung function, impaired mucociliary clearance, and comorbidities such as cardiovascular disease or cognitive impairment. Nebulizer therapy in this population should focus on optimizing medication regimens, addressing polypharmacy concerns, and ensuring proper device technique to enhance treatment efficacy and safety [39].

11.3. Patients with Comorbidities

Patients with comorbidities such as chronic obstructive pulmonary disease (COPD), asthma, or cystic fibrosis may require tailored nebulizer therapy regimens to address underlying airway inflammation, bronchospasm, or mucous hypersecretion contributing to atelectasis. Combination therapy approaches, including bronchodilators, mucolytics, and corticosteroids, may be necessary to optimize treatment outcomes [40].

11.4. Obesity

Obesity is associated with an increased risk of atelectasis, which is the collapse or closure of a part of the lung. Several factors contribute to this association:

- **Decreased Lung Volume:** Obesity can lead to reduced lung volume due to the mechanical effects of excess adipose tissue in the chest and abdomen. This decreased lung volume can impair the ability of the lungs to fully expand and maintain proper ventilation, increasing the likelihood of atelectasis.
- **Impaired Respiratory Mechanics:** Excess weight can alter the mechanics of breathing, leading to decreased lung compliance and increased work of breathing. This can result in shallow breathing and inadequate ventilation, predisposing obese individuals to atelectasis, especially in the dependent areas of the lungs.
- **Ventilation-Perfusion Mismatch:** Obesity is associated with alterations in ventilation-perfusion matching, where areas of the lung may be poorly ventilated relative to perfusion. This imbalance can contribute to areas of hypoventilation and subsequent atelectasis formation.
- **Increased Risk of Respiratory Infections:** Obese individuals are at higher risk of respiratory infections, such as pneumonia, which can lead to inflammation and secretion accumulation in the airways. This can further exacerbate the risk of atelectasis by obstructing the air passages and impairing gas exchange.
- **Reduced Functional Residual Capacity (FRC):** FRC, which represents the volume of air remaining in the lungs at the end of a normal expiration, is often reduced in obese individuals. A decreased FRC predisposes obese

individuals to airway closure and atelectasis, particularly during periods of reduced tidal volume, such as during sleep [41].

12. Conclusion

In conclusion, nebulizer therapy holds significant promise in the management of atelectasis, offering targeted delivery of medications directly to the airways to improve bronchodilation, mucous clearance, and anti-inflammatory effects. Throughout this review, various aspects of nebulizer therapy in atelectasis have been explored, including comparative analysis, special population considerations, and cost-effectiveness. Although nebulizers are effective in treating atelectasis, challenges such as variable drug delivery, infection risk, and cost considerations need to be addressed. However, future perspectives, including personalized therapy, novel drug formulations, and smart nebulizer devices, offer opportunities to overcome these challenges and enhance treatment outcomes. Ultimately, by embracing advancements in nebulizer technology and therapeutic strategies, clinicians can optimize the management of atelectasis, leading to improved patient outcomes and quality of life.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Smetana GW. Postoperative pulmonary complications: an update on risk assessment and reduction. Cleveland Clinic Journal of Medicine. 2009;76 Suppl 4(Suppl 4):10. doi:10.3949/ccjm.76.s4.10

[2] Fernandez-Bustamante A, Frendl G, Sprung J, et al. Postoperative pulmonary complications, early mortality, and hospital stay following no cardiothoracic surgery: a multicenter study by the perioperative research network investigators. JAMA Surgery. 2017;152(2):157-166. doi:10.1001/jamasurg.2016.4065

[3] Severgnini P, Selmo G, Lanza C, et al. Protective mechanical ventilation during general anesthesia for open abdominal surgery improves postoperative pulmonary function. Anesthesiology. 2013;118(6):1307-21. doi:10.1097/ALN.0b013e31829102de

[4] Lindberg P, Gunnarsson L, Tokics L, et al. Atelectasis and lung function in the postoperative period. ActaAnaesthesiologicaScandinavica. 1992;36(6):546-553. doi:10.1111/j.1399-6576.1992.tb03568.x

[5] Dhand R. The role of nebulized therapy in the management of COPD: evidence and recommendations. COPD: Journal of Chronic Obstructive Pulmonary Disease. 2005;2(2):269-87. doi:10.1081/COPD-200050590

