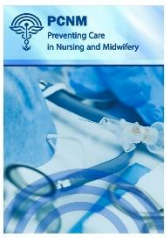
Prev Care Nurs Midwifery J (PCNM)
http://dx.doi.org/10.61882/pcnm.15.4.60

PCNM. 2025;15(4):60-69
Peer-Reviewed | Open Access

Preventive Care in Nursing and Midwifery Journal



Original Article

The Effect of Jet Nebulizer Placement Relative to the Heat and Moisture Exchange (HME) Filter on Pulmonary Parameters in Mechanically Ventilated Adults: A Randomized, Double-Blind Controlled Clinical Trial

Zahra Khezerlou[1], Akram Khadiri[2], Farhad Ramezani-Badr[2*], Mohammadreza Dinmohammadi[2], Samad Ghodrati[3], Mahtab Aligholipour[2]

[1] Medical Surgical Nursing Department, School of Nursing and Midwifery, Zanjan University of Medical Sciences, Zanjan, Iran.

[2] Critical Care and Emergency Nursing Department, School of Nursing and Midwifery, Zanjan University of Medical Sciences, Zanjan, Iran.

[3] Pulmonology Department, Vali-e-Asr Hospital, Zanjan University of Medical Sciences, Zanjan, Iran.

Received: 29 Oct 2025 **Accepted:** 12 Nov 2025 **Published:** 27 Nov 2025

Article Info

Keywords:
Nebulizers
Heat and Moisture Exchangers
Airway Resistance
Lung Compliance
Mechanical Ventilation

[*]Corresponding author:
Farhad Ramezani-Badr
Critical Care and Emergency Nursing Department, School of Nursing and Midwifery, Zanjan University of Medical Sciences, Zanjan, Iran.
Email:
Ramezanibadr@gmail.com

How to Cite This Article:
Khezerlou Z, Khadiri A, Ramezani-Badr F, Dinmohammadi MR, Ghodrati S, Aligholipour M. The Effect of Jet Nebulizer Placement Relative to the Heat and Moisture Exchange (HME) Filter on Pulmonary Parameters in Mechanically Ventilated Adults: A Randomized, Double-Blind Controlled Clinical Trial. Prev Care Nurs Midwifery J. 2025;15(4):60-69.

Abstract

Background: Heat and moisture exchanger (HME) filters are essential for mechanically ventilated patients but can hinder aerosol delivery.

Objectives: This study compared jet nebulizer placement positions relative to the HME filter on pulmonary parameters.

Methods: This double-blind randomized controlled trial assessed 86 patients for eligibility. After excluding 13, 73 were randomized into two groups: the intervention group (n=36), where the nebulizer was placed between the patient and the HME filter, and the control group (n=37), where it was placed between the ventilator and the HME. During the trial, 3 patients died (intervention: 1, control: 2), resulting in a final analysis of 70 patients (35 per group). Parameters were measured at baseline and at 90 minutes after each of four bronchodilator doses administered over 24 hours. Data analysis included repeated measures ANOVA via SPSS v.22.

Results: Significant within-group time effects were found for mean airway pressure (MAP), SpO_2, lung compliance (Cst), and airway resistance (Raw) (P<0.05). Tidal volume (VT) and minute ventilation (MV) showed no significant temporal changes (P>0.05). The time×group interaction was significant only for Raw and SpO_2 (P<0.05). Between-group analysis revealed significant differences in VT, MAP, SpO_2, Raw, and MV (P<0.05), but not for Cst (P=0.222).

Conclusion: Nebulizer placement relative to the HME filter affects temporal changes in Raw and SpO_2. Considering small-to-moderate effect sizes, differences are primarily physiological; thus, placement should be guided by clinical status and specific protocols.

Implications for Nursing and Midwifery Preventive Care

- Both placements are clinically safe, granting nurses flexibility in circuit management while ensuring stable respiratory parameters and effective bronchodilator delivery.
- Stable outcomes allow nurses to prioritize vital preventive care, including infection control, without concerns regarding nebulizer positioning-related respiratory complications.

Introduction

Intensive care units (ICU) represent the central setting for the management of critically ill patients, many of whom develop acute respiratory failure and therefore require mechanical ventilation [1, 2]. Mechanical ventilation is a common and vital intervention in this population, with more than 90% of critically ill patients relying on this therapeutic modality [3]. In the ICU setting, mechanical ventilation is used as a fundamental treatment for patients who have lost the ability to breathe spontaneously. This intervention is particularly essential in patients with respiratory failure, shock, those undergoing complex surgical procedures, or those with acute illnesses [4]. Mechanical ventilation can significantly improve the clinical condition of patients; however, its success is not limited to the ventilator device and its settings, as multiple other factors also play a role in the effectiveness of the therapy [5].

One of the essential components of care for mechanically ventilated patients is ensuring adequate temperature and humidity of the inspired gases. Endotracheal intubation bypasses the upper airways, disrupting the natural mechanisms of warming and humidifying inhaled air. Inhalation of cold and dry gases can lead to respiratory epithelial damage, impaired ciliary function, increased secretion viscosity, endotracheal tube obstruction, and elevated airway resistance, all of which negatively affect lung mechanics and gas exchange [6, 7]. Therefore, the use of humidification systems is considered essential in patients receiving mechanical ventilation.

In ICU clinical settings, humidification is typically achieved either through active heated humidifiers or heat and moisture exchanger (HME) filters. HMEs are widely used due to their ease of use, reduced water accumulation in the ventilator circuit, lower risk of microbial contamination, and lower cost [7–9]. However, evidence suggests that the presence of an HME in the ventilator circuit may negatively affect aerosol drug delivery, as these filters act as a physical barrier by trapping aerosol particles, thereby reducing the efficiency of drug deposition in the lungs [9].

Aerosol therapy, particularly the administration of bronchodilators, is a common intervention in mechanically ventilated patients and plays a crucial role in reducing airway resistance and improving pulmonary parameters. However, studies have shown that only a limited portion of the nominal drug dose (approximately 10 to 20%) actually reaches the patients' lungs, while the majority remains within the ventilator circuit, endotracheal tube, and ancillary equipment [10]. The type of nebulizer, ventilator settings, structure of the breathing circuit, and the positioning of equipment are all factors that influence the effectiveness of aerosol drug delivery. In this context, while the use of an HME is essential for maintaining appropriate humidity and temperature in the airway and preserving lung function, it can affect the amount of aerosolized medication delivered. Studies have shown that placing the HME between the nebulizer and the patient significantly reduces drug delivery; therefore, the placement of equipment within the ventilator circuit is of critical importance [1].

Preclinical and ex vivo studies have demonstrated that the placement of the nebulizer relative to the HME filter and the Y-piece can play a decisive role in the amount of drug delivered. Hou and colleagues reported that positioning the nebulizer 15 centimeters upstream of the Y-piece resulted in the highest drug deposition [11]. Findings by Montigaud and colleagues also demonstrated that this nebulizer position significantly increases drug deposition in the lungs, even under humidified conditions [1]. Heat and moisture exchanger (HME) filters play an important role in maintaining airway humidity and temperature in mechanically ventilated patients. However, a study by Ari et al. (2018) showed that placing the HME filter between the nebulizer and the patient can reduce the delivery of inhaled medications. Therefore, in certain situations, the use of an HME without a filter or temporary removal of the filter during aerosol therapy is recommended [12]. In another study, Reilly and colleagues (2024) used modeling in mechanically ventilated adults and children to examine drug deposition, finding that lung health status (healthy vs. diseased) has a greater impact on the deposited drug dose than nebulizer

placement or the type of humidification, particularly in adults [13].

However, most of this evidence is based on laboratory or animal models, and clinical evidence from randomized trials in ICU patients remains limited.

Objectives

Given the importance of effective inhaled drug delivery and the potential role of jet nebulizer and HME filter placement in enhancing or reducing therapeutic efficacy, well-designed clinical studies are warranted.

Therefore, the present study aimed to compare the effects of jet nebulizer placement relative to the heat and moisture exchanger (HME) filter on pulmonary parameters in mechanically ventilated adult patients in the ICU.

Methods

Study Design and Setting

This study was a double-blind randomized clinical trial with a parallel-group, repeated measures design, conducted as a pre-test–post-test on mechanically ventilated patients admitted to the intensive care unit of Vali-e-Asr Educational and Medical Center, Zanjan University of Medical Sciences. Patient recruitment for the study took place from August 2019 to June 2020.

Participants

The study population consisted of patients aged 18 to 65 years who were receiving mechanical ventilation in the ICU of Vali-e-Asr Educational and Medical Center, Zanjan University of Medical Sciences. Inclusion criteria were patients with an artificial airway (endotracheal tube or tracheostomy), connected to a ventilator in volume-controlled mode, receiving aerosolized bronchodilators, and having vital signs within normal ranges.

Inclusion Criteria

Patients aged 18 to 65 years, with an artificial airway (endotracheal tube or tracheostomy), connected to a ventilator in volume-controlled mode, receiving aerosolized bronchodilators, and with vital signs within normal ranges.