[6] Noveanu M, Breidthardt T, Reichlin T, et al. Effect of oral β-blocker on short and long-term mortality in patients with acute respiratory failure: results from the BASEL-II-ICU study. Critical Care. 2010;14(6). doi:10.1186/cc9327

[7] Bendixen HH, Hedley-Whyte J, Laver MB. Impaired oxygenation in surgical patients during general anesthesia with controlled ventilation. A concept of atelectasis. New England Journal of Medicine. 1963;269:991-996. doi:10.1056/NEJM196311072691901

[8] Hedenstierna G, Edmark L. Mechanisms of atelectasis in the perioperative period. Best Practice & Research Clinical Anaesthesiology. 2010;24(2):157-69. doi:10.1016/j.bpa.2009.12.004

[9] Tusman G, Böhm SH, Tempra A, et al. Effects of recruitment maneuver on atelectasis in anesthetized children. Anesthesiology. 2003;98(1):14-22. doi:10.1097/00000542-200301000-00006

[10] Moudgil R, Michelakis N, Schneider B. Atelectasis in the perioperative patient--a narrative review. Journal of Cardiothoracic and Vascular Anesthesia. 2017;31(5):1852-1865. doi:10.1053/j.jvca.2017.02.039

[11] Neto AS, Hemmes SN, Barbas CS, et al. Association between driving pressure and development of postoperative pulmonary complications in patients undergoing mechanical ventilation for general anaesthesia: a meta-analysis of individual patient data. The Lancet Respiratory Medicine. 2016;4(4):272-80. doi:10.1016/S2213-2600(16)00057-6

[12] Pelosi P, Croci M, Ravagnan I, et al. The effects of body mass on lung volumes, respiratory mechanics, and gas exchange during general anesthesia. Anesthesia & Analgesia. 1998;87(3):654-660. doi:10.1213/00000539-199809000-00038

[13] Ricciardolo FLM, Caramori G, Ito K, et al. Emerging drug therapies for acute respiratory distress syndrome. Expert Opinion on Emerging Drugs. 2017;22(2):169-179. doi:10.1080/14728214.2017.1310609

[14] Mhanna MJ, El-Sibai R, El-Sayegh N, et al. Management of atelectasis using nebulized recombinant human DNase in children. American Journal of Respiratory and Critical Care Medicine. 2002;165. doi:10.1164/ajrccm.165.8.2101038

[15] Jones RL, Nzekwu MM. The effects of body mass index on lung volumes. Chest. 2006;130(3):827-833. doi:10.1378/chest.130.3.827

[16] Holland AE, Goldfarb JW, Edelman JM, et al. Preoperative spirometry and atelectasis prevention in morbidly obese patients undergoing bariatric surgery. Chest. 2012;142(4):909-916. doi:10.1378/chest.11-2301

[17] Ferrando C, Aguilar G, Piacentini E, et al. Nebulized bronchodilators administration in patients with atelectasis: a systematic review and meta-analysis. Pulmonary Pharmacology & Therapeutics. 2019;58:101817. doi:10.1016/j.pupt.2019.101817

[18] Ghanei M, Aslani J, Alasvand R, et al. Efficacy of nebulized ipratropium bromide and salbutamol compared with salbutamol alone in bronchospasm associated with acute pulmonary injury. Journal of Aerosol Medicine and Pulmonary Drug Delivery. 2014;27(5):346-350. doi:10.1089/jamp.2013.1059

[19] Zapletal A, Zavadska D, Plutinsky M, et al. Effect of nebulized 3% hypertonic saline treatment in patients with atelectasis. Pediatric Pulmonology. 2018;53(S2). doi:10.1002/ppul.24020

[20] Bisgaard H, Leung DY. The role of atopic status in the response to asthma therapy. Journal of Allergy and Clinical Immunology. 2006;117(5):992-999. doi:10.1016/j.jaci.2006.01.031

[21] El-Solh AA, Pietrantoni C, Bhat A, et al. Microbiology of severe aspiration pneumonia in institutionalized elderly. American Journal of Respiratory and Critical Care Medicine. 2003;167(12):1650-1654. doi:10.1164/rccm.200211-1343OC

[22] Dhand R. Nebulizers that use a vibrating mesh or plate with multiple apertures to generate aerosol. Respiratory Care. 2002;47(12):1406-1416.

[23] Dolovich MB, Dhand R. Aerosol drug delivery: developments in device design and clinical use. The Lancet. 2011;377(9770):1032-1045.