Exclusion Criteria

Patients with brain lesions; those receiving dopamine, dobutamine, nitroglycerin, or other vasoactive medications; patients who were weaned from the ventilator, or received more than six doses of aerosolized medication within 24 hours.

Sampling Method and Sample Size

A convenience sampling method was employed. Initially, 86 patients were assessed for eligibility. Of these, 13 patients were excluded prior to randomization for not meeting the inclusion criteria or meeting one or more exclusion criteria. Consequently, 73 eligible patients were enrolled and randomized into two groups: the intervention group (n=36) and the control group (n=37). The allocation sequence was generated using random blocks of four with SPSS software, version 22. To ensure allocation concealment, the sequence was placed in sequentially numbered, sealed, opaque envelopes. An independent nurse, not involved in outcome assessment, was responsible for maintaining the envelopes and opening the next envelope in numerical order after each patient's enrollment to reveal the group assignment. To assign 73 patients into two groups using the block method, predetermined blocks of four (with a 2:2 allocation ratio) were randomly selected and concatenated. This process naturally resulted in the final slightly uneven group sizes (36 and 37) while preserving randomness and balance within each block. This study was conducted as a double-blind trial: due to their clinical condition, patients were unaware of the technical intervention details. The outcome assessor (who recorded pulmonary parameters from the ventilator monitor) was blinded to group assignments. The statistical analyst remained unaware of the group codes until the final analysis was complete.

The sample size was calculated based on a 95% confidence level, 80% statistical power, and a standard deviation of 14.34 for airway resistance, according to Hart et al. (2009) [14]. The calculation

determined a requirement of 35 patients per group. To account for potential attrition, 73 patients were randomized. During the trial, three patients died (intervention: 1, control: 2). Therefore, the final per-protocol analysis was completed for 70 patients (35 in each group).

Data Collection Instruments

The data collection form included three sections: demographic characteristics (gender and age), clinical characteristics (type of artificial airway, underlying disease, type and frequency of breaths, and breath sounds), and pulmonary parameter measurements, which consisted of lung compliance, airway resistance, tidal volume, minute volume, mean airway pressure, and oxygen saturation. These pulmonary parameters were evaluated as functional lung outcomes in response to the intervention. In addition, any potential adverse events related to the intervention (such as changes in blood pressure or heart rate requiring intervention) were recorded and monitored throughout the study as safety outcomes.

To ensure the validity and reliability of the measurement instruments, the monitoring devices used in the ICU were calibrated before initiating data collection.

To establish the content validity of the data collection form, the opinions of eight faculty members from the School of Nursing and Midwifery at Zanjan University were consulted.

The ventilator used in the ICU of Hazrat Vali-e-Asr (AJ) Hospital was an AVEA model manufactured by the American company CareFusion. The vital signs monitors were produced by Pooyandegan Rah Saadat, and all devices in each unit were calibrated uniformly according to the manufacturer's standards [15].

Intervention and Data Collection

Bronchodilators were administered to patients as aerosols via a nebulizer. Before drug administration, pulmonary parameters were measured and recorded in both groups. At this stage, the HME filter was placed in the ventilator circuit without the nebulizer. In the intervention group, the nebulizer was positioned between the patient and the HME filter, whereas in the control group, the nebulizer was placed between the ventilator and the HME filter. To control for confounding variables, all patients were ventilated in volume-controlled mode with fixed settings for tidal volume and respiratory rate, as determined by the attending physician independent of the study. These settings were maintained unchanged throughout the data collection period.

The bronchodilator medication (Combivent: 2.5 mg Albuterol and 0.5 mg Ipratropium in 3 mL) was administered via jet nebulizer every six hours for a total of four doses over a 24-hour period. Pulmonary parameters were recorded at baseline (pre-intervention) and at 90 minutes after each dose administration. Thus, data were collected at five time points: Baseline (T0), and then post-dose at T1 (1.5 hours after dose 1), T2 (7.5 hours after dose 1 / 1.5 hours after dose 2), T3 (13.5 hours after dose 1 / 1.5 hours after dose 3), and T4 (19.5 hours after dose 1 / 1.5 hours after dose 4). The total duration of active intervention and data collection was 21 hours from the first post-dose measurement to the last. Measurements taken before drug administration and after the four subsequent doses were compared between the two groups. The complete study flowchart, prepared according to the CONSORT guidelines, is presented in Figure 1. It illustrates the number of participants assessed for eligibility, those excluded prior to randomization, randomized participants, and those included in the final analysis. No participants were lost to follow-up during the study period.

Data Analysis

Descriptive statistics, including means and standard deviations, were used to summarize the data, and the normality of distribution was assessed using the Kolmogorov-Smirnov test, which indicated that the data were normally distributed. To compare pulmonary parameters between the two groups across the four repeated measurement time points after the intervention, repeated measures analysis of variance (Repeated Measures ANOVA) was performed using the general linear model (GLM). The sphericity assumption was assessed using Mauchly's test, and if violated, the Greenhouse-

Geisser correction was applied. Within-group controls (pre- and post-intervention) were performed using paired t-tests, and baseline variables between the two groups were compared using independent t-tests or chi-square tests, as appropriate. Statistical analyses were conducted using SPSS software, version 22, and a significance level of $p < 0.05$ was considered.

Result

A total of 86 patients were assessed for eligibility for the study. Of these, 13 patients were excluded due to the use of vasoconstrictive medications, separation from mechanical ventilation, and the presence of brain lesions. Consequently, 73 patients with a mean age of 51.79 years (SD: 9.94) were enrolled and randomly assigned to either the control or intervention group, with 35 patients in each group. During the study period, 2 patients in the control group and 1 patient in the intervention group were lost to follow-up due to mortality.

Ultimately, data analysis was completed for 70 patients. As shown in Table 1, the two groups were homogeneous in terms of baseline demographic characteristics, including age and gender distribution, with no statistically significant differences observed between them ($p > 0.05$).Before the intervention, pulmonary parameters were compared between the two groups (Table 1).

Table 1. Baseline Demographic and Pulmonary Characteristics of the Participants

Parameter / Characteristic	Control Group (n=35)	Intervention Group (n=35)	*p*
Age (years), Mean (SD)	50.80 (10.70)	52.77 (9.13)	0.410
Gender, n (%)			0.811
Male	17 (48.6%)	18 (51.4%)	
Female	18 (51.4%)	17 (48.6%)	
Tidal Volume (VT), mL	457.43(46.36)	404.57(55.00)	<0.001
Minute Ventilation (MV), mL	5854.29(1192.96)	6968.57(737.55)	<0.001
Mean Airway Pressure (MAP), cmH_2O	10.11(1.66)	9.86(3.43)	0.691
O_2 Saturation (SpO_2), %	96.06(1.89)	95.06(2.44)	0.059
Compliance (Cst), mL/cmH_2O	25.77(8.39)	42.39(34.35)	0.008
Resistance (Raw), $cmH_2O/L/s$	18.39(8.30)	22.68(9.64)	0.050

Table 2. Results of Repeated Measures ANOVA for Pulmonary Parameters

Parameter	Effect	F (Hypothesis df, Error df)	*p*	Partial η^2
Tidal Volume (VT), mL	Time	2.783 (2.07,138.73)	0.063	0.040
	Time × Group	0.298 (2.07,138.73)	0.750	0.004
	Group	4.750 (1, 67)	0.033	0.066
Mean Airway Pressure (MAP), cmH_2O	Time	9.935 (2.4, 160.79)	<0.001	0.129
	Time × Group	0.804 (2.4, 160.79)	0.469	0.012
	Group	31.86 (1, 67)	0.020	0.078
O_2 Saturation (SpO_2), %	Time	2.785 (3,201)	0.042	0.040
	Time × Group	3.266 (3,201)	0.022	0.046
	Group	5.181 (1, 67)	0.026	0.072
Compliance (Cst), mL/cmH_2O	Time	17.910 (2.56, 171.49)	<0.001	0.211
	Time × Group	0.792 (2.56, 171.49)	0.482	0.012
	Group	1.517 (1, 67)	0.222	0.022
Resistance (Raw), $cmH_2O/L/s$	Time	4.824 (1.56, 104.58)	0.016	0.067
	Time × Group	18.165 (1.56, 104.58)	<0.001	0.213
	Group	9.326 (1, 67)	0.003	0.122
Minute Ventilation (MV), mL/min	Time	2.62 (1.82, 123.97)	0.082	0.37
	Time × Group	1.77 (1.82, 123.97)	0.177	0.25
	Group	8.70 (1, 68)	0.004	0.113

The results showed that the mean tidal volume (VT) was significantly higher in the control group compared to the intervention group ($p < 0.001$). In contrast, the mean minute volume (MV) ($P < 0.001$), airway resistance (Raw) ($p = 0.050$), and lung compliance (Cst) ($p = 0.008$) were significantly higher in the intervention group. No significant differences were observed between the two groups in terms of mean airway pressure (MAP) and oxygen saturation (SpO_2) at baseline. Variables that showed statistically significant differences between the two groups at baseline were controlled as covariates in the subsequent analyses.