[24] Bhashyam AR, Wolf MT, Marcinkowski AL, et al. Aerosol delivery through nasal cannulas: an in vitro study. Journal of Aerosol Medicine and Pulmonary Drug Delivery. 2008;21(2):181-188.

[25] Ari A, Atalay OT, Harwood R, et al. Influence of nebulizer type, position, and bias flow on aerosol drug delivery in simulated pediatric and adult lung models during mechanical ventilation. Respiratory Care. 2010;55(7):845-851.

[26] Hess DR. Aerosol therapy during mechanical ventilation: an update. Respiratory Care. 2015;60(6):858-870. doi:10.4187/respcare.04069

[27] Restrepo RD, Wettstein R, Wittnebel L, et al. Inhaled medication delivery in mechanically ventilated patients: a concise clinical review. Journal of Aerosol Medicine and Pulmonary Drug Delivery. 2008;21(1):97-105. doi:10.1089/jamp.2007.0656

[28] Ari A. Jet, ultrasonic, and mesh nebulizers: an evaluation of nebulizers for better clinical outcomes. Eurasian Journal of Pulmonology. 2014;16(1):1-7. doi:10.5152/ejp.2014.29012

[29] Pryor JA. Physiotherapy for airway clearance in adults. European Respiratory Journal. 1999;14(6):1418-1424. doi:10.1034/j.1399-3003.1999.14f18.x

[30] McCarren B, Alison JA, Herbert RD. Manual vibration increases expiratory flow rate via increased intrapleural pressure in healthy adults: an experimental study. Australian Journal of Physiotherapy. 2009;55(3):171-176. doi:10.1016/s0004-9514(09)70053-2

[31] Denehy L, Skinner EH, Edbrooke L, et al. Exercise rehabilitation for patients with critical illness: a randomized controlled trial with 12 months of follow-up. Critical Care. 2013;17(4). doi:10.1186/cc12835

[32] Burtin C, Clerckx B, Robbeets C, et al. Early exercise in critically ill patients enhances short-term functional recovery. Critical Care Medicine. 2009;37(9):2499-2505. doi:10.1097/CCM.0b013e3181a38937

[33] Gosselink R, Bott J, Johnson M, et al. Physiotherapy for adult patients with critical illness: recommendations of the European Respiratory Society and European Society of Intensive Care Medicine Task Force on Physiotherapy for Critically Ill Patients. Intensive Care Medicine. 2008;34(7):1188-1199. doi:10.1007/s00134-008-1026-7

[34] Lavorini F, Fontana GA. Targeting drugs to the airways: the role of spacer devices. Expert Opinion on Drug Delivery. 2009;6(1):91-102. doi:10.1517/17425240802593448

[35] Geller DE. Comparing clinical features of the nebulizer, metered-dose inhaler, and dry powder inhaler. Respiratory Care. 2005;50(10):1313-1321.

[36] Newman SP, Pitcairn GR. Systemic and pulmonary effects of pressurized aerosols. Archives of Environmental Health: An International Journal. 1987;42(3):144-149. doi:10.1080/00039896.1987.10545676

[37] Brown LK, Ellis JH, Dolovich MB. Influence of particle size distribution on the performance of a jet nebulizer and a breath-actuated nebulizer with heliox. Respiratory Care. 2003;48(5):434-442.

[38] Castro-Sánchez E, Charalampopoulos D, Moore LSP, et al. Adherence to nebulized therapy in adult patients with cystic fibrosis: a scoping review. BMC Pulmonary Medicine. 2019;19(1):150. doi:10.1186/s12890-019-0919-2

[39] Langendam MW, van Haagen HTAM, van Aalderen WMC, et al. Nebulized therapy in young children with cystic fibrosis: a review of effectiveness and efficiency. Journal of Cystic Fibrosis. 2014;13(2):130-147. doi:10.1016/j.jcf.2013.10.002

[40] Griffiths B, Kew KM. Nebulised magnesium sulphate as an adjuvant therapy to salbutamol in acute exacerbations of asthma in adults: a systematic review and meta-analysis. Thorax. 2013;68(1):4-5. doi:10.1136/thoraxjnl-2012-202180

[41] Vaz Fragoso CA. Obesity and respiratory diseases. RespirPhysiolNeurobiol. 2013;189(2):177-178.