Mauchly's test indicated that the sphericity assumption was violated for tidal volume, airway resistance, minute volume, lung compliance, and mean airway pressure ($p < 0.05$); therefore, results for these variables are reported using the Greenhouse-Geisser correction. A summary of these analyses is presented in Table 3.

Table 3. Within-Group Changes from Baseline to First Post-Intervention Measurement

Parameter & Group	Pre-Intervention Mean (SD)	Post-Intervention Mean (SD)	Mean Difference (SD)	t (df)	*p*
Tidal Volume (VT), mL					
Control	457.43 (46.36)	482.57 (68.23)	-25.14 (59.18)	-2.514 (34)	0.017
Intervention	404.57 (55.00)	412.86 (65.42)	-8.29 (29.05)	-1.687 (34)	0.101
Minute Ventilation (MV), mL/min					
Control	5854.29 (1192.96)	6288.57 (1413.33)	-434.29 (539.58)	-4.762 (34)	<0.001
Intervention	6968.57 (737.55)	6841.14 (778.23)	127.43 (552.66)	1.364 (34)	0.182
Mean Airway Pressure (MAP), cmH_2O					
Control	10.11 (1.66)	9.26 (1.48)	0.86 (1.48)	3.431 (34)	0.002
Intervention	9.86 (3.43)	8.66 (2.86)	1.20 (1.43)	4.962 (34)	<0.001
O_2 Saturation (SpO_2), %					
Control	96.06 (1.89)	96.69 (1.64)	-0.63 (2.95)	-1.260 (34)	0.216
Intervention	95.06 (2.44)	96.11 (1.76)	-1.06 (1.49)	-4.186 (34)	<0.001
Compliance (Cst), mL/cmH_2O					
Control	25.77 (8.39)	34.00 (13.66)	-8.23 (11.23)	-4.335 (34)	<0.001
Intervention	42.39 (34.35)	41.34 (17.04)	1.05 (24.42)	0.253 (34)	0.802
Airway Resistance (Raw), $cmH_2O/L/s$					
Control	18.39 (8.30)	17.52 (11.06)	0.87 (5.04)	1.026 (34)	0.312
Intervention	22.68 (9.64)	20.05 (9.03)	2.63 (6.43)	2.425 (34)	0.021

Repeated measures ANOVA revealed significant within-group changes over time for mean airway pressure (MAP), oxygen saturation (SpO_2), lung compliance (Cst), and airway resistance (Raw) ($p < 0.05$), indicating that these parameters changed significantly across the four post-intervention measurement points. Minute ventilation (MV) and tidal volume (VT) did not show significant changes over time ($p = 0.082$ and $p = 0.063$, respectively, after Greenhouse-Geisser correction). The time × group interaction was significant only for SpO_2 ($F=3.266$, $p=0.022$, partial $\eta^2=0.046$) and Raw ($F=18.165$, $p<0.001$, partial $\eta^2=0.213$), suggesting that the pattern of change over time for these two parameters differed between the groups. For VT, MV, MAP, and Cst, the non-significant interaction

($p > 0.05$) indicates that their temporal trends were similar in both groups. Between-group comparisons (the main effect of group) showed significant overall differences for VT, MAP, SpO_2, MV, and Raw ($p < 0.05$), meaning that, when data from all-time points were combined, the average values of these parameters differed between the control and intervention groups. Lung compliance (Cst) remained comparable between groups in this overall comparison ($p= 0.222$).

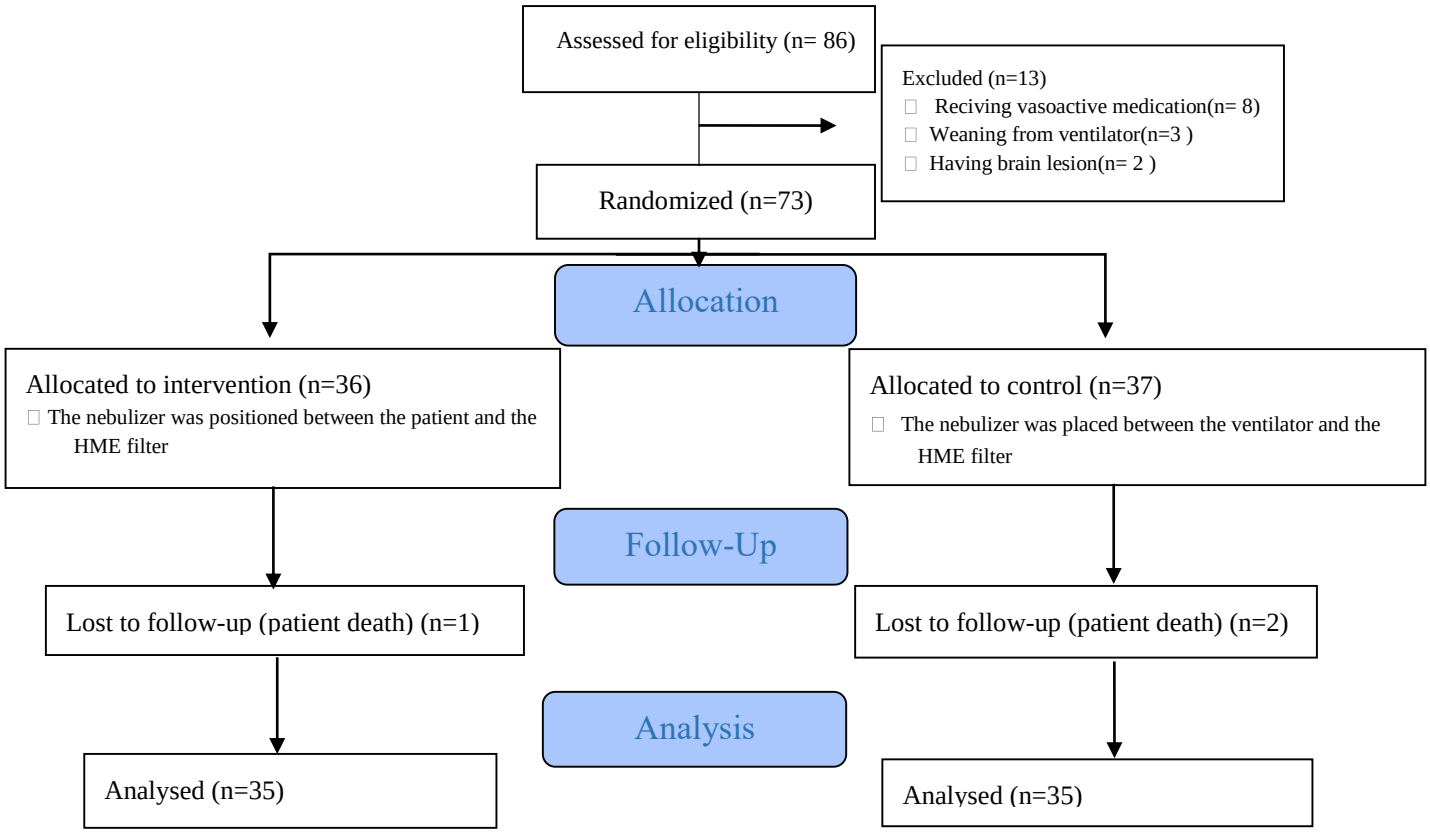


Figure 1. Flow Diagram of Study Selection and Data Collection Process

Discussion

The findings of the present study indicate that, although statistically significant differences were observed in favor of the intervention group for specific parameters such as airway resistance and oxygen saturation, no significant between-group difference was found for lung compliance, which followed a similar temporal pattern in both groups. This suggests that the fundamental bronchodilator effect on improving lung elasticity may be achieved irrespective of the nebulizer's position relative to the HME filter. Our results provide a clinical perspective to laboratory findings, such as those by Montigaud et al. [1], who demonstrated that while aerosol deposition is highly position-dependent in simulated models, the resulting physiological endpoints may not differ as dramatically. This distinction between aerosol deposition efficiency and measurable clinical effect is critical, implying that under real-world ICU conditions, both nebulizer positions can deliver a therapeutically adequate dose to elicit a target physiological response in lung compliance. The data analysis indicated that the two groups were homogeneous in terms of demographic variables (age and gender). Although statistically significant differences were observed between the groups in some baseline pulmonary parameters, the use of repeated measures ANOVA allowed us to focus on the patterns of change over time. The significant time×group interaction for SpO_2 and Raw

underscores that the placement of the nebulizer specifically modulates the temporal evolution of these parameters. This finding aligns with the principles outlined in bench studies, such as that by Hou et al. [11], which emphasize the importance of nebulizer positioning in the circuit. However, our clinical data show that this positional influence does not uniformly translate to all measured pulmonary parameters, highlighting the moderating effect of complex patient physiology.

Within-group controls showed that, in the control group, tidal volume increased significantly and mean airway pressure decreased significantly after the first dose, whereas in the intervention group, a significant increase in oxygen saturation was observed. The present findings regarding the short-term improvement of certain pulmonary parameters are consistent with the therapeutic effects reported in studies of inhaled therapies, such as the meta-analysis by Axson et al. [16]. However, our study contextualizes this effect within the specific technical constraint of HME filter placement, demonstrating that acute bronchodilator response is preserved even with the nebulizer placed between the ventilator and the HME.

Under the conditions of this research, the use of HME filters did not prevent the physiological effects of bronchodilators, though the nebulizer's position influenced the pattern of changes in airway resistance. This observation supports and extends the work of Ari et al. [12], who demonstrated in a simulated model that an HME does not drastically reduce drug delivery from jet nebulizers. Our study moves beyond simulation by showing that this preserved delivery translates into a measurable, position-dependent physiological response in critically ill patients. Furthermore, it resonates with the international consensus by Li et al. [4], which states that HMEs are not an absolute barrier to effective aerosol therapy and calls for more clinical trial data. Our findings directly address this call, providing evidence from a randomized controlled trial.

The compatibility of HME filters with effective therapy is supported by advancements in delivery systems. Cuccia et al. [17] demonstrated that using breath-actuated nebulizers with bypassable HMEs can optimize delivery. While our study used standard jet nebulizers, the shared conclusion, that circuit design can be managed without negating efficacy, highlights a consistent principle.

The modest effect sizes in our study likely stem from the transition from controlled models to the heterogeneous ICU environment. As noted by Reilly et al. [13], patient-specific factors like lung health may exert a greater influence on deposition than circuit configuration alone. Factors inherent to our patient population, such as varied pulmonary secretions and disease severity, may attenuate the precise positional advantages seen in vitro, leading to the more comparable overall outcomes we observed. Minor differences in study results may thus stem from various factors, such as the complex physiology of patients, the presence of pulmonary secretions, and differences in research models. These factors highlight the importance of conducting controlled clinical studies in real-world settings to accurately assess the effectiveness of aerosol interventions. The limitations of this study include the absence of long-term follow-up and the inability to blind ICU staff due to the nature of the intervention. Additionally, the study did not control for certain potential confounding variables, such as specific underlying pulmonary diagnoses. These limitations emphasize the importance of conducting larger, more controlled studies.

Conclusion

Although the intervention resulted in statistically significant changes in some pulmonary parameters, the small to moderate effect sizes suggest that, under the conditions of this study, the nebulizer placement does not have a decisive impact on the overall patient status. Therefore, the choice of nebulizer placement can be guided by practical considerations, safety, and the preferences outlined in ICU protocols, granting clinicians flexibility in circuit management while ensuring effective bronchodilator delivery.

Ethics Consideration

This study was conducted in full accordance with ethical standards, with approval from the Ethics

Committee of Zanjan University of Medical Sciences (Ethics Code: IR.ZUMS.REC.1397.113) and registered in the clinical trial database (Clinical Trial Code: IRCT20130124012257N8). Participation in the study was entirely voluntary, and participants were granted the right to withdraw at any stage of the research. Written informed consent was obtained from the legal guardians of all participants. Participant confidentiality was fully maintained, and they were instructed not to include their names on any study documents.

Acknowledgements

The authors express their sincere gratitude to the staff of the Intensive Care Unit at Vali-Asr (AJ) Hospital and to all the patients who participated in this study. We also sincerely appreciate the guidance and scientific support provided by Dr. Hanifi throughout the course of the research.

Conflict of Interest

The authors declare no financial, personal, or professional conflicts of interest related to this research.

Funding

This research was financially supported by Zanjan University of Medical Sciences. The funding sources had no influence on the study design, data collection, data analysis, or manuscript preparation.

Authors' Contributions

Khezerlou Z: Writing the manuscript and contributing to data analysis

Ramezani-Badr F: Contributing to data analysis, manuscript writing, and reviewing

Din Mohammadi, MR: Data analysis, reviewing, and contributing to manuscript writing

Ghodrati S: Data collection, reviewing, and contributing to manuscript writing

Khadiri A: Data collection, Contributing to data analysis

Aligholipour M: Writing the manuscript and contributing to data analysis

Artificial Intelligence

Utilization for Article Writing Artificial intelligence was utilized to enhance the fluency and coherence of the English text.

Data Availability Statement

The data are available from the corresponding author

References

1. Montigaud Y, Georges Q, Leclerc L, Clotagatide A, Louf-Durier A, Pourchez J, et al. Impact of gas humidification and nebulizer position under invasive ventilation: preclinical comparative study of regional aerosol deposition. Sci Rep. 2023;13(1):11056-67. https://doi.org/10.1038/s41598-023-38281-9

2. Marshall JC, Bosco L, Adhikari NK, Connolly B, Diaz JV, Dorman T, et al. What is an intensive care unit? A report of the task force of the World Federation of Societies of Intensive and Critical Care Medicine. J Crit Care. 2017;37:270-6. https://doi.org/10.1016/j.jcrc.2016.07.015

3. Pham T, Brochard LJ, Slutsky AS. Mechanical ventilation: State of the art. Mayo Clin Proc. 2017;92(9):1382-400. https://doi.org/10.1016/j.mayocp.2017.05.004

4. Li J, Liu K, Lyu S, Jing G, Dai B, Dhand R, et al. Aerosol therapy in adult critically ill patients: a consensus statement regarding aerosol administration strategies during various modes of respiratory support. Ann Intensive Care. 2023;13(1):63-88. https://doi.org/10.1186/s13613-023-01147-4

5. Battaglini D, Pelosi P, Robba C. Ten rules for optimizing ventilatory settings and targets in post-cardiac arrest patients. Crit Care. 2022;26(1):390-401. https://doi.org/10.1186/s13054-022-04268-7

6. Wilkins RL, Stoller JK, Kacmarek RM, Egan DF. Egan's fundamentals of respiratory care. St. Louis: Mosby; 2003.

7. Vargas M, Chiumello D, Sutherasan Y, Ball L, Esquinas AM, Pelosi P, et al. Heat and moisture exchangers (HMEs) and heated humidifiers (HHs) in adult critically ill patients: a systematic review, meta-analysis and meta-regression of randomized controlled trials. Crit Care. 2017;21(1):123-137. https://doi.org/10.1186/s13054-017-1710-5

8. Re R, Lassola S, De Rosa S, Bellani G. Humidification during Invasive and non-invasive ventilation: a starting tool kit for correct setting. Med Sci. 2024;12(2):26-37. https://doi.org/10.3390/medsci12020026

9. Dhand R. Mitigating Viral Dispersion during Respiratory Support Procedures in the ICU. Am J Respir Crit Care Med. 2021 May 1;203(9):1051-1053. PMID: 33617748; PMCID: PMC8314900. https://doi.org/10.1164/rccm.202102-0317ed

10. Lin HL, Fink JB, Ge H. Aerosol delivery via invasive ventilation: a narrative review. Ann Transl Med. 2021;9(7):588-605. https://doi.org/10.21037/atm-20-5665

11. Hou H, Xu D, Dai B, Zhao H, Wang W, Kang J, et al. Position of different nebulizer types for aerosol delivery in an adult model of mechanical ventilation. Front Med (Lausanne). 2022;9:950569-78. https://doi.org/10.3389/fmed.2022.950569

12. Ari A, Dang T, Al Enazi FH, Alqahtani MM, Alkhathami A, Qoutah R, et al. Effect of Heat Moisture Exchanger on Aerosol Drug Delivery and Airway Resistance in Simulated Ventilator-Dependent Adults Using Jet and Mesh Nebulizers. J Aerosol Med Pulm Drug Deliv. 2018;31(1):42-8. https://doi.org/10.1089/jamp.2016.1347
13. Reilly L, Mac Giolla Eain M, Murphy S, O'Sullivan A, Joyce M, MacLoughlin R. An in vitro study of the effects of respiratory circuit setup and parameters on aerosol delivery during mechanical ventilation. Front Med. 2024;10:1307301-9. https://doi.org/10.3389/fmed.2023.1307301
14. Hart MT. The Effects of Aerosol Drug Delivery on Airway Resistance through Heat-Moisutre Exchangers. Respiratory Therapy Theses. 2009:4.
15. Sundaramurthy A, Vaithiyalingam C. Advancements in calibration techniques for ensuring accuracy and reliability of medical devices: A comprehensive report. In: Gupta N, editor. Hybrid and Advanced Technologies. Boca Raton: CRC Press; 2025. p. 413-22. https://doi.org/10.1201/9781003559139-60
16. Axson EL, Lewis A, Potts J, Pang M, Dickinson S, Vioix H, et al. Inhaled therapies for chronic obstructive pulmonary disease: a systematic review and meta-analysis. BMJ Open. 2020;10(9):e036455.
https://doi.org/10.1136/bmjopen-2019-036455
17. Cuccia AD, Ashraf S, McPeck M, Samuel J, Smaldone GC. Wet-side breath-enhanced jet nebulization: Controlling drug delivery during mechanical ventilation. Respir Care. 2020;65(8):1077-89. https://doi.org/10.4187/respcare.07